Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act

Guidance for Industry

DRAFT GUIDANCE

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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)
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October 2021
Procedural

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Contains Nonbinding Recommendations

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Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the FD&C Act Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

The Food and Drug Administration (FDA) is issuing this draft guidance to assist registrants of drug establishments in submitting to FDA reports on the amount of each listed drug manufactured, prepared, propagated, compounded, or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) (21 U.S.C. 360(j)(3)), as added by section 3112(e) of the Coronavirus Aid, Relief, and Economic Security Act (CARES Act).

This guidance describes the process that should be used for reporting such information by each person who registers with FDA under section 510 of the FD&C Act with regard to a listed drug (including a finished dosage form product, an active pharmaceutical ingredient (API), and other types of listed drugs, except for biological products or categories thereof exempted by an order under section 510(j)(3)(B)).[2] The process described in this guidance applies to such reporting with respect to listed drugs including medical gases,[3] homeopathic products, products marketed in accordance with requirements under section 505G of the FD&C Act (21 U.S.C. 355h),[4] often referred to as over-the-counter monograph drugs, and animal drug products that are not

[1] This guidance has been prepared by the Office of Regulatory Policy and the Office of Pharmaceutical Quality in 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.

[2] 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 a Proposed Order that, if finalized, would exempt 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 86 FR 59395 (October 27, 2021). See also Question & Answer IV.J.

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

[4] 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.

approved, conditionally approved, or indexed under sections 512, 571, and 572 of the FD&C Act.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, 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

An establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a drug in the United States is required to be registered with the FDA.[5] Likewise, any establishment within a foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug that is imported or offered for import into the United States is also required to be registered with the FDA.[6] Further, domestic and foreign registrants are required to list with FDA all the drugs being manufactured, prepared, propagated, compounded, or processed by their registered establishments for commercial distribution.[7] Each registrant must provide certain information[8] for each listed drug it manufactures for commercial distribution,[9] including unfinished drugs[10] and APIs. This information helps the FDA maintain a catalog of all drugs in commercial distribution in the United States.

On March 27, 2020, the CARES Act[11] was enacted to aid response efforts and ease the economic impact of the Coronavirus Disease 2019 (COVID-19). In addition, the CARES Act included authorities to enhance FDA's ability to identify, 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 new section 510(j)(3) of the FD&C Act, which requires that each person (including repackers and relabelers) who registers with FDA under section 510 of the FD&C Act with regard to a drug must report to FDA annually on the amount of each listed drug that was manufactured, prepared, propagated, compounded, or processed by such person for commercial distribution.

[5] Section 510(b) of the FD&C Act; § 207.17 (21 CFR 207.17).
[6] Section 510(i) of the FD&C Act; § 207.17.
[7] Section 510(j)(1) of the FD&C Act; 21 CFR 207.41. Manufacturers, repackers, relabelers or salvagers of Type B or Type C mediated feed are exempt from drug listing (section 510(g)(5) of the FD&C Act; 21 CFR 207.13(g)).
[8] Section 510(j) of the FD&C Act; 21 CFR 207.49(a) (e.g., § 207.49(a)(4); § 207.49(a)(8)).
[9] See 21 CFR 207.1 (21 CFR 207.1) (defining "manufacture" and "commercial distribution").
[10] *Unfinished drug* means an active pharmaceutical ingredient either alone or together with one or more other ingredients but does not include finished drug products (§ 207.1).
[11] Public Law 116-136.

III. DISCUSSION

A. Content of Reports

Each registrant that lists a drug must report to FDA annually on the amount of such drug that it manufactured, prepared, propagated, compounded, or processed (including repacking and relabeling[12]) for commercial distribution.[13]

The report should provide the amount of each listed drug, identified by National Drug Code (NDC), that was released by each registered establishment during the reported year, organized by the amount of drug released in each month.[14] Repackers and relabelers should also include in their reports the source NDC (i.e., the full three-segment NDC assigned to the drug received by the repacker/relabeler for repacking or relabeling), if available.

Registrants should also report the single business operation that is most relevant to the overall business operations performed for the listed drug at the registered establishment in that year.[15] The business operation information provided in the section 510(j)(3) report may be different from the business operation(s) included in the drug listing because the drug listing file may identify multiple business operations, whereas the 510(j)(3) report should identify a single business operation.

1. Finished Dosage Form Products

For the purposes of this guidance, a *finished dosage form product* is a drug that is in finished dosage form (e.g., finished tablet, capsule, or solution), whether or not it is in a package form suitable for distribution to pharmacies, hospitals, or other sellers or dispensers of the drug product to patients or consumers.

Each registrant that lists a *finished dosage form product* must report to FDA annually the amount of such drug that it manufactured, prepared, propagated, compounded, or processed (including repacking and relabeling[16]) for commercial distribution.[17]

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[12] See section 510(a)(1) of the FD&C Act.

[13] See section 510(j)(3)(A) of the FD&C Act.

[14] For the purposes of this guidance, "released" means that the batch or lot has been determined to conform to final specifications (see 21 CFR 211.165; FDA guidance for industry *ICH Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* (ICH Q7) (September 2016), section 11.2), and the production and control records have been reviewed and approved by the quality control unit (see 21 CFR 211.192; ICH Q7 section 6.7). Additional information regarding how to report the amount of each listed drug under section 510(j)(3) is available in FDA's Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[15] Additional information regarding the business operation to include in a section 510(j)(3) report is available in FDA's Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide.

[16] See section 510(a)(1) of the FD&C Act; also see definition of "manufacture" at § 207.1 (i.e., "the term 'manufacture, preparation, propagation, compounding, or processing,' as used in section 510 of the Federal Food, Drug, and Cosmetic Act, includes relabeling, repackaging, and salvaging").

[17] See section 510(j)(3)(A) of the FD&C Act.

If the product is listed with FDA as having a single level of packaging, the amount reported should correspond only to the quantity of that package type associated with the NDC assigned to the product released. For example, if the NDC is for a drug packaged in a bottle containing 500 film-coated tablets, the registrant should report the number of bottles released, not the number of tablets. Table 1 provides an illustration of the relationship between the NDC, the package description, and the quantity reported.[18]

Table 1: Relationship Between the NDC, Package Description, and Quantity Reported for Products with a Single Level of Packaging

NDC	Package Description	Quantity of Bottles Released	Package Type Quantity To be Reported
00000-000-00	500 TABLET, FILM COATED in 1 BOTTLE	10,000	10,000

If the product is listed with FDA as having multiple levels of packaging and the product is not listed as a kit, then the product should be reported using the NDC assigned to the outermost layer of packaging, and the amounts reported should correspond to the package types associated with both the outermost layer of packaging and the innermost layer of packaging. The outermost layer of packaging is the package type associated with the NDC assigned to the drug released. The innermost layer of packaging is the package type directly enclosing the product. For example, a case (outermost layer of packaging) of 48 cartons, each carton containing one bottle (innermost layer of packaging) of 30 tablets, should be reported by the NDC assigned to the case, with the amounts reported using both the number of cases and the number of bottles released.[19] Table 2 provides an illustration of the relationship between the NDC, the package description, and the quantity reported.[20]

[18] For information about how to submit the amount of each listed drug in a section 510(j)(3) report, refer to FDA's Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide.

[19] We are requesting that this information be reported at both of these packaging levels for multiple reasons. First, having this information, combined with the information in the self-reported drug listing files will help us validate the data submitted and identify certain possible reporting errors. Second, having this volume information at multiple reporting levels will increase the utility of the data. Although the Agency may have the capability to use some of the data from the drug listing files to convert from one packaging level to the other, the Agency has identified discrepancies between the package descriptions included in self-reported drug listing files and packaging descriptions included in product labeling. These discrepancies could impact the validity of the data if the Agency were to try to convert amounts from one packaging level to the other. Accordingly, the Agency currently believes that, with respect to drug products listed as having multi-level packaging, reporting of drug amount information by both the outermost layer of packaging and the innermost layer of packaging would ensure the data is provided in the most useful way to the Agency.

[20] For information about how to submit the amount of each listed drug in a section 510(j)(3) report, refer to FDA's Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide.

Table 2: Relationship Between the NDC, Package Description, and Quantity Reported for Products with Multiple Levels of Packaging

NDC	Package Description (Inclusive of all levels)	Quantity of Cases Released	Quantity of Bottles Released	Outermost Package Type Quantity To be Reported	Innermost Package Type Quantity To be Reported
11111-1111-1	1 CASE (11111-1111-1) contains 48 CARTONS; 1 CARTON contains 1 BOTTLE; 1 BOTTLE contains 30 TABLETS	20,000	960,000	20,000	960,000

If the product is listed as a kit,[21] the amount reported should be based on the outermost layer of packaging associated with the NDC assigned to the kit released.

In some instances, a product that has been assigned an NDC (NDC #1) may be both commercially distributed on its own and commercially distributed (and listed) as a part of a kit or as an inner packaging layer for another product that is assigned a separate NDC (NDC #2). Reports submitted under NDC #1 should only include amounts released on their own and should not include amounts of the product that are a part of the kit or an inner packaging layer for the other product assigned NDC #2, as those would be accounted for in the amount reported for NDC #2.

Registrants should not submit section 510(j)(3) reports to FDA based on the number of tablets, volume, or mass of the product.[22]

[21] For purposes of this guidance, a kit is a co-packaged product that includes at least one or more drug items.

[22] Medical gas manufacturers should report to the Agency each year the number of units (e.g., cylinder, dewar, tank) of each medical gas released from each registered establishment. FDA recognizes that, during normal manufacturing, storage, and filling operations for medical gases, venting may result in some product loss, and that manufacturers reuse containers that may contain residual gas from previous use. Registrants that list a medical gas need not, in preparing a report under section 510(j)(3), determine what amount has vented during normal operations or what amount of gas released consisted of residual gas from previous use.
Additionally, FDA recognizes that some designated medical gas manufacturers produce and distribute the same gas for both medical and non-medical (e.g., industrial) purposes and may not be able to determine how much of the gas will be used for medical purposes. Registrants that list a designated medical gas need not, in preparing a report under section 510(j)(3), determine whether the gas will be ultimately used for a medical or non-medical purpose; rather, they should report to the Agency each year the number of units of each designated medical gas released from each registered establishment, regardless of its ultimate use.

142 *2. API*
143
144 Each registrant that lists an API[23] must report to FDA annually the amount of API that it has
145 manufactured, prepared, propagated, compounded, or processed (including repacking and
146 relabeling[24]) for commercial distribution for the reporting year.[25] The amount should be
147 reported in terms of the appropriate unit containers as reported in drug listing (e.g., tanks, drums,
148 cylinders, bags) rather than by weight, mass, or volume using metric or imperial system units.[26]
149
150 *3. Other Listed Drugs*
151
152 Each registrant that lists a drug that consists of API with other ingredient(s) and that is not a
153 finished dosage form product,[27] must report to FDA annually the amount of such drug
154 manufactured, prepared, propagated, compounded, or processed (including repacking and
155 relabeling[28]) for commercial distribution for the reporting year.[29] The amount should be
156 reported in the appropriate unit containers as reported in the drug listing, rather than metric or
157 imperial system units.[30]
158
159 *4. Private Label Distribution*
160
161 As noted above, the report should provide the amount of each listed drug, identified by NDC,
162 that was released by each registered establishment during the reported year, organized by the
163 amount of drug released in each month. For drugs that are manufactured, prepared, propagated,
164 compounded, or processed (including repacking and relabeling) by a registrant for commercial
165 distribution under the trade name or label of a private label distributor, the data should be
166 submitted separately by the NDC associated with the registrant's labeler code and the NDC
167 associated with the private label distributor's labeler code.
168

[23] *Active pharmaceutical ingredient* (API) means any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body. API does not include intermediates used in the synthesis of the substance (§ 207.1). Additionally, for the purposes of this guidance, API includes *drug substance* as defined by FDA's guidance for industry: Q6B, Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products (ICH Q6B) (August 1999).

[24] See section 510(a)(1) of the FD&C Act. Also see the definition of "manufacture" at § 207.1 (i.e., "the term 'manufacture, preparation, propagation, compounding, or processing,' as used in section 510 of the Federal Food, Drug, and Cosmetic Act, includes relabeling, repackaging, and salvaging").

[25] See section 510(j)(3)(A) of the FD&C Act.

[26] For API that is in multi-level packaging, the principles underlying the recommendations for reporting multi-level packaged finished dosage form products should apply (see section III.A.1).

[27] See definition of *finished dosage form product* in section III.A.1.

[28] See section 510(a)(1) of the FD&C Act.

[29] See section 510(j)(3)(A) of the FD&C Act.

[30] For other listed drugs that are in multi-level packaging, the principles underlying the recommendations for reporting multi-level packaged finished dosage form products should apply (see section III.A.1).

B. Timing of Reports

Reports on the amount of each registrant's listed drugs must be submitted annually.[31] Such reports should include information regarding the amount of drug released[32] for the respective calendar year (January 1 – December 31).

Reports for calendar year 2020[33] should be submitted no later than February 15, 2022,[34] and reports for calendar year 2021 should be submitted no later than May 16, 2022. Reports for subsequent calendar years should be submitted no later than February 15 of the following calendar year. For instance, registrants that manufactured, prepared, propagated, compounded, or processed listed drugs for commercial distribution at any time in calendar year 2022 should submit reports to FDA reporting the drug amounts for calendar year 2022 no later than February 15, 2023.[35]

C. Process for Report Submission

FDA is authorized to require registrants to submit section 510(j)(3) reports in an electronic format, as determined by the Agency.[36] Registrants should submit reports via the NextGen Portal, available at edm.fda.gov. Additional information regarding technical specifications for submissions is available on FDA's website.[37] 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 (CDER) DrugVolumeReporting@fda.hhs.gov, (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010, or (CVM) Office of Surveillance and Compliance, 240-402-7082 or CVMSurveillance@fda.hhs.gov, as applicable.)

[31] Section 510(j)(3)(A) of the FD&C Act.

[32] See footnote 14.

[33] The effective date of section 510(j)(3) of the FD&C Act, as added by section 3112(e) of the CARES Act, was September 23, 2020.

[34] Firms that were not registered with listed drugs at any point in calendar year 2020 are not required to submit a section 510(j)(3) report for that year.

[35] In addition to annual reporting requirements, FDA is authorized under section 510(j)(3)(A) of the FD&C Act to require registrants to submit reports on the amount of listed drugs at the time a public health emergency is declared by the Secretary under section 319 of the Public Health Service Act. FDA intends to continue to assess the need for such additional reporting during public health emergencies, including the public health emergency declared by the Secretary of the Department of Health and Human Services (HHS) on January 31, 2020. This includes any renewals made by the HHS Secretary in accordance with section 319(a) of the Public Health Service Act (42 U.S.C. 247d(a)). Report submissions related to a public health emergency under section 510(j)(3)(A) of the FD&C Act do not satisfy the requirement to submit a separate report for the calendar year under such section.

[36] Section 510(j)(3)(A) of the FD&C Act.

[37] See FDA's Reporting Amount of Listed Drugs and Biological Products Technical Conformance Guide.

IV. QUESTIONS AND ANSWERS

A. What type of drug reporting is the subject of this guidance?

This guidance describes the process that registrants should use for annually reporting the amount of each listed drug that was manufactured, prepared, propagated, compounded, or processed for commercial distribution. Under section 510(j)(3) of the FD&C Act, such information must be reported by each person who registers with FDA under section 510 of the FD&C Act with regard to a listed drug (including a finished dosage form product, an API, and other listed drugs, except for biological products or categories thereof exempted by an order under section 510(j)(3)(B)).[38] The process described in this guidance applies to such reporting with respect to listed drugs including medical gases, homeopathic products, products marketed in accordance with requirements under section 505G of the FD&C Act (21 U.S.C. 355h),[39] 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.

B. If an applicant submits a report containing distribution data under 21 CFR 314.81(b)(2)(ii)(*a*) or 21 CFR 600.81(a) for human drugs or biological products, respectively, does the registrant of an establishment(s) identified in the application also need to annually submit a separate report under section 510(j)(3) of the FD&C Act containing the amount of the listed drug that was manufactured, prepared, propagated, compounded, or processed at the establishment for commercial distribution?

A registrant[40] of a listed drug must submit a report as required under section 510(j)(3) of the FD&C Act.[41] FDA acknowledges that applicants with approved applications[42] provide to FDA certain drug product distribution data in reports under § 314.81 (21 CFR 314.81) and § 600.81 (21 CFR 600.81); however, such data is aggregated and reflects the total amount distributed by an applicant but does not include reporting specific to each establishment of the listed drug. If an application includes multiple establishments, the information reported under § 314.81 and § 600.81 would not be specific to each establishment, which can introduce challenges for the Agency in identifying, preventing, and mitigating

[38] See footnote 2.

[39] 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.

[40] *Registrant* means any person that owns or operates an establishment that manufactures, repacks, relabels, or salvages a drug, and is not otherwise exempt from establishment registration requirements under section 510 of the FD&C Act or 21 CFR part 207. See § 207.1.

[41] See section 510(j)(3)(A) of the FD&C Act.

[42] For the purposes of this Question & Answer IV.B, *applicant* includes (i) any person who submits a new drug application (NDA) under section 505(b) of the FD&C Act, abbreviated new drug application (ANDA) under section 505(j) of the FD&C Act, or a biologics license application (BLA) under section 351 of the PHS Act (or an amendment or supplement to any such NDA, ANDA, or BLA), and (ii) any person who owns an approved NDA, ANDA, or BLA. See 21 CFR 314.3, 21 CFR 601.2(a).

drug shortages. In contrast, reports submitted under section 510(j)(3) of the FD&C Act should be submitted for each establishment, which would enhance the Agency's ability to identify, prevent, and mitigate possible drug shortages.[43]

FDA does not intend to take action against an applicant regarding the requirement to submit distribution data in annual reports[44] submitted under §314.81(b)(2)(ii)(a), if:

(1) Each registrant of establishments identified in the application submits a timely and complete report under section 510(j)(3) of the FD&C Act;
(2) Each registrant of establishments identified in the application adds to its section 510(j)(3) report the amount of listed drug product (organized by NDC number) that was distributed for foreign use during the reporting period;[45] and
(3) The applicant's annual report submitted under § 314.81(b)(2) provides:
    - The NDC number(s) and strength(s) of drug product for which each registrant submitted its report under section 510(j)(3) of the FD&C Act; and
    - The date(s) of the report(s) submitted under section 510(j)(3) of the FD&C Act.

FDA believes that this enforcement policy would maintain the Agency's access to information that would enhance the Agency's ability to identify, prevent, and mitigate possible drug shortages, and would also address the potential reporting burden for applicants that are subject to both § 314.81(b)(2)(ii)(a) and section 510(j)(3) of the FD&C Act.[46]

[43] Additionally, reports that the Agency receives under § 314.81(b)(2)(ii)(a) and § 600.81(a) are limited to the finished drug product and do not include information about the API, drug substance, or unfinished drug product. Moreover, these reports arrive at the Agency from numerous applicants at different times throughout the year, which makes it challenging for the Agency to identify, prevent, and mitigate drug shortages at any particular point in time. In contrast, under FDA's recommendations for reports submitted under section 510(j)(3) of the FD&C Act, the data from all applicable registrants should arrive at the Agency during the same timeframe (see section III.B), which would enhance the Agency's ability to identify, prevent, and mitigate possible drug shortages.

[44] For the purposes of this enforcement policy, the § 314.81(b)(2) annual report would be submitted no later than 1 year after the submission of the section 510(j)(3) report(s) by each registrant of establishments identified in the application. Additionally, annual reports submitted under § 314.81(b)(2) are required to provide as applicable, among other information, a brief summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product; labeling information; chemistry, manufacturing, and control change information, nonclinical laboratory studies, clinical data; and status reports of postmarketing study commitments.

[45] § 314.81(b)(2)(ii)(*a*) requires applicants to provide to the Agency information about the quantities of drug product distributed for foreign use.

[46] The Agency does not intend to extend this enforcement policy to the submission of distribution reports under § 600.81. Distribution reports submitted under § 600.81 contain certain information relating to the quantity of biological product distributed by the applicant by lot, which is not required for reports submitted under section 510(j)(3) of the FD&C Act. For example, distribution reports submitted under § 600.81 include the fill lot numbers for the total number of dosage units of each strength or potency distributed, the label lot number (if different from fill lot number), the number of doses in fill lot/label lot, and the date of release of fill lot/label lot for distribution. See § 600.81(a). Additionally, distribution reports under § 600.81 are generally submitted once every 6 months, while reports under section 510(j)(3) of the FD&C Act are submitted annually.

C. If an applicant submits a report containing distribution data for animal drugs under 21 CFR 514.80(b)(4)(i), and/or 21 CFR 514.87(b)(4)-(5), does the registrant of an establishment(s) in the application also need to submit a separate report under section 510(j)(3) of the FD&C Act containing the amount of the listed drug that was manufactured, prepared, propagated, compounded, or processed at the establishment for commercial distribution?

Yes, a registrant of a listed animal drug must submit a separate report under section 510(j)(3) of the FD&C Act containing the amount of the listed drug that was manufactured, prepared, propagated, compounded, or processed by such person for commercial distribution. This is in addition to the reporting requirements of applicants[47] under § 514.80(b)(4)(i) (21 CFR 514.80(b)(4)(i)) and § 514.87(b)(4)-(5) (21 CFR 514.87(b)(4)-(5)).[48]

FDA understands that applicants provide to FDA certain distribution data in reports under § 514.80(b)(4)(i) and § 514.87(b)(4)-(5); however, such data is limited to the applicants and it does not include reporting specific to each establishment of the listed drug. If an application includes multiple establishments, the information reported under § 514.80(b)(4)(i) and § 514.87(b)(4)-(5) would not be specific to each establishment, which can introduce challenges for the Agency in identifying, preventing, and mitigating drug shortages. In contrast, for reports submitted under section 510(j)(3) of the FD&C Act, reports should be submitted for each establishment, which would enhance the Agency's ability to identify, prevent, and mitigate possible drug shortages.[49]

D. Can an authorized agent of a registrant submit a report under section 510(j)(3) of the FD&C Act on the registrant's behalf?

An agent that has knowledge regarding the amount of drug released and who has been authorized by the registrant to submit the registrant's report under section

[47] For the purposes of this Question & Answer IV.C, *applicant* is a person or entity who owns or holds on behalf of the owner the approval for a new animal drug application (NADA) or an abbreviated new animal drug application (ANADA), and is responsible for compliance with the applicable provisions of the FD&C Act and regulations. See 21 CFR 514.3.

[48] The Agency does not intend to extend a policy similar to that described for § 314.81(b)(2)(ii)(a) (see Question & Answer IV.B), with respect to reports containing distribution data submitted under 21 CFR 514.80(b)(4)(i) or § 514.87(b)(4)-(5). In contrast to annual reports submitted under § 314.81, distribution reports submitted under § 514.80(b)(4)(i) are generally submitted once every 6 months for the first 2 years following approval of an NADA or ANADA. Further, FDA is required to publish annual summary reports of data and information it receives under § 514.87, and these published reports are required to include a summary of distribution data received under § 514.87. See § 514.87(f); see also section 512(l)(3)(E) of the FD&C Act.).

[49] Additionally, reports that the Agency receives under § 514.80(b)(4)(i) and § 514.87(b)(4)-(5) are limited to the finished drug product and do not include information about the API or unfinished drug product. Moreover, these reports arrive at the Agency from numerous applicants at different times throughout the year, which makes it challenging for the Agency to identify, prevent, and mitigate drug shortages at any particular point in time. In contrast, under FDA's recommendations for reports submitted under section 510(j)(3) of the FD&C Act, the data from all applicable registrants would arrive at the Agency during the same time frame, which would enhance the Agency's ability to identify, prevent, and mitigate possible drug shortages.

510(j)(3) of the FD&C Act may submit such a report on the registrant's behalf to the Agency. Accordingly, a private label distributor with knowledge of the amount of drug released and who has been authorized as an agent to submit a report under section 510(j)(3) on the registrant's behalf may do so. Additionally, an applicant (e.g., holder of an NDA, ANDA, BLA, NADA, or ANADA) that has been authorized as an agent on behalf of a contract manufacturer (registrant) to submit a report under section 510(j)(3) on the contract manufacturer's behalf may do so.[50] However, each registrant is ultimately responsible for ensuring that an accurate and timely report under section 510(j)(3) is submitted on its behalf.

E. Should the registrant report the amount of listed drug released based on theoretical yield or actual yield?

Registrants should report the actual yield—the actual amount of drug that is released during the reporting period. Percent yield is the percent ratio of actual yield to theoretical or predicted yield and can only be 100% if there are no losses or errors during actual production. Registrants should not report the amount of listed drug available for commercial distribution based on a theoretical assumption of 100% yield.

F. In determining the amount of drug to report in a section 510(j)(3) report, should a registrant include amounts of drug that were returned and/or recalled?

Registrants are required to report "on the amount" of listed drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution.[51] There is no exemption for drugs that have been returned or recalled. For that reason, the report must not subtract amounts that have been returned[52] or recalled.[53]

G. If a registrant manufactured, prepared, propagated, compounded, or processed an applicable drug for commercial distribution during only part of the calendar year, does the registrant still need to submit an annual volume report under section 510(j)(3) of the FD&C Act?

Yes, the registrant should submit a report to FDA no later than the recommended date each year (see section III.B).

H. If a registrant had a drug listed with FDA during the calendar year, but did not ultimately manufacture, prepare, propagate, compound, or process any

[50] Contract facilities should consider outlining the reporting arrangements in a written quality agreement or other written contract.

[51] Section 510(j)(3)(A) of the FD&C Act.

[52] See 21 CFR 211.204.

[53] See 21 CFR part 7, subpart C.

of the drug for commercial distribution during that calendar year, does the registrant need to submit a report under section 510(j)(3) of the FD&C Act?

Registrants are required to report "on the amount" of listed drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution.[54] If such amount for an individual registrant is zero, the registrant still must submit a report under section 510(j)(3) of the FD&C Act.

I. What amount should a registrant of a foreign establishment report if some, but not all, of the listed drug it manufactures is imported or offered for import into the United States?

If a listed drug was manufactured, prepared, propagated, compounded, or processed in a foreign establishment for commercial distribution (i.e., in the United States[55]) and the registrant of the foreign establishment knows how much of the listed drug was imported or offered for import into the United States, then the registrant must report that amount.[56] However, if a listed drug was manufactured, prepared, propagated, compounded, or processed for commercial distribution in a foreign establishment but the registrant does not know how much of the listed drug was imported or offered for import into the United States, then the registrant should report the total amount of the listed drug that it manufactured, prepared propagated, compounded or processed (including repacked or relabeled) during the reporting period.

J. Should a registrant of a listed biological product submit a section 510(j)(3) report to FDA, if the biological product falls within a category of biological products identified in FDA's Proposed Order as being proposed for exemption from section 510(j)(3)(A) reporting requirements?

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 a Proposed Order that, if finalized, would exempt 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.[57]

Until the effective date of an order finalizing the Proposed Order or the date of withdrawal of the Proposed Order, whichever comes first, FDA does not intend to take action if a registrant does not submit a report required under section

[54] See section 510(j)(3)(A) of the FD&C Act.
[55] See § 207.1 (defining "commercial distribution").
[56] See section 510(j)(3)(A) of the FD&C Act.
[57] See 86 FR 59395 (October 27, 2021).

510(j)(3)(A) of the FD&C Act with respect to a biological product that falls within a category of biological products identified in the Proposed Order as being proposed for exemption from section 510(j)(3)(A) reporting requirements.

K. Should a registrant of a listed drug submit a section 510(j)(3) report to FDA, if the registrant's only business operation in the drug listing file is sterilize, analysis, particle size reduction, and/or salvage?

FDA does not intend to take action if registrants whose only business operation in the drug listing file is sterilize, analysis, particle size reduction, and/or salvage do not submit reports under section 510(j)(3) of the FD&C Act. FDA believes the data reported by other registrants (e.g., registrants with business operations of manufacture, repack, or relabel in the drug listing file) will be sufficient.