

Electronic Submission of Lot Distribution Reports

Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-7800, or email ocod@fda.hhs.gov, or from the Internet at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above or (CDER) Office of Communications, Division of Drug Information at 301-796-3400.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
March 2015**

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Contains Nonbinding Recommendations

Table of Contents

I. INTRODUCTION..... 1

II. BACKGROUND 2

III. LOT DISTRIBUTION REPORTS..... 2

IV. PROCESS 3

V. WAIVER REQUESTS 4

A. Content of Waiver Requests 4

B. Where to Submit Waiver Requests 5

C. FDA Response to Waiver Requests..... 5

The technical specifications associated with this guidance entitled “Structured Product Labeling Implementation Guide with Validation Procedures” is provided in a separate document and is updated periodically. The technical specifications document is incorporated by reference into this guidance document. To ensure that you have the most recent version of the technical specifications document, check the CBER Electronic Submissions Web page at: <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>.

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This guidance represents the Food and Drug Administration's (FDA's or Agency's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance using the contact information on the title page of this guidance.

I. INTRODUCTION

This guidance provides you, licensed manufacturers of products distributed under an approved biologics license application (BLA) (henceforth referred to as applicants), with recommendations on how to submit lot distribution reports (LDRs) for biological products in an electronic format that FDA can process, review, and archive.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA'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 FDA's guidances means that something is suggested or recommended, but not required.

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II. BACKGROUND

On June 10, 2014, FDA issued a final rule which, among other things, amended the requirements as to biological LDRs required under Title 21 of the Code of Federal Regulations 600.81 (21 CFR 600.81). Specifically, under this rule, applicants are required to submit LDRs to FDA in an electronic format that the Agency can process, review and archive (79 FR 33072). This reporting requirement is effective as of June 10, 2015.¹ Note that the rule does not change the content of these reports.

In addition, 21 CFR 600.81 provides that the Agency will issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files). The purpose of this guidance is to provide that information. This guidance represents the Agency's current thinking on this topic.

For example, as discussed later in this document, the guidance sets forth the Structured Product Labeling (SPL) standard and vocabulary for electronic submission of LDRs. Within this guidance, you also are directed to additional resources, such as an implementation guide, validation procedures, and links with further information. Note that we recommend using the same message exchange format that is currently used for establishment registration and drug product listing (<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>).

FDA is developing links between the Center for Biologics Evaluation and Research's (CBER's) lot distribution database and FDA's Adverse Event Reporting System (FAERS) and Vaccine Adverse Event Reporting System (VAERS) databases. We anticipate that this linkage will allow for better monitoring of safety patterns by product lot.

III. LOT DISTRIBUTION REPORTS

Under 21 CFR 600.81, applicants must submit to CBER or to the Center for Drug Evaluation and Research (CDER), as appropriate, LDRs containing certain specified information every 6 months about the quantity of the product distributed under their BLAs (including to distributors). As needed, FDA may require an applicant to submit more detailed product distribution information.

¹ Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 379k-1), added by section 1136 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144), provides that submissions under section 505(b), (i), or (j) of the FD&C Act or section 351(a) or (k) of the Public Health Service Act shall be submitted in such electronic format as specified by FDA in guidance. In section 745A(a), Congress granted explicit statutory authority to FDA to implement the electronic format for submissions requirement by guidance. This grant of authority, however, does not preclude FDA from implementing such requirements by notice and comment rulemaking (5 U.S.C. 553). Accordingly, at this time, even though FDA has concluded that certain submissions that are addressed in the rule entitled "Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements" are also within the scope of section 745A(a), FDA has determined that it is appropriate to amend the regulations on the submission of certain reports to remove references to paper submissions and to specify that such reports be submitted in an electronic format that FDA can process, review, and archive. FDA may consider, at a future date, whether to include information pertaining to submission of reports in electronic format in guidance pursuant to section 745A(a) of the FD&C Act.

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Furthermore, upon written notice, the Agency may request distribution reports at times other than every 6 months.

The following link lists the elements to be included when you submit your electronic LDRs for each final container lot distributed during the reporting period - [Structured Product Labeling Implementation Guide with Validation Procedures](#).

Where feasible, parameter values for each field should be drawn from FDA's electronic data standards for SPL Resources. The most current information on these electronic data standards is located at

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

If an appropriate value does not appear to meet the needs for a particular product, you should submit a request for additional values to spl@fda.hhs.gov.

IV. PROCESS

The lot distribution file should be included in eCTD Module 3, section 3.2.R Regional Information. Applicants should name the leaf title, "Lot-Distribution-Report-[Date of the submission]." The lifecycle for this file should be updated as appropriate, in accordance with the current eCTD² specification.

Lot distribution files should be formatted in the same electronic messaging standard used for drug registration and listing information and for the content of labeling for BLAs. This standard, known as Health Level Seven (HL7) 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.

Required information may be created using the following information to generate a Lot Distribution SPL file:

A free tool for generating SPL files is available at

<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm189651.htm>.

Step-by-step instructions for electronically creating, validating, and submitting self-identification information are available at

<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>; or software tools developed internally by generic manufacturers utilizing the SPL technical specifications.

Additional information is available at

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

² eCTD guidance and specifications are available at

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>.

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Once a Lot Distribution SPL file is created and finalized, the file should be transmitted to FDA as a BLA eCTD submission through the Electronic Submissions Gateway (ESG), FDA's electronic information portal. Information on the ESG is available at <http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm>.

If any questions arise, you should call 240-402-8622 or communicate via email to LDD@fda.hhs.gov.

V. WAIVER REQUESTS

Under 21 CFR 600.90, an applicant required to submit an LDR under 21 CFR 600.81 may ask FDA to waive temporarily the requirement that the report be submitted in electronic format. We anticipate that temporary waivers from the electronic submission requirement will be needed only in rare circumstances. Companies experiencing technical difficulties with transmission of their electronic submissions to FDA should consult FDA for technical assistance rather than submitting a waiver request.

A. Content of Waiver Requests

Under 21 CFR 600.90(a), an applicant's request to waive the electronic format requirement must include one of the following as supporting documentation: An explanation why the applicant's compliance with the requirement is unnecessary or cannot be achieved (e.g., acts of nature, widespread internet outages, temporary issues with the manufacturer's database(s)); a description of an alternative submission format that satisfies the purpose of the requirement; or other information justifying a waiver.

We recommend that this request be submitted to FDA in writing by mail. The request should reference all products that are to be covered by the waiver. If not already provided as justification for the waiver for purposes of meeting the requirements under 21 CFR 600.90(a), the waiver request should include the reason for the request (i.e., the nature of the inability to comply), and the anticipated time to recover. The waiver request also should include a proposed end date for the waiver and a description of any proposed alternative reporting method, as relevant to the circumstances. Potential alternative reporting methods could include (but are not limited to) physical media and fax. The waiver request should be clearly titled "**WAIVER REQUEST – LOT DISTRIBUTION REQUIREMENTS**" in bold capital letters at the top of the first page of the submission.

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B. Where to Submit Waiver Requests

For licensed biological products regulated by CDER, waiver requests should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Therapeutics Biological Products Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

For licensed biological products regulated by CBER, waiver requests should be addressed to:

Document Control Center
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Building 71, Room G112
Silver Spring, MD 20993-0002

C. FDA Response to Waiver Requests

FDA reviews waiver requests on a case-by-case basis. FDA intends to respond in writing to the requestor,³ stating whether or not the waiver is granted. If the waiver is granted, FDA intends to also include in its response letter a description of the alternate submission method(s) the Agency intends to accept. **Waivers of the requirement to submit reports in electronic format, if granted, will be temporary.**

³ To follow up with the company, FDA intends to contact the individual who submitted the waiver request unless an alternate contact person is provided.