U.S. FOOD & DRUG ADMINISTRATION

FDA FACT SHEET

Human Drug Exports

Deciphering Why FDA Returned Your Electronic Certificate of Pharmaceutical Product (eCPP) Application

The FDA Center for Drug Evaluation and Research (CDER) works to promote and protect public health by promoting supply chain integrity of human drugs. Facilities exporting human drugs are often asked by foreign customers or foreign governments to provide documentation of the facility's compliance with FDA standards.

FDA issues electronic certificates of pharmaceutical product (eCPP) for drugs approved or licensed by the FDA, over-the-counter drugs that follow an FDA monograph, and unapproved drugs that meet FDA's statutory requirements. FDA eCPPs conform to the World Health Organization format and are intended for importing countries considering whether to license products for sale in that country. eCPPs provide information about a drug's U.S. marketing status and the manufacturer's compliance with current good manufacturing practice (CGMP).

For various reasons, CDER may not be able to issue an eCPP to an applicant and will return the application with a Return for Action request. A Return for Action request gives the applicant an opportunity to provide information that will allow CDER to reconsider the eCPP application.

CPP applications are automatically cancelled by the system after two Return for Action requests or when the applicant fails to respond within three business days to the Return for Action request from the date of receipt.

CDER may return an eCPP application if it does not include all the required information or if information provided is out of date.

Other possible reasons include:

- FDA has initiated an enforcement action, such as a seizure or injunction.
- The manufacturing facility is not registered with FDA or not in compliance with CGMP.
- The drug is not listed with FDA.
- The requisite labeling documents submitted as part of the eCPP application are outdated or not in correspondence with Agency documentation.

The CDER Exports Program reviews thousands of eCPP applications a year. In 2021, CDER reviewed and issued approximately 7,820 export certificates with 3,172 corresponding copies. CDER has Returned for Action a total of 16,923 CPP applications from 2017 to April 2022.

A table explaining the most frequent reasons for a Return for Action request is shown below. Please refer to the table below as a guide for responding to a Return for Action request.

Top reason codes for why CDER issues a Return for Action request, based on historical data

FACILITY

Review Reason Code	Case scenario	Resolution
Unacceptable CGMP I CGMP discrepancies	Inspection history shows Official Action Indicated (OAI) status for the manufacturer.	Applicant should contact the manufacturer to determine CGMP compliance status before re-submitting a response to the Return for Action request for the CPP application. *Note: No Action Indicated (NAI) and Voluntary Action Indicated (VAI) are acceptable CGMP decisions for manufacturing sites.*
Profile class not associated with facility	Profile class of drug for which CPP is being sought was never inspected for by FDA and shows no inspection history for the corresponding profile class (e.g., the profile class subject to the CPP application is a capsule but FDA's database does not indicate that capsules were covered during facility inspection). Facility inspection records show discontinued or missing profile class.	Applicant should provide supporting documentation showing that the facility was inspected to manufacture/package the profile class of the drug subject to their request.
No inspection history	Agency database shows no history of inspection for manufacturer. No CGMP records noted for inspection of product under review.	Applicant should ensure the correct manufacturer FEI/ Data Universal Numbering System (DUNS) number is listed for your product's CPP application. *Note: In the event that the FDA has been unable to visit the manufacturing site for an on-site inspection, we will not be able to approve that specific site as part of the CPP application until inspection protocols are completed. Contact the nearest FDA field office to request further information.*
Inspection report not finalized	Agency database shows facility has a history of inspection, but the most recent inspection is pending finalization.	Applicant should resubmit the application when the inspection report is finalized. The most recent inspection report for the inspection dated {MM/DD/YYYY} and associated with {MANUFACTURING/PACKAGING FACILITY NAME, ADDRESS} is not finalized.
Facility Registration not updated in the electronic Drug Registration and Listing System (eDRLS)	The product's drug listing shows an expired registration date for an identified manufacturing site. The product's drug listing shows the facility noted in the CPP has been omitted from the listing.	Applicant should update drug listing in the electronic Drug Registration and Listing System (eDRLS).

Review Reason Code	Case scenario	Resolution
Facility not approved for drug	Referenced facility not found in Agency approval documents for products approved under NDA, ANDA or BLA drug type.	Applicant should provide documentation to support the manufacture of products at this site.
Manufacturer specific number (DUNS) does not match facility	The manufacturer specific number (DUNS) stated in the CPP differs from that which is noted for the manufacturing site stated in the drug listing (eDRLS).	Applicant should provide the correct manufacturing site (i.e., address that corresponds to that site's DUNS number) which matches information in the product's approval documents.
Facility not registered in electronic Drug Registration and Listing System (eDRLS)	The referenced facility noted in the CPP application cannot be found in the electronic Drug Registration and Listing System (eDRLS). The facility noted in the CPP application lacks an FEI/DUNS number or an incorrect FEI/DUNS number has been provided.	Applicant should ensure the registration information for the stated manufacturing site is appropriately updated in the drug listing system.
Other	Discrepancy in manufacturer's address or responsibilities (i.e., a site is noted for shipping, warehousing and production planning as opposed to the Finished Dose Manufacturing process stated in application). Manufacturer FEI # provided by applicant pulls an address that does not correspond to that which is noted in FDA's database.	Applicant should ensure FEI # and stated location match documentation submitted as part of the Agency drug approval process. *Note: Only applies to Rx and OTC drugs that retain their NDA and ANDA approval numbers.*

PRODUCT

Review Reason Code	Case scenario	Resolution
Product License Holder (PLH) address does not match	Applicant provided an address (e.g., manufacturer site location) that does not correspond with the PLH name/address noted in Agency approval documents (Form 356h).	Applicant should ensure PLH name and address are validated with the information specified in the Agency's initial product approval submission or what is currently denoted in the most recently submitted FDA Form 356h.
National Drug Code (NDC) does not match drug	The drug listing link does not populate due to incorrect product NDC number. The NDC number displayed on the attached container or carton label document is not consistent with the NDC denoted in NDC section of CPP application.	Applicant should ensure the product's NDC number is correctly noted in the electronic Drug Registration and Listing System (eDRLS) before attaching the drug listing link to the CPP application.

Review Reason Code	Case scenario	Resolution
Not an Approval Letter	Applicant provides an attachment of an unrelated document (e.g., product formulation sheet instead of the Agency approval letter) in the product section of the CPP application.	Applicant should verify that the corresponding FDA product marketing approval letter is attached in this section.
Approval number does not match drug	The approval number for the NDA, BLA or ANDA do not correspond with the requested drug subject to the CPP application under review. Product has been switched from an NDA (per original approval) to ANDA or BLA marketing status, but applicant designates drug as NDA drug type.	Applicant should provide the appropriate number and Drug Type (NDA, ANDA, BLA) for the product to conform with the one currently denoted in the FDA form 356h approval documents.
Approval Letter does not match drug	The original FDA approval letter does not correspond to the drug subject to the CPP application under review. For NDA products switched to BLA: The application provided the product's initial or supplemental NDA approval letter.	Applicant should provide the initial application (Original-1) approval letter or the supplemental letter (Supplement-1) that shows approval of a subsequent product strength. Applicant should provide the associated 'Deemed BLA' letter. However, retain the original marketing approval date for the product in the CPP application.
U.S. License Number in Approval Letter does not match	Product incorrectly designated as an NDA and not a BLA thus omitting the entry of the applicant's US License number.	Applicant should verify that the correct designation has been selected for the product (i.e., BLA) and provide the requisite License number for the biologic drug product.
Other	Drug Type differs from approval documents (e.g., ANDA or BLA denoted as NDA). Approval date does not match. Applicant provided approval dates for subsequent application supplements or that of a completely different drug.	Applicant should provide appropriate drug type per current Agency documentation. E.g.: Applications for insulin and other NDAs were changed to BLA applications in 03/2020. Applicant should note that the requested approval date refers to the date of the original approval (Original-1) for that product (or supplemental approval date - only for introduction of a new product strength) being requested for export via the CPP application.

LABELING

Review Reason Code	Case scenario	Resolution
Listing not updated	Package Insert (PI) attached to CPP application is not the most recently updated document posted in the electronic Drug Registration and Listing System (eDRLS). The product's drug listing shows a "future, inactive or discontinued" product status in the overview tab. The manufacturer specified for the product under review is not associated with the product in its drug listing.	Applicant should provide the most recently approved labeling (package insert) as the revision date for the currently attached PI is outdated. Applicant should update the drug listing to reflect an "active" product status. Applicant should update the provided drug listing link with this specified manufacturer if appropriate.
NDC does not match drug	The NDC number noted in eDRLS differs from that shown on the attached carton and container label. The Drug listing link does not populate due to incorrect product NDC number The NDC number displayed on attached container or carton label documents is not consistent with that which is specified in the NDC section of the CPP application.	Applicant should update the product container and carton label pictorials with the requisite NDC number to match drug listing pictorials.
Drug not listed	Product under review cannot be found in eDRLS.	Applicant should ensure the drug has been listed and is active in eDRLS.
Illegible drug label	Hard to decipher script on the attached container or carton label documents.	Applicant should provide English language labeling attachments that are easy to read.
Label missing "CAUTION" statement	Refers specifically to Active Pharmaceutical Ingredient (API) labels that do not bear the statement: "Caution: For manufacturing, processing or repacking."	Applicant should provide a label that includes the appropriate cautionary statement for API products.
Label not in compliance	The requested CPP application for an Unapproved Drug Product utilizes labeling and the NDC number of an approved NDA for a proprietary drug.	Applicant should amend the application by providing the correct label and NDC number for the unapproved product and ensure the active ingredient name of the drug is used instead of an approved brand or proprietary name.
Not a Drug Label	The back panel of the product label denotes "Supplement Facts" or dissolution mediums (i.e., syrups) as opposed to "Drug Facts." Formulation page does not populate as currently attached in drug label section.	Applicant should contact CDERICFSAN for guidance on regulations regarding exportation of food supplements or dissolution mediums/ vehicles. Applicant should delete from current location (drug labels) and re-attach under "Supplemental Attachments."

Review Reason Code	Case scenario	Resolution
Other	Drug listing shows Product Status as Active: Future (i.e., the drug listing shows future active date (e.g., 2030) and yet there is a current request for issuance of an export certificate. Applicant provides a response to our Return for Action in the supplemental attachments section and incorrectly indicates that the document be printed as part of the CPP certificate.	Applicant should update the drug listing to reflect a current marketing start date of "NOW" (or at least within the current year). Applicant should not click "Yes" to print a supplemental attachment document that is in response to Agency comments.

OTHER REVIEW REASONS THAT RESULT IN RETURN FOR ACTION

REMARKS SECTION

Review Reason Code	Case scenario	Resolution
Statements that should not be noted for printing with the CPP application	For instance, "This packaging facility is CGMP compliant" appears to suggest a reference to CGMP Compliance letters that are issued separately upon request.	Applicant should note that this comment is not allowed for printing with the CPP in the Remarks section. ECB will provide a courtesy email to confirm that the information will be removed, and the statement box can be unchecked so as not to have it print on the certificate. However, if there are other discrepancies noted on the application, then a Return for Action will be issued.