5. DESI No. 6270 (36 FR 23330, December 8, 1971), ''Certain Preparations Containing Hexachlorophene''.

[40 FR 14033, Mar. 27, 1975, as amended at 42 FR 63773, Dec. 20, 1977; 55 FR 11577, Mar. 29, 1990; 67 FR 4906, Feb. 1, 2002; 69 FR 18763, Apr. 8, 2004]

PART 251—SECTION 804 IMPORTATION PROGRAM

Subpart A—General Provisions

Subpart B—Section 804 Importation Program Proposals and Pre-Import Requests

Subpart C—Certain Requirements for Section 804 Importation Programs

AUTHORITY: 21 U.S.C. 351, 352, 353, 355, 360, 360eee–1, 371, 374, 381, 384.

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Subpart A—General Provisions

§ 251.1 Scope of the part.

(a) This part sets forth the procedures that Section 804 Importation Program sponsors (SIP Sponsors) must follow when submitting plans to implement time-limited programs to begin importation of drugs from Canada under section 804 of the Federal Food, Drug, and Cosmetic Act. This part also sets forth certain requirements that are necessary for such programs to be authorized by the Food and Drug Administration (FDA). Additionally, this part sets forth requirements for eligible prescription drugs and requirements for entities that engage in importation of eligible prescription drugs.

(b) This part includes provisions that exempt eligible prescription drugs that meet certain requirements from section 502(f)(1) of the Federal Food, Drug, and Cosmetic Act. This part also includes provisions that exempt certain transactions involving eligible prescription drugs from certain requirements in section 582 of the Federal Food, Drug, and Cosmetic Act.

§ 251.2 Definitions.

The definitions of terms in section 804 of the Federal Food, Drug, and Cosmetic Act apply to the terms used in this part, if not otherwise defined in this section. The following definitions apply to this part:

Active ingredient has the meaning set forth in § 314.3 of this chapter.

Adverse event means any untoward medical occurrence associated with the use of a drug product in humans, whether or not it is considered related to the drug product. An adverse event can occur in the course of the use of a drug product; from overdose of a drug product, whether accidental or intentional; from abuse of a drug product; from discontinuation of the drug product (e.g., physiological withdrawal); and it includes any failure of expected pharmacological action.

Combination product has the meaning set forth in § 3.2(e) of this chapter.

Constituent part has the meaning set forth in § 4.2 of this chapter.

Disability means a substantial disruption of a person's ability to conduct normal life functions.

Eligible prescription drug:

(1) Means a drug subject to section 503(b) of the Federal Food, Drug, and Cosmetic Act that has been approved and has received a Notice of Compliance and a Drug Identification Number (DIN) from the Health Products and

Food Branch of Health Canada (HPFB) and, but for the fact that it deviates from the required U.S. labeling, also meets the conditions in an FDA-approved new drug application (NDA) or abbreviated new drug application (ANDA) for a drug that is currently commercially marketed in the United States, including those relating to the drug substance, drug product, production process, quality controls, equipment, and facilities.

(2) The term *eligible prescription drug* does not include:

(i) A controlled substance (as defined in section 102 of the Controlled Substances Act (21 U.S.C. 802));

(ii) A biological product (as defined in section 351(i)(1) of the Public Health Service Act (42 U.S.C. 262(i)(1)));

(iii) An infused drug (including a peritoneal dialysis solution);

(iv) An intravenously injected drug;

(v) A drug that is inhaled during surgery;

(vi) An intrathecally or intraocularly injected drug;

(vii) A drug that is subject to a risk evaluation and mitigation strategy under section 505–1 of the Federal Food, Drug, and Cosmetic Act; or

(viii) A drug that is not a ''product'' for purposes of section 582 as defined in section 581(13) of the Federal Food, Drug, and Cosmetic Act.

Entered (or entry) for consumption has the meaning set forth in 19 CFR 141.0a(f).

Entry means the information or data filed electronically in the Automated Commercial Environment (ACE) or any other U.S. Customs and Border Protection (CBP)-authorized electronic data interchange system to secure the release of imported merchandise from CBP, or the act of filing that information or data.

Foreign Seller means an establishment within Canada engaged in the distribution of an eligible prescription drug that is imported or offered for importation into the United States. A Foreign Seller must have an active Drug Establishment License to wholesale drugs by Health Canada. A Foreign Seller must be registered with provincial regulatory authorities to distribute HPFB-approved drugs. A Foreign Seller must not be licensed by a provincial regulatory authority with an international pharmacy license that allows it to distribute drugs that are approved by countries other than Canada and that are not HPFB-approved for distribution in Canada. A Foreign Seller must also be registered with FDA under section 804 of the Federal Food, Drug, and Cosmetic Act in accordance with the requirements described in this part.

Illegitimate foreign product means a drug purchased by a Foreign Seller from a manufacturer, and intended for sale to the Importer in the United States, where the Foreign Seller has credible evidence that shows that the product:

(1) Is counterfeit, diverted, or stolen;

(2) Is intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;

(3) Is the subject of a fraudulent transaction; or

(4) Appears otherwise unfit for distribution such that the product would be reasonably likely to result in serious adverse health consequences or death to humans.

Importer means a pharmacist or wholesaler. An Importer must be a State-licensed pharmacist, or a State- or FDA-licensed wholesale distributor, who is the U.S. owner of an eligible prescription drug at the time of entry into the United States. The Importer's pharmacist license or wholesale distributor license (if issued by a State and not FDA) must be issued by a State that is a SIP Sponsor or SIP Co-Sponsor. An Importer's pharmacist or wholesale distributor license must be in effect (*i.e.*, not expired) and the Importer's license must be in good standing with the licensor.

Individual case safety report (ICSR) means a description of an adverse event related to an individual patient or subject.

ICSR attachments means any document related to the adverse event described in an ICSR, such as medical records, hospital discharge summaries, or other documentation.

Life-threatening adverse event means any adverse event that places the patient, in the view of the initial reporter, at immediate risk of death from the adverse event as it occurred,

i.e., it does not include an adverse event that, had it occurred in a more severe form, might have caused death.

Manufacturer means an applicant, as defined in § 314.3 of this chapter, or a person who owns or operates an establishment that manufactures an eligible prescription drug. Manufacturer also means a holder of a drug master file containing information necessary to conduct the Statutory Testing, prepare the manufacturer's attestation and information statement, or otherwise comply with section 804 of the Federal Food, Drug, and Cosmetic Act or this part.

Minimum data set for an adverse event means the minimum four elements required for reporting an ICSR of an adverse event: An identifiable patient, an identifiable reporter, a suspect drug product, and an adverse event.

Pharmacist means a person licensed by a State to practice pharmacy, including the dispensing and selling of prescription drugs.

Pre-Import Request means a request made to FDA by an Importer that must be granted by FDA before the Importer can start importation under a Section 804 Importation Program.

Qualifying laboratory means a laboratory in the United States that has been approved by FDA for the purposes of section 804 of the Federal Food, Drug, and Cosmetic Act.

Relabel has the meaning set forth in § 207.1 of this chapter.

Relabeler has the meaning set forth in § 207.1 of this chapter.

Repack or repackage has the meaning set forth in § 207.1 of this chapter.

Responsible individual(s) means an individual or individuals who are designated in the Section 804 Importation Program compliance plan. Such individuals are responsible for ensuring compliance with the requirements of the Section 804 Importation Program under their oversight and with the applicable provisions of the Federal Food, Drug, and Cosmetic Act and this part.

Section 804 Importation Program (''SIP'') means a program under section 804 of the Federal Food, Drug, and Cosmetic Act, and this part, that has been authorized by FDA for the importation of eligible prescription drugs from Canada.

Section 804 Importation Program Sponsor (''SIP Sponsor'') means a State or Indian Tribe that regulates wholesale drug distribution and the practice of pharmacy that submits a proposal to FDA that describes a program to facilitate the importation of prescription drugs from Canada under section 804 of the Federal Food, Drug, and Cosmetic Act and is responsible for oversight of the implementation of the program. After an initial 2-year period beginning on the date of the first import entry under any SIP authorized under this part, the Secretary may determine, based on experience under the program, that there is a sufficient likelihood that a proposal that does not include a State or Indian Tribe as the SIP sponsor could provide the same level of assurance of safety as a proposal that does include such a sponsor, such that FDA may begin receiving, reviewing, and potentially authorizing applications for SIPs without such a sponsor. After the Secretary makes such a determination, a pharmacist or wholesaler may propose a SIP that does not include a State or Indian Tribe as a sponsor, and FDA may authorize such a SIP if the sponsor demonstrates that the SIP meets the criteria for authorization with the same level of assurance of safety as a proposal that includes a State or Indian Tribe as the SIP sponsor, which FDA shall evaluate consistent with any considerations described in the Secretary's determination, including by evaluating whether the application demonstrates that the proposed sponsor has sufficient relevant experience, such as participating in a SIP and demonstrating compliance with the requirements of the Federal Food, Drug, and Cosmetic Act and this part.

Section 804 Importation Program Co-Sponsor (''SIP Co-Sponsor'') means any other State or Indian Tribe, or a pharmacist or a wholesale distributor that, with the SIP Sponsor, signs a proposal to FDA that describes a program to facilitate the importation of prescription drugs from Canada under section 804 of the Federal Food, Drug, and Cosmetic Act.

Section 804 Serial Identifier (''SSI'') means a unique alphanumeric serial number of up to 20 characters that is

assigned and placed on or affixed by the Foreign Seller to each package and homogenous case of the product that the Foreign Seller intends to sell to an Importer. For purposes of the SSI, ''package'' means the smallest individual saleable unit of product for distribution that is intended by the Foreign Seller for sale to an Importer located in the United States, and ''individual saleable unit'' means the smallest container of product sold by the Foreign Seller to the Importer.

Serious adverse event means:

(1) An adverse event is considered ''serious'' if it results in any of the following outcomes:

(i) Death;

(ii) A life-threatening adverse event;

(iii) Inpatient hospitalization or prolongation of existing hospitalization;

(iv) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; and/or

(v) A congenital anomaly/birth defect.

(2) Other events that may be considered serious adverse events: Important medical events that may not result in one of the listed outcomes in this definition may be considered serious adverse events when, based upon appropriate medical judgment, they may jeopardize the patient or study subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples include: Allergic bronchospasm requiring intensive treatment in an emergency department or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of product dependency or product abuse.

Statutory Testing means the testing of an eligible prescription drug as required by section 804(d)(1)(J) and (L) and section 804(e) of the Federal Food, Drug, and Cosmetic Act, including for authenticity, for degradation, and to ensure that the prescription drug is in compliance with established specifications and standards.

Suspect foreign product means a drug purchased by a Foreign Seller from a manufacturer, and intended for sale to an Importer in the United States, for which the Foreign Seller has reason to believe that such product:

(1) Is potentially counterfeit, diverted, or stolen;

(2) Is potentially intentionally adulterated such that the product would result in serious adverse health consequences or death to humans;

(3) Is potentially the subject of a fraudulent transaction; or

(4) Appears otherwise unfit for distribution such that the product would result in serious adverse health consequences or death to humans.

Transaction means the transfer of product between persons in which a change of ownership occurs, in accordance with section 581(24) of the Federal Food, Drug, and Cosmetic Act. For the purposes of this part, ''transaction'' includes the sale and transfer of product between the manufacturer and Foreign Seller. The sale and transfer of product between Foreign Seller and Importer also constitutes a ''transaction.''

Unexpected adverse event means an adverse event that is not included in the current U.S. labeling for the drug product. Events that may be symptomatically or pathophysiologically related to an adverse event included in the labeling but differ from the labeled event because of greater severity or specificity would be considered unexpected. ''Unexpected,'' as used in this definition, also refers to adverse events that are mentioned in the product labeling as occurring with a class of products or anticipated from the pharmacological properties of the product but are not specifically mentioned as occurring with the particular product.

(1) *Example of greater severity*. Under this definition, hepatic necrosis would be unexpected if the labeling referred only to elevated hepatic enzymes or hepatitis.

(2) *Example of greater specificity*. Cerebral thromboembolism and cerebral hemorrhage would be unexpected if the labeling included only cerebrovascular accidents.

Unique facility identifier means the identifier required to be submitted by the registrant for drug establishment registration under section 510 of the Federal Food, Drug, and Cosmetic Act in accordance with § 207.25 of this chapter. For Foreign Sellers registering

under section 804 of the Federal Food, Drug, and Cosmetic Act, the term ''unique facility identifier'' means the identifier required to be submitted under § 251.9 in accordance with the system specified under section 510 of the Federal Food, Drug, and Cosmetic Act.

Wholesaler means a person licensed as a wholesale distributor, as the terms ''licensed'' and ''wholesale distributor'' are defined in section 581(9)(A) and 581(29), respectively. The term ''wholesaler'' does not include a person authorized to import drugs under section 801(d)(1).

Subpart B—Section 804 Importation Program Proposals and Pre-Import Requests

§ 251.3 SIP proposal submission requirements.

(a) A SIP Sponsor may delegate implementation activities to a SIP co-sponsor but the SIP Sponsor remains responsible for oversight of the implementation of the program.

(b) A SIP Sponsor must only designate one Foreign Seller and one Importer per initial proposal. Additional Foreign Sellers and Importers may be added to an authorized SIP through a supplemental proposal under § 251.8.

(c) A SIP Sponsor that intends to implement a SIP under this part must submit a proposal to FDA in electronic format via FDA's Electronic Submissions Gateway (ESG) or to an alternative transmission point identified by FDA. The proposal must include:

(1) A cover sheet containing the following:

(i) Name or names of SIP Sponsor and co-sponsors, if any;

(ii) Name and contact information for a person authorized to serve as the point of contact with FDA during its review of the proposal; and

(iii) The signature of the SIP Sponsor and co-sponsors, if any, or authorized representative who is an employee or agent of the Sponsor or co-sponsor and has been authorized to sign the proposal for the Sponsor or co-sponsor. The signatory must reside or have a place of business within the United States, and the proposal cover sheet must contain the name, title, and business address of the signatory.

(2) A table of contents;

(3) An introductory statement that includes an overview of the SIP Sponsor's SIP Proposal; and

(4) The SIP Sponsor's importation plan.

(d) The overview of the SIP Proposal must include:

(1) The name of the SIP, if any, and the name or names and address or addresses of the SIP Sponsor and co-sponsors, if any;

(2) The name, email address, and telephone number of the responsible individual(s);

(3) The name and DIN of each eligible prescription drug that the SIP Sponsor seeks to include in the SIP;

(4) The name and address of the applicant that holds the approved NDA or ANDA for each eligible prescription drug's FDA-approved counterpart, and the approved NDA or ANDA number;

(5) The name and address of the manufacturer of the finished dosage form of the eligible prescription drug, if known or reasonably known;

(6) The name and address of the manufacturer of the active ingredient or ingredients of the eligible prescription drugs, if known or reasonably known;

(7) The name and address of the Foreign Seller;

(8) A copy of the Foreign Seller's Health Canada Drug Establishment License;

(9) The name and address of the Importer;

(10) The name and address of the FDA-registered repackager or relabeler, if different from the Importer, that will relabel the eligible prescription drugs (including any limited repackaging in accordance with the requirements in this part), along with adequate evidence of registration and of satisfactory resolution of any objectionable conditions or practices identified during its most recent FDA inspection, if applicable; and

(11) A summary of how the SIP Sponsor will ensure that:

(i) The imported eligible prescription drugs meet the Statutory Testing requirements;

(ii) The supply chain is secure;