Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide

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)
Center for Veterinary Medicine (CVM)

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Procedural

Revision 1

Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide

Guidance for Industry

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Contains Nonbinding Recommendations

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Contains Nonbinding Recommendations

Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide 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

FDA is issuing this Technical Conformance Guide (guide) to assist registrants of drug establishments (or their authorized agents) in submitting reports on the amount of each listed drug manufactured,[2] prepared, propagated, compounded, or processed for commercial distribution, as required by section 510(j)(3) of the Federal Food, Drug, and Cosmetic Act (FD&C Act),[3] as added by section 3112(e) of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act).[4] This guide supplements the guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (February 2024).[5] The guide describes 1) how first-time users can access FDA's NextGen Portal[6] (the portal) to submit these reports, 2) the different methods for submitting the reports through the portal, and 3) the data elements to be included in the reports.

This guide describes the data elements that should be submitted for reporting information under section 510(j)(3) by each person who registers with FDA under section 510 of the FD&C Act with regard to a listed drug (including a drug product that is in finished package form, a drug product that is not in finished package form, an active pharmaceutical ingredient (API), and other types of listed drugs, except for biological products or categories thereof exempted by an order

[1] This guidance has been prepared by the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research and the Center for Veterinary Medicine, at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2017-D-6821 (available at https://www.regulations.gov/docket?D=FDA-2017-D-6821). See the instructions in that docket for submitting comments on this and other Level 2 guidances.

[2] For the purposes of this guidance, "manufacture" means the manufacture, preparation, propagation, compounding, and processing of a drug. "Manufacture, preparation, propagation, compounding, or processing" also includes repackaging and relabeling. See section 510(a) of the FD&C Act; section 207.1 (21 CFR 207.1) (definitions of *manufacture* and *manufacturer*).

[3] 21 U.S.C. 360(j)(3)

[4] Public Law 166-136

[5] We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[6] All registrants (not just registrants of CDER-regulated drug establishments) should use the NextGen Portal to submit reports that are required under section 510(j)(3) of the FD&C Act, available at: https://edm.fda.gov/.

under section 510(j)(3)(B)).[7] Listed drugs subject to reporting include human drug products (including non-exempt biological products) marketed under an approved application; animal drug products marketed under an approved application; medical gases;[8] homeopathic products; products marketed in accordance with requirements under section 505G of the FD&C Act (21 U.S.C. 355h),[9] often referred to as over-the-counter monograph drugs; and animal drug products that are not approved, conditionally approved, or indexed under sections 512, 571, and 572 of the FD&C Act.

In general, FDA's guidance documents 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.

II. BACKGROUND

On March 27, 2020, the CARES Act was enacted to aid response efforts and ease the economic impact of the Coronavirus Disease 2019 (COVID-19). The CARES Act includes authorities to enhance FDA's ability to assess, prevent, and mitigate possible drug shortages by, among other things, improving FDA's visibility into drug supply chains. Section 3112(e) of the CARES Act added section 510(j)(3) to the FD&C Act. Under section 510(j)(3), each person (including repackers and relabelers) who registers under section 510 of the FD&C Act with regard to a drug must report to FDA annually the amount of each listed drug that was manufactured, prepared, propagated, compounded, or processed by such person for commercial distribution.

III. USING THE NEXTGEN PORTAL

All registrants or their authorized agents should use the portal to submit reports on the amount of each listed drug that was manufactured for commercial distribution. If you are a first-time user, you will need to register and create an account.[10] You may submit reports through the portal by 1) manually entering information, or 2) uploading data from a comma-separated values (CSV) file.[11]

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[7] Under section 510(j)(3)(B) of the FD&C Act, FDA may issue an order to exempt certain biological products or categories of biological products regulated under section 351 of the Public Health Service Act from some or all of the reporting requirements under section 510(j)(3)(A) of the FD&C Act, if FDA determines that applying such reporting requirements is not necessary to protect the public health. FDA has issued an order that exempts from section 510(j)(3)(A) reporting requirements the following categories of biological products: (i) blood and blood components for transfusion; and (ii) cell and gene therapy products, where one lot treats a single patient. See 88 FR 22454 (April 13, 2023).

[8] For purposes of this guidance, *medical gas* and *designated medical gas* have the meanings set forth in section 575 of the FD&C Act.

[9] Under section 505G of the FD&C Act, certain nonprescription drug products may be lawfully marketed without an approved application under section 505 of the FD&C Act if applicable requirements are met.

[10] For further instruction, see the reference guide available at https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts

[11] The three CSV templates showing the data elements are available under the NextGen Resources section at https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts

FDA recommends using the manual entry option in the portal for smaller submissions. To enter data into the portal manually, you will use the portal's interface to provide the appropriate information by following a series of prompts, using drop-down boxes, and entering free text. A user guide with step-by-step instructions for entering the data manually and submitting reports is available via the portal and the website.[12]

FDA strongly recommends using the option to upload data from a CSV file for larger submissions that would be time consuming to enter manually using the portal. If you choose to upload data to the portal from a CSV file, it is important that you use the correct template which will depend on the reporting pathway (type of drug and its packaging).[13,14] Templates for each pathway are available via the portal and the website.[15] A user guide with step-by-step instructions for creating the CSV file and submitting the report using this method is available via the portal and the website.[16]

Technical questions regarding the submission process should be sent to EDMSupport@fda.hhs.gov. For questions regarding the content to be submitted in a section 510(j)(3) report, please contact the appropriate FDA center:

- CDER: DrugAmountReporting@fda.hhs.gov
- CBER: Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010, ocod@fda.hhs.gov
- CVM: Office of Surveillance and Compliance, 240-402-7002, AskCVM@fda.hhs.gov as applicable

IV. DATA ELEMENT SPECIFICATIONS

In general, the submission process includes three steps:

1. Verifying the submitter information: The submitter's information is displayed. This information automatically populates based on information you submitted when registering for your NextGen account.
2. Describing the submission: The system will prompt you to provide information about the submission. Specifically, you will be asked to identify your role with respect to the submission, which calendar year the submission will cover, which reporting pathway (type of drug and its packaging) the submission will cover, and how you will complete the report (i.e., by submitting manually or by uploading data from a CSV file). If you

[12] The website is available at https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts

[13] For further instruction, see the summary diagram and the recommended reporting structures in the guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (February 2024).

[14] For the purposes of this guidance, "type of drug" refers to the following categories: (i) drug that consists of API alone; (ii) drug that consists of API with other ingredient(s) but that is not in finished dosage form; (iii) drug product that is not in finished package form; and (iv) drug product that is in finished package form.

[15] See footnote 12.

[16] See footnote 12.

have more than one type of drug, you should submit a separate report for each type of drug.

3. Completing the report: The system will prompt you to either complete the report by using manual entry or by uploading data from an appropriately formatted CSV file.

We describe the data elements relevant to each of these steps in more detail below. These descriptions will help you complete the process and understand what information to include for the various data elements at each step. For additional information, illustrative examples are also included in the Appendix to facilitate reporting amounts of listed drugs.

A. Submitter Information

The following data elements come directly from your NextGen account profile and are displayed for identity verification purposes. These data elements are read-only on this display; you can change them by updating your NextGen account profile.[17]

1. First Name and Last Name

This is the first and last name you provided during portal registration.

2. Email

This is the email address you provided during portal registration.

3. Phone Number and Extension

This is the phone number and optional extension you provided during portal registration.

4. Organization Name

This is the organization name you provided during portal registration.

5. Organization Address

This is the address you provided during portal registration. This data element is separated as Address Line 1, Address Line 2, City, State/Province, Zip/Postal Code, and Country.

B. Submission Description Elements

You will enter the following data elements into the portal interface regardless of whether you plan to submit the report manually or by uploading data from a CSV file.

[17] If you are submitting as an authorized agent, see section IV.B.1 for further detail.

A separate submission is needed for each report, but each report may include multiple establishments and multiple national drug codes (NDCs). The elements selected for the following fields will apply to every establishment and NDC included in the submission.

1. Submitter Type

The system will prompt you to indicate whether you are submitting the information as the registrant of the reporting establishment or as an authorized agent on behalf of the registrant of the reporting establishment.

- If you are an employee of the reporting establishment or of another organization with or under common control or ownership of the reporting establishment (e.g., parent, subsidiary, affiliate), you should indicate that you are submitting this information as a registrant.
- If you are not an employee of the reporting establishment or of another organization under or with common control or ownership of the reporting establishment, and you are authorized by the registrant to submit the information on behalf of the registrant, you should indicate that you are reporting as an authorized agent.
- If your role differs based on the establishment for which you are reporting (i.e., you will be submitting as a registrant for some and as an authorized agent for others), you should submit these reports separately because the submitter type will apply to every establishment and NDC included in the report. For example, if you are an employee of a registrant that manufactures its own drugs but also relies on contract manufacturers to manufacture drugs that your organization distributes as a private-label distributor, and you plan to submit a report for the drugs your establishment manufactures and on behalf of your contract manufacturer for the drugs your organization distributes as a private-label distributor, you should submit one report in which you identify your role as registrant and another report in which you identify your role as authorized agent.

2. Reporting Year

The system will prompt you to select which calendar year the submission covers.

3. Data Submission Method

The system will prompt you to indicate whether you will submit the report manually or by uploading data from a CSV file.

4. Type of Drug and its Packaging

The system will prompt you to select the type of drug and its packaging for the report you plan to submit. You should follow the recommended reporting pathways in the guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (section III. B. 5) based on the appropriate type of drug and its packaging.

C. Data Elements for Reporting the Amount of Listed Drug

The data elements described in this section comprise the specific information for reporting (whether manually or by uploading data from a CSV file) the amount of listed drug manufactured, prepared, propagated, compounded, or processed for commercial distribution.

A report will not be considered ready for submission unless, at a minimum, it:

- Identifies at least one establishment by Data Universal Numbering System (DUNS) number
- Identifies at least one drug by NDC at that establishment
- Identifies the single most relevant business operation performed at that establishment with respect to that drug

The portal will automatically check the entered DUNS number and NDC against FDA's internal database. If an entered DUNS number or NDC is not found in the internal FDA database, that entry will be flagged and a message will display on the screen. If the entry is flagged, you can change the entry,[18] or you can proceed with your submission if you know the number is valid and accurate even though it was not found in the internal FDA database.

The submission format allows you to provide a single report for multiple establishments. Recognizing that each establishment may perform different business operations with respect to different drugs, instead of identifying the business operations for each NDC, the report is designed to allow establishments to identify the different business operations performed and then identify the specific drugs, by NDC, for which they perform that business operation. However, as explained in more detail below, you should generally associate an NDC with only a single business operation at each establishment.

You should select the single business operation that best describes the manufacturing activities the establishment performs for each NDC for which you reported for that establishment. This business operation should generally match the business operation for that establishment that was included in the drug listing.

- MANUFACTURE is the default selection. You should select this option unless one of the other business operations applies to the NDC for which you are reporting.[19]
- API MANUFACTURE applies only if the NDC for which you are reporting identifies an API (active pharmaceutical ingredient) and the establishment performed operations besides repackaging or relabeling the API.

[18] For a manual submission, you can change the number manually in the portal. To change the number for a CSV submission, you need to update the CSV file and resubmit it.

[19] If the business operation from the drug listing file that best describes the activities performed for the listed drug, or the single business operation for the listed drug, for that establishment is "pack" or "label," then the registrant should, for the purposes of a section 510(j)(3) report, identify "manufacture" as the single business operation that best describes the activities performed for the listed drug.

- REPACK applies only if the establishment repackaged[20] the drug and that drug was manufactured at a different establishment.
- RELABEL applies only if the establishment relabeled[21] the drug and that drug was manufactured at a different establishment.
- TRANSFILL applies only if the NDC for which you are reporting is a medical gas and the establishment transfills that medical gas.
- POSITRON EMISSION TOMOGRAPHY DRUG PRODUCTION applies only if the NDC for which you are reporting identifies a positron emission tomography drug.

Generally, you should not enter an NDC in association with more than one business operation at a specific establishment. For example, if you manufacture both the API and the finished dosage form at a single establishment, you should not enter the NDC for the finished dosage form under both MANUFACTURE and API MANUFACTURE; you should just enter the NDC under MANUFACTURE.[22]

In some circumstances, it may be appropriate to enter the same NDC under separate business operations at a single establishment. For example, if you are a repackager and a relabeler for a specific drug, and sometimes you repackage the drug and sometimes you just relabel the drug, then you should include the NDC under both REPACK and RELABEL and include the appropriate amounts with respect to each business operation.

The guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (section III. B. 5) describes three reporting pathways based on the type of drug and its packaging. The data elements listed below are specific to each reporting pathway.

D. Reporting Amount of Drug Products in Finished Package Form

1. Establishment DUNS

You should include the DUNS number for each establishment covered by the submission. The DUNS number is a 9-digit number, including any leading zero(s), but without dashes or spaces.

[20] For purposes of selecting the appropriate business operation, *repackaging* involves removing the drug from the container in which it was received by the establishment and placing the drug into a different container without manipulating, changing, or affecting the composition or formulation of the drug (see 21 CFR 207.1). Although the establishment may have placed a different label on the repackaged drug, this operation is included within the activities associated with repackaging a drug.

[21] For purposes of selecting the appropriate business operation, *relabeling* involves changing the existing label or labels on the drug's package, or changing or altering the drug's existing label, without repackaging or manipulating, changing, or affecting the drug's composition or formulation (see 21 CFR 207.1).

[22] However, if you manufacture both the API and the finished dosage form at a single establishment, and you separately list the API with its own NDC, then you should include the NDC for the finished dosage form under MANUFACTURE and the NDC for the API under API MANUFACTURE.

2. Business Operation

For each establishment you identify, specify the business operation performed for each drug product. To simplify reporting, we have limited the types of business operations for drug products in finished package form to:

- MANUFACTURE
- REPACK
- RELABEL
- TRANSFILL
- POSITRON EMISSION TOMOGRAPHY DRUG PRODUCTION

3. NDC

To identify each drug product for which you are reporting, you should use the 10-digit NDC for the drug product as listed with FDA. You should provide the NDC in the appropriate format (i.e., using hyphens between the labeler code, the product code, and the package code). Appropriately formatted NDCs should have one of the following configurations: 4-4-2 (e.g.,1234-5678-90), 5-4-1 (e.g., 12345-6789-1), 5-3-2 (e.g., 12345-678-90).[23]

4. Source NDC

For a drug product listed under REPACK or RELABEL, you should provide the source NDC in the appropriate format (i.e., using hyphens between the labeler code, the product code, and the package code) using the 10-digit NDC assigned to the drug product received by the repacker or relabeler for repacking or relabeling. Appropriately formatted NDCs should have one of the following configurations: 4-4-2 (e.g.,1234-5678-90), 5-4-1 (e.g., 12345-6789-1), 5-3-2 (e.g., 12345-678-90). This field is used to identify the drug product that was repacked or relabeled, so that FDA can avoid double counting this drug product when analyzing the data.

5. Amount Per

The amount of each listed drug product manufactured for commercial distribution in a particular year should be organized by month. You should enter the name of each of the 12 months (i.e., January, February, …, November, and December) followed by "Annual Total" in the CSV file.

6. Outermost Quantity Manufactured

You should enter the quantity of the drug product that the establishment manufactured for commercial distribution during the relevant time period. We suggest that you provide this amount based on the relevant time period in which the drug product was released. This quantity should be based on the drug product's outermost packaging. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug product

[23] For certain minimally manipulated human cell and tissue products, you may use an alternatively formatted NDC approved for use by the relevant center director.

was manufactured during the relevant time period. For manually entered data in the portal, based on the monthly data provided, the system will calculate the annual sum.

7. Outermost Quantity Distributed (Non-US)

If you entered "Yes" (in the CSV file) or clicked the checkbox (for manual entry) in the *Intended to Fulfill 21 CFR 314.81* data element, you should enter only the amount of a listed drug product that the establishment manufactured for commercial distribution and distributed to the non-US market during the reporting period that would have been included in an annual report as required by 21 CFR 314.81(b)(2)(ii)(*a*). Because this is an alternative reporting process for drug products with an approved application, for the purposes of this field, you should only include the amount of drug product that would otherwise have been provided in the respective annual report under 21 CFR 314.81(b)(2)(ii)(*a*) and provide this amount based on the relevant time period that the drug product was distributed. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug product was distributed during the relevant time period. You should not leave it blank even for time periods when no drug product was distributed. For manually entered data, based on the monthly data provided, the system will calculate the annual sum.

If you entered "No" (in the CSV file) or left the checkbox unchecked (for manual entry) in the *Intended to Fulfill 21 CFR 314.81* data element, then you should leave this field blank. If a listed drug product is not subject to an approved application for which an annual report is required under 21 CFR 314.81(b)(2)(ii)(*a*), then you should leave this field blank.

8. Outermost Package Type

You should enter the package type associated with the NDC for which you are submitting data. Values entered here should adhere to the FDA-recognized package types as outlined in the portal.

9. Innermost Quantity Manufactured

You should use this field for multi-level packaged drug product only. You should enter the quantity of the drug product that the establishment manufactured for commercial distribution during the relevant time period. We suggest that you provide this amount based on the relevant time period in which the drug product was released. This quantity should be based on the drug product's innermost packaging. You should enter data into this field using a positive number (integer only) or a zero depending on whether the drug product was manufactured during the relevant time period. For manually entered data in the portal, based on the monthly data provided, the system will calculate the annual sum.

10. Innermost Quantity Distributed (Non-US)

You should use this field for multi-level packaged drug products only. If you entered "Yes" (in the CSV file) or clicked the checkbox (for manual entry) in the *Intended to Fulfill 21 CFR 314.81* data element, you should enter only the amount of a listed drug product that the

establishment manufactured for commercial distribution and distributed to the non-US market during the reporting period that would have been included in an annual report as required by 21 CFR 314.81(b)(2)(ii)(*a*). Because this is an alternative reporting process for drug product with an approved application, for the purpose of this field, you should only include the amount of drug products that would otherwise have provided in the respective annual report under 21 CFR 314.81(b)(2)(ii)(*a*) and provide this amount based on the relevant time period in which the drug product was distributed. You should enter data into this field using a positive number (integer only) or a zero depending on whether the drug product was distributed during the relevant time period. You should not leave it blank even for time periods when no drug product was distributed. For manually entered data in the portal, based on the monthly data provided, the system will calculate the annual sum.

If you entered "No" (in the CSV file) or left the checkbox unchecked (for manual entry) in the *Intended to Fulfill 21 CFR 314.81* data element, then you should leave this field blank. If a listed drug product is not subject to an approved application for which an annual report is required under 21 CFR 314.81(b)(2)(ii)(*a*), then you should leave this field blank.

11. Innermost Package Type

You should use this field for multi-level packaged drug products only. If you are submitting information for a listed drug product that has multiple levels of packaging, this field should reflect the package type directly enclosing the drug product for which you are reporting data. Values entered here should adhere to the FDA-recognized package types as outlined in the portal.

12. Intended to Fulfill 21 CFR 314.81

The guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* explains the circumstances under which FDA does not intend to take action against an applicant regarding the requirement to submit distribution data in an annual report under section 314.81(b)(2)(ii)(*a*) if certain data is included in a report that is submitted through the portal.

If the drug product's application holder is not seeking to use the alternative reporting process for the distribution data required in an annual report under section 314.81(b)(2)(ii)(*a*) or a listed drug product is not subject to an approved application for which such an annual report is required (i.e., the listed drug product is not subject to an approved new drug application or an abbreviated new drug application), then you should enter "No" (in the CSV file) or leave the checkbox unchecked (for manual entry). If the drug product's application holder is seeking to use the alternative reporting process for the distribution data required in an annual report under section 314.81(b)(2)(ii)(*a*), then you should enter "Yes" (in the CSV file) or click the checkbox (for manual entry).

E. Reporting Amount of Drug Products Not in Finished Package Form

1. Establishment DUNS

You should include the DUNS number for each establishment covered by the submission. The DUNS number is a 9-digit number, including any leading zero(s), but without dashes or spaces.

2. Business Operation

For each establishment you identify, specify the business operation performed for each drug product. To simplify the reporting, we have limited the types of business operations for drug products not in finished package form to:

- MANUFACTURE
- REPACK
- RELABEL
- TRANSFILL
- POSITRON EMISSION TOMOGRAPHY DRUG PRODUCTION

3. NDC

To identify each drug product for which you are reporting, you will use the 10-digit NDC for the drug product as listed with FDA. You should provide the NDC in the appropriate format (i.e., using hyphens between the labeler code, the product code, and the package code). Appropriately formatted NDCs should have one of the following configurations: 4-4-2 (e.g.,1234-5678-90), 5-4-1 (e.g., 12345-6789-1), 5-3-2 (e.g., 12345-678-90).[24]

4. Source NDC

For a drug product listed under REPACK or RELABEL, you should provide the source NDC in the appropriate format (i.e., using hyphens between the labeler code, the product code, and the package code) using the 10-digit NDC assigned to the drug product received by the repacker or relabeler for repacking or relabeling. Appropriately formatted NDCs should have one of the following configurations: 4-4-2 (e.g.,1234-5678-90), 5-4-1 (e.g., 12345-6789-1), 5-3-2 (e.g., 12345-678-90). This field is used to identify the drug product that was repacked or relabeled, so that FDA can avoid double counting this drug product when analyzing the data.

5. Amount Per

The amount of each listed drug product manufactured for commercial distribution in a particular year should be organized by month. You should enter the name of each of the 12 months (i.e., January, February, …, November, and December) followed by "Annual Total" in the CSV file.

[24] For certain minimally manipulated human cell and tissue products, you may use an alternatively formatted NDC approved for use by the relevant center director.

6. Quantity Manufactured

You should enter the quantity of the drug product that the establishment manufactured for commercial distribution during the relevant time period. We suggest that you provide this amount based on the relevant time period in which the drug product was released. This quantity should be based on the drug product's dosage form unit. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug product was manufactured during the relevant time period. You should not leave it blank even for time periods when no drug product was manufactured. For manually entered data in the portal, based on the monthly data provided, the system will calculate the annual sum.

7. Quantity Distributed (Non-US)

If you entered "Yes" (in the CSV file) or clicked the checkbox (for manual entry) in the *Intended to Fulfill 21 CFR 314.81* data element, you should enter only the amount of a listed drug product that the establishment manufactured for commercial distribution and distributed to the non-US market during the reporting period that would have been included in an annual report as required by 21 CFR 314.81(b)(2)(ii)(*a*). Because this is an alternative reporting process for drug products with an approved application, for the purpose of this field, you should only include the amount of drug product that would otherwise have been provided in the respective annual report under 21 CFR 314.81(b)(2)(ii)(*a*) and provide this amount based on the relevant time period that the drug product was distributed. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug product was distributed during the relevant time period. You should not leave it blank even for time periods when no drug product was distributed. For manually entered data, based on the monthly data provided, the system will calculate the annual sum.

If you entered "No" (in the CSV file) or left the checkbox unchecked (for manual entry) in the *Intended to Fulfill 21 CFR 314.81* data element, then you should leave this field blank. If a listed drug product is not subject to an approved application for which an annual report is required under 21 CFR 314.81(b)(2)(ii)(*a*), then you should leave this field blank.

8. Dosage Form Units

You should enter the dosage form units associated with the NDC for which you are submitting data. Values entered here should adhere to a list of permissible values provided in the portal.

9. Intended to Fulfill 21 CFR 314.81

The guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* explains the circumstances under which FDA does not intend to take action against an applicant regarding the requirement to submit distribution data in an annual report under section 314.81(b)(2)(ii)(*a*) if certain data is included in a report that is submitted through the portal.

If the drug product's application holder is not seeking to use the alternative reporting process for the distribution data required in an annual report under section 314.81(b)(2)(ii)(*a*) or a listed drug product is not subject to an approved application for which such an annual report is required (i.e., the listed drug product is not subject to an approved new drug application or an abbreviated new drug application), then you should enter "No" (in the CSV file) or leave the checkbox unchecked (for manual entry). If the drug product's application holder is seeking to use the alternative reporting process for the distribution data required in an annual report under section 314.81(b)(2)(ii)(*a*), then you should enter "Yes" (in the CSV file) or click the checkbox (for manual entry).

F. Reporting Amount of Drugs That Are Not Drug Products

Drugs that are not drug products[25] include drugs that consist of API alone and drugs that consist of API with other ingredient(s) but that are not in finished dosage form. If you manufacture drugs that are not drug products, you should enter the amount of drugs using the data elements described below.

1. Establishment DUNS

You should include the DUNS number for each establishment covered by the submission. The DUNS number is a 9-digit number, including any leading zero(s), but without dashes or spaces.

2. Business Operation

For each establishment you identify, the drugs for which you are reporting for that establishment will be grouped by business operation performed. To simplify the reporting, we have limited the types of business operations to:

- MANUFACTURE
- API MANUFACTURE
- REPACK
- RELABEL
- TRANSFILL
- POSITRON EMISSION TOMOGRAPHY DRUG PRODUCTION

3. NDC

To identify each drug for which you are reporting, you will use the 10-digit NDC for the drug as listed with FDA. You should provide the NDC in the appropriate format (i.e., using hyphens between the labeler code, the product code, and the package code). Appropriately formatted NDCs should have one of the following configurations: 4-4-2 (e.g.,1234-5678-90), 5-4-1 (e.g., 12345-6789-1), 5-3-2 (e.g., 12345-678-90).[26]

[25] See guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (Part III.B.5.a.)

[26] For certain minimally manipulated human cell and tissue products, you may use an alternatively formatted NDC approved for use by the relevant center director.

4. Amount Per

The amount of each listed drug manufactured for commercial distribution in a particular year should be organized by month. You should enter the name of each of the 12 months (i.e., January, February, …, November, and December) followed by "Annual Total" in the CSV file.

5. Mass/Volume

You should enter the quantity of drug by mass or volume. We suggest that you provide this amount based on the relevant time period in which the drug was released. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug was manufactured during the relevant time period. You should not leave it blank even for time periods when no drug was manufactured. For manually entered data in the portal, based on the monthly data provided, the system will calculate the annual sum.

6. Unit of Measure

You should enter the unit of measure for reporting the amount of each listed drug. Values entered here should adhere to a list of permissible values provided in the portal.

7. Activity (Unit of Measure)

The guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* specifies that API registrants (or authorized agents) should also provide activity for drugs that are formulated by activity (e.g., heparin). For example, 1 mL of penicillin with an activity of 1,000,000 units per mL has a five times greater bactericidal effect than 1 mL of penicillin with an activity of 200,000 units per mL. Botulinum toxin dosages are also expressed in units, but 1 U of botulinum toxin of one product may not have the same biological effect or represent the same amount as 1 U of botulinum toxin of another product.

This field should only be used by API registrants (or their authorized agents) to report activity of drugs. Values entered here should adhere to the units provided in the portal.

8. Average Activity

This field should only be used by API registrants (or their authorized agents) to provide average activity information for drugs that are formulated by activity. We suggest that you provide the average activity from all batches based on the relevant time period in which the drug was released. The average activity value corresponds only to the number of batches; this is not a weighted average. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug was manufactured during the relevant time period. For example, if four batches were manufactured in a month with activity values of 90 U/mL, 91 U/mL, 92 U/mL, and 93 U/mL, then the average activity for that month is the sum of the four activity values divided by four, which is 91.5 U/mL. For reporting the annual total, you should use the total activity values from all batches released in a reporting year divided by the total number of batches.

9. Minimum Activity

This field should only be used by API registrants (or their authorized agents) to provide minimum activity information for drugs that are formulated by activity. We suggest that you provide the minimum activity from all batches based on the month in which the drug was released. You should enter data into this field using a positive number (integer or decimal) or a zero depending on whether the drug was manufactured during the relevant time period. For example, if four batches were manufactured in a month with activity values of 90 U/mL, 91 U/mL, 92 U/mL, and 93 U/mL, respectively, then you should enter 90 U/mL as the minimum activity value for that month. For reporting the annual total, you should enter the minimum activity value from all batches released in a reporting year.

V. RESOURCES

- Reference Guide for Reporting Amount of Listed Drugs and Biological Products[27]
- Guidance for industry *Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act* (February 2024)
- NextGen Portal[28]
  - Frequently Asked Questions web page
  - Technical Support
  - Reference Guide: Account Registration and Multi-Factor Authentication (MFA) Enrollment Process

[27] https://www.fda.gov/drugs/drug-shortages/coronavirus-aid-relief-and-economic-security-act-cares-act-drug-shortage-mitigation-efforts
[28] Available at https://edm.fda.gov/

APPENDIX

The following examples illustrate how to submit amounts of listed drugs based on the type of drug and its packaging in different scenarios.

Reporting Amount for Drug Products in Finished Packaged Form

Example 1 — Finished Dosage Form With Single-Level Packaging

Drug A is listed under national drug code (NDC) 12340-567-89 with the package description in its drug listing shown in Table 1.

Table 1. Drug A Package Description

Package NDC	Package description
12340-567-89	100 TABLET in 1 BOTTLE

Scenario 1 — Drug Manufactured for Commercial Distribution

An establishment (in a particular month) manufactured for commercial distribution and released 2,000 bottles of Drug A. The amount should be entered using the fields shown in Table 2. The registrant is not seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(*a*), so the *Intended to Fulfill 21 CFR 314.81* field should indicate "No" and the *Outermost Quantity Distributed (Non-US)* field is also left blank. In this scenario, there is no innermost packaging, so those fields should be left blank.

Table 2. Amounts Entered if Drug A Is Manufactured for Commercial Distribution

NDC	Outermost Quantity Manufactured	Outermost Quantity Distributed (Non-US)	Outermost Package Type	Innermost Quantity Manufactured	Innermost Quantity Distributed (Non-US)	Innermost Package Type	Intended to Fulfill 21 CFR 314.81
12340-567-89	2000		BOTTLE				No

Scenario 2 — Drug Manufactured for Commercial Distribution, and Submission Intended to Fulfill 21 CFR 314.81

An establishment (in a particular month) manufactured for commercial distribution and released 1,700 bottles of Drug A. Of those 1,700 bottles, 200 were distributed to a non-US market. If Drug A is subject to an approved application for which an annual report is required under 21 CFR 314.81(b)(2)(ii)(*a*), and the application holder is seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(a), then the amount should be entered using the fields shown in Table 3. The *Intended to Fulfill 21 CFR 314.81* field should indicate "Yes," and "200" should be entered into the *Outermost Quantity Distributed (Non-US)* field for the 200 bottles of Drug A that were distributed to a non-U.S. market during the relevant time period. In this scenario, there is no innermost packaging, so those fields should be left blank.

Table 3. Amounts Entered if Drug A is Manufactured for Commercial Distribution, and the Submission is Intended to Fulfill 21 CFR 314.81

NDC	Outermost Quantity Manufactured	Outermost Quantity Distributed (Non-US)	Outermost Package Type	Innermost Quantity Manufactured	Innermost Quantity Distributed (Non-US)	Innermost Package Type	Intended to Fulfill 21 CFR 314.81
12340-567-89	1700	200	BOTTLE				Yes

Example 2 — Finished Dosage Form With Multi-Level Packaging and a Single NDC

Drug B is listed under NDC 12340-567-01 with the package description in its drug listing shown in Table 4. In this example, the case is the outermost packaging because it is the highest level of packaging assigned an NDC. The innermost packaging is the bottle, since it directly encloses the drug (in this case, the capsules).

Table 4. Drug B Package Description

Package NDC	Package description
12340-567-01	96 CARTON in 1 CASE
	5 BOTTLE in 1 CARTON
	60 CAPSULE in 1 BOTTLE

An establishment (in a particular month) manufactured for commercial distribution and released 20 cases of Drug B. The amount should be entered using the fields shown in Table 5. In this scenario, the innermost packaging amount should be entered based on the quantities in the package description in its drug listing. The application holder is not seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(a), so the *Intended to Fulfill 21 CFR 314.81* field should indicate "No" and the *Outermost Quantity Distributed (Non-US)* and *Innermost Quantity Distributed (Non-US)* fields are left blank.

Table 5. Amounts Entered if Drug B Has a Single NDC

NDC	Outermost Quantity Manufactured	Outermost Quantity Distributed (Non-US)	Outermost Package Type	Innermost Quantity Manufactured	Innermost Quantity Distributed (Non-US)	Innermost Package Type	Intended to Fulfill 21 CFR 314.81
12340-567-01	20		CASE	9600		BOTTLE	No

Example 3 — Finished Dosage Form With Multi-Level Packaging and Multiple NDCs

Drug C is listed under NDC 12340-999-02 with the package description in its drug listing shown in Table 6. In this example, the outermost packaging should be the carton, and the innermost packaging should be the blister pack because the blister pack directly encloses the drug (i.e., the tablets). The pouches also have been assigned an NDC.

Table 6. Drug C Package Description

Package NDC	Package description
12340-999-02	3 POUCH in 1 CARTON
12340-999-01	5 BLISTER PACK in 1 POUCH
12340-999-03	21 TABLET in 1 BLISTER PACK

Scenario 1 — Single Innermost Package Presentation

An establishment (in a particular month) manufactured for commercial distribution and released 20 cartons of Drug C (NDC 12340-999-02). The amount should be entered using the fields shown in Table 7. In this scenario, the innermost packaging amount should be

entered based on the package description in its drug listing. The application holder is not seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(a), so the *Intended to Fulfill 21 CFR 314.81* field should indicate "No" and the *Outermost Quantity Distributed (Non-US)* and *Innermost Quantity Distributed (Non-US)* fields are left blank.

Table 7. Amounts Entered if Drug C Has a Single Innermost Package Presentation

NDC	Outermost Quantity Manufactured	Outermost Quantity Distributed (Non-US)	Outermost Package Type	Innermost Quantity Manufactured	Innermost Quantity Distributed (Non-US)	Innermost Package Type	Intended to Fulfill 21 CFR 314.81
12340-999-02	20		CARTON	300		BLISTER PACK	No

Scenario 2 — Multiple Innermost Package Presentations

An establishment (in a particular month) manufactured for commercial distribution and released 20 cartons of Drug C (NDC 12340-999-02) and separately manufactured for commercial distribution and released 500 pouches of Drug C (NDC 12340-999-01) on their own (not in cartons). The amount should be entered using the fields shown in Table 8. In this scenario, the innermost packaging amount should be entered based on the package description in its drug listing. The application holder is not seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(a), so the *Intended to Fulfill 21 CFR 314.81* field should indicate "No" and the *Outermost Quantity Distributed (Non-US)* and *Innermost Quantity Distributed (Non-US)* fields are left blank.

Table 8. Amounts Entered if Drug C Has Multiple Innermost Package Presentations

NDC	Outermost Quantity Manufactured	Outermost Quantity Distributed (Non-US)	Outermost Package Type	Innermost Quantity Manufactured	Innermost Quantity Distributed (Non-US)	Innermost Package Type	Intended to Fulfill 21 CFR 314.81
12340-999-02	20		CARTON	300		BLISTER PACK	No
12340-999-01	500		POUCH	2500		BLISTER PACK	No

Example 4 — Kit With Multiple Components

Kit X is listed under NDC 23451-999-11 with the package description in its drug listing shown in Table 9 and the parts quantities shown in Table 10.

Table 9. Kit X Package Description

Package NDC	Package description
23451-999-11	1 in 1 CARTON

Table 10. Kit X Parts Quantities

Part number	Package quantity
1	Drug 1 (1 VIAL, MULTI-DOSE)
2	Drug 2 (1 VIAL, SINGLE-DOSE)
3	Drug 3 (1 PACKET)

An establishment (in a particular month) manufactured for commercial distribution and released 200 cartons. The amount should be entered using the fields shown in Table 11. For kits, the fields for innermost packaging should be left blank. The application holder is not seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(a), so the *Intended to Fulfill 21 CFR 314.81*field should indicate "No" and the *Outermost Quantity Distributed (Non-US)* and *Innermost Quantity Distributed (Non-US)* fields are left blank.

Table 11. Amounts Entered for Kit X With Multiple Components

NDC	Outermost Quantity Manufactured	Outermost Quantity Distributed (Non-US)	Outermost Package Type	Innermost Quantity Manufactured	Innermost Quantity Distributed (Non-US)	Innermost Package Type	Intended to Fulfill 21 CFR 314.81
23451-999-11	200		CARTON				No

Reporting Amount for Drug Products Not in Finished Packaged Form

Example 5 — Drug Products Not in Finished Package Form

Drug D is listed under NDC 23450-678-01 with the package description in its drug listing shown in Table 12. In this example, the dosage form unit is tablet, and the amount reported should correspond only to the dosage form associated with the NDC assigned to the manufactured product, regardless of whether the product is in single- or multi-level packaging.

Table 12. Drug D Package Description

Package NDC	Package description
23450-678-01	50,000 TABLET in 1 DRUM

An establishment (in a particular month) manufactured for commercial distribution and released 5 drums of Drug D, four containing 50,000 tablets and one partially-filled drum with 12,000 tablets. The amount should be entered using the fields shown in Table 13. The application holder is not seeking to use the alternative reporting process for the distribution data required for the annual report under 21 CFR 314.81(b)(2)(ii)(a), so the *Intended to Fulfill 21 CFR 314.81* field should indicate "No" and the *Quantity Distributed (Non-US)* field is left blank.

Table 13. Amounts Entered for Drug D

NDC	Quantity Manufactured	Quantity Distributed (Non-US)	Dosage Form Units	Intended to Fulfill 21 CFR 314.81
23450-678-01	212000		TABLET	No

Reporting Amount for Drugs That Are Not Drug Products

Example 6 — Reporting API for Drugs That are Not Formulated by Activity

Drug E is listed under NDC 23450-567-01 with the package description in its drug listing shown in Table 14.

Table 14. Drug E Package Description

Package NDC	Package description
23450-567-01	100 kg in 1 DRUM

An establishment (in a particular month) manufactured for commercial distribution and released 5 drums of Drug E, with four drums each containing 100 kg, and one partially-filled drum with 36.5 kg, for a total of 436.5 kg. The amount should be entered using the fields shown in Table 15. In this scenario, Drug E is not formulated by activity, so those fields should be left blank.

Table 15. Amounts Entered for Drug E

NDC	Mass/Volume	Unit of Measure	Activity (Unit of Measure)	Average Activity	Minimum Activity
23450-567-01	436.5	kg			

Example 7 — Reporting API for Drugs That are Formulated by Activity

Drug F is listed under NDC 34560-123-01 with the package description in its drug listing shown in Table 16.

Table 16. Drug E Package Description

Package NDC	Package description
34560-123-01	100 kg in 1 DRUM

An establishment (in a particular month) manufactured for commercial distribution and released 5 drums of Drug F (e.g., heparin sodium). These drums contained four batches of Drug F with activity specification ranging from 90 U to 120 U. The batch size for drug F is 100 kg, and the establishment manufactured 4 batches of Drug F in this particular month. Three batches weigh 100 kg and

one batch weighs 90kg, and the activities reported for each batch are 90 U, 91 U, 92 U, and 93 U, respectively. For that month, the mass/volume should be 390 kg, the average activity should be 91.5 U, and the minimum activity should be 90 U. The amount should be entered using the fields shown in Table 17.

Table 17. Amounts Entered for Drug F

NDC	Mass/Volume	Unit of Measure	Activity (Unit of Measure)	Average Activity	Minimum Activity
34560-123-01	390	kg	U	91.5	90