Electronic Submissions of Biological Product Lot Distribution Data

ELECTRONIC SUBMISSION INSTRUCTIONS FOR LOT DISTRIBUTION DATA (eLDD)

Please submit comments and questions concerning these instructions via email to LDDDISTRIBUTION@CBER.FDA.GOV

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

Providing Post marketing Lot Distribution Reports in Electronic Format

GENERAL INFORMATION AND LOT DATA SUBMISSION INSTRUCTIONS

INTRODUCTION

This procedure is intended to assist manufacturers of vaccines and other biological products to electronically submit post marketing lot distribution data to CBER's Lot Distribution Database (LDD). In the past, these data primarily came to CBER under 21 CFR 600.81 as paper reports. Conversion to uniform electronic submissions will improve accuracy, efficiency, and timeliness. We outline below the necessary file format, physical media, and submission procedures for the lot distribution reports.

BACKGROUND

Most manufacturers have submitted biological product lot distribution reports required under 21 CFR 600.81 in the form of printed paper reports, sometimes accompanied by electronic data files as American Standard Code for Information Interchange (ASCII) flat files or in other formats. CBER staff then manually compiles the data into the LDD system for use in post marketing safety surveillance. In accordance with current Agency automation initiatives, the FDA is moving toward electronic submission of all regulatory data in computer-readable and achievable formats. Although establishing electronic reporting will initially require additional effort by both FDA and regulated industry, the resultant process will increase the accuracy, efficiency, and timeliness of the data.

CBER's LDD did not previously support automated electronic loading of received data. Manual data entry imposed substantial labor costs and introduced inevitable typographic errors. Inconsistent reporting formats and limited software accuracy precluded reliable transcription through computerized Optical Character Recognition. The improved data file format provides a standardized and consistent presentation of lot distribution information that can be automatically transferred and validated against CBER's Regulatory Management system, which tracks licensed CBER products and manufacturers.

§ 600.81 Distribution reports.
The licensed manufacturer shall submit to the Center for Biologics Evaluation and Research or the Center for Drug Evaluation and Research (see mailing addresses in §600.2), information about the quantity of the product distributed under the biologics license, including the quantity distributed to distributors. The interval between distribution reports shall be 6 months. Upon written notice, FDA may require that the licensed manufacturer submit distribution reports under this section at times other than every 6 months. The distribution report shall consist of the bulk lot number (from which the final container was filled), the fill lot numbers for the total number of dosage units of each strength or potency distributed (e.g., fifty thousand per 10-milliliter vials), the label lot number (if different from fill lot number), labeled date of expiration, number of doses in fill lot/label lot, date of release of fill lot/label lot for distribution at that time. If any

significant amount of a fill lot/label lot is returned, include this information. Disclosure of financial or pricing data is not required. As needed, FDA may require submission of more detailed product distribution information. Upon written notice, FDA may require that the licensed manufacturer submit reports under this section at times other than those stated. Requests by a licensed manufacturer to submit reports at times other than those stated should be made as a request for a waiver under §600.90.
[59 FR 54042, Oct. 27, 1994, as amended at 64 FR 56449, Oct. 20, 1999; 70 FR 14983, Mar. 24, 2005]

(If bulk and/or fill lot data are pertinent to the manufacturing of a given product, then they must be included, unless CBER waives this requirement on a case by case basis.)

We anticipate expansion to electronic data submission of post marketing lot distribution data for all vaccine and other biological products marketed for human use with biologic license applications (BLAs) regulated by CBER. (Electronic Lot Distribution Data submission is only for biological products regulated by CBER. It does not apply to therapeutic biologics transferred to the Center for Drug Evaluation and Research (CDER) on June 30, 2003. The FDA CBER website http://www.fda.gov/cber/ lists these products.)

Because FDA authority is limited to the United States, the scope of LDD submissions should similarly focus on product lots intended for "domestic" distribution, i.e., distribution within the U.S. or to U.S. military bases abroad. Lots intended for distribution to other countries should not be included. However, we retain a field to distinguish between domestic and foreign distribution for consistency with previous file formats and in case special circumstances might warrant tracking of non-domestic lots.

REPORTING REQUIREMENTS

Lot Distribution Data must be reported by the company that manufactures the product. In situations where a licensed manufacturer sells a product to a second manufacturer, if the second one conducts further manufacturing steps under its own license, such as packaging with a diluent or another primary product or modifying the package labeling, then the second manufacturer has the reporting obligation. Alternatively, if the second simply distributes the unchanged product to wholesalers, retailers, doctors' offices, and other parties, then the second is a distributor, and the first retains the reporting obligation. By understanding this difference, we can avoid receiving duplicate reports for the same product. CBER may grant waivers to allow alternative reporting arrangements on a case by case basis.

Distribution Type: The kind of distribution data reported may be Interval, Cumulative, or Anticipated Total. Interval refers to product distribution between the identified start and end dates. Cumulative would refer to reporting of all product distributed thus far (as of the end date provided), including amounts previously reported. Anticipated Total would describe an entire lot’s size, not all of which would necessarily have been distributed during a given reporting interval. For consistency with previous data submissions, LDD retains the distinction between these three types of distribution. However, CBER currently prefers that routine submissions employ the Interval format.

SUBMISSION INSTRUCTIONS FOR LOT DISTRIBUTION DATA (LDD)

FDA has implemented the regulatory and infrastructure changes to support electronic submissions for post marketing Lot Distribution Data (LDD) of vaccines and other biological products under 21 CFR 600.81.
Manufacturers may submit LDD reports via the FDA Electronic Submission Gateway (ESG), which is the central transmission point for sending information electronically to the FDA.
Lot distribution data submission reports do not apply to the therapeutic biologics transferred to the Center for Drug Evaluation and Research (CDER) on June 30, 2003. The FDA CBER website http://www.fda.gov/cber/ lists these products.

Manufacturers may submit LDD reports via the FDA Electronic Submission Gateway (ESG), which is the central transmission point for sending information electronically to the FDA or using physical media.

Please follow these steps to begin submitting LDD Reports electronically:

Step 1

- Contact the LDD Electronic Submission Coordinator to advise FDA of your intent to begin submitting LDD Reports electronically.

  Bridget Davis
  Office of Biostatistics and Epidemiology
  Center for Biologics Evaluation and Research, FDA
  1401 Rockville Pike, 200S/HFM-220
  Rockville, MD 20852-1448

  Phone: (301)827-9426
  Fax: (301) 827-5218
  mailto:LDDDistribution@fda.hhs.gov

Step 2

- Review FDA's technical requirements for Lot Distribution Data

Step 3

- Submit a test file to the LDD Electronic Submission Coordinator via email.
- If test file is compliant with technical requirements the LDD system will return an email test acknowledgment receipt with notification for data acceptance.
- If test file is NOT successful, review Step 2.
- If test file is successful notify LDD Electronic Submission Coordinator on your intention to submit data electronically.
- Once the test file is processed successfully, you may begin submitting electronic reports via the FDA Electronic Submission Gateway (ESG) or on physical media.

Step 4

- Prepare the LDD submission package, which should contain:

A. Cover Letter should be filled out and saved with a designated naming convention, such as prefix LDD, company name, and reporting period.

B. Electronic file(s) with Lot Distribution Data per technical requirements.

For data submitted in XML format: - Validation should be done against LDD XML Schema (any appropriate program can be used).
- XML Style Sheet can be used for viewing data summary and detail.
- All files should be packaged together under the folder name "LDD_MM_DD_YYYY" and sent as a single submission. A folder named "LDD_MM_DD_YYYY" should be created on the client site and all files should be copied into this folder before they are submitted to the FDA.

Step 5

For Electronic Submission via FDA ESG:

- First time users should review FDA's Electronic Submission Gateway (ESG) User Guide (HTML) that provides industry participants with information and guidance on how to use the FDA ESGI
- Setup an FDA ESG **test** Account
- Submit LDD prepared package (Step 4) through the test gateway during the gateway hours of operation. See the status page for the current status of the gateway.
- The gateway will return an acknowledgment of receipt of the transmission when submitted file is successfully received and decrypted. The LDD system will return an ICH M2 compliant acknowledgment test message when the LDD Report has been processed and loaded into the FDA database.
- If test was successful Setup an FDA ESG **production** Account
- Submit production package using FDA ESG **production** account
- The gateway will return an acknowledgment of receipt of the transmission when submitted file is successfully received and decrypted. The LDD system will return an ICH M2 compliant acknowledgment production message when the LDD Report has been processed and loaded into the FDA database.

For more information regarding electronic submissions via the FDA ESTRI Gateway, go to the Gateway Frequently Asked Questions web page.

For Electronic Submission using Physical Media:

- Prepare a submission package that contains the CD-ROM along with the Cover Letter
- Mail the submission package to the address below:

Two copies of the electronic files should be submitted on CD-ROM to:
FDA Center for Biologics Evaluation and Research
Office of Biostatistics and Epidemiology HFM 220M
1401 Rockville Pike
Rockville, MD 20852-1448

TECHNICAL REQUIREMENTS

Lot distribution data submissions include required information defined in 21 CFR 600.81 and portions of the suggested format provided in the guidance for industry entitled *Post marketing Safety Reporting for Human Drug and Biological Products Including Vaccines (March 2001)*.

Although FDA recognizes that the content and structure of each company database can and will differ, there are high-level steps that every organization needs to follow in preparing compliant files. Companies must map their output data to the specifications for the file and data layout. Instructions for mapping have not been included, since this is highly dependent on the structure and content of individual databases. Where feasible, values for each field should be drawn from FDA electronic data standards (http://www.fda.gov/oc/datacouncil/splncicodes.html). If no appropriate value appears to meet the needs for a particular product, requests for additional values should be submitted via: http://www.fda.gov/cder/dsm/Vocabulary_Change_Request_Form.pdf,

FDA accepts submission reports in two formats:

ASCII file format
This file format will be accepted from the manufacturers who previously submitted LDD reports in the ASCII format. FDA encourages manufactures to participate in the pilot program to convert the existing ASCII file submissions into the XML Format as the old ASCII format will be discontinued in the nearest future.

XML file Format
This is a new format and FDA encourages manufactures to participate in the pilot program to convert the existing ASCII file submissions into the XML Format