(b) [Reserved]

[39 FR 11680, Mar. 29, 1974, as amended at 42 FR 36994, July 19, 1977; 52 FR 15892, Apr. 30, 1987; 52 FR 30055, Aug. 12, 1987; 55 FR 31779, Aug. 3, 1990; 57 FR 58374, Dec. 9, 1992; 58 FR 49898, Sept. 23, 1993; 59 FR 4218, Jan. 28, 1994; 60 FR 52507, Oct. 6, 1995; 72 FR 15043, Mar. 30, 2007; 72 FR 67640, Nov. 30, 2007]

Subpart D—Records and Reports

§ 310.305 Records and reports concerning adverse drug experiences on marketed prescription drugs for human use without approved new drug applications.

(a) *Scope.* FDA is requiring manufacturers, packers, and distributors of marketed prescription drug products that are not the subject of an approved new drug or abbreviated new drug application to establish and maintain records and make reports to FDA of all serious, unexpected adverse drug experiences associated with the use of their drug products. Any person subject to the reporting requirements of paragraph (c) of this section must also develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences to FDA.

(b) *Definitions.* The following definitions of terms apply to this section:

Adverse drug experience. Any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: An adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action.

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

Individual case safety report (ICSR). A description of an adverse drug experience related to an individual patient or subject.

ICSR attachments. Documents related to the adverse drug experience described in an ICSR, such as medical records, hospital discharge summaries, or other documentation.

Life-threatening adverse drug experience. Any adverse drug experience that places the patient, in the view of the initial reporter, at *immediate* risk of death from the adverse drug experience as it occurred, *i.e.*, it does not include an adverse drug experience that, had it occurred in a more severe form, might have caused death.

Serious adverse drug experience. Any adverse drug experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Unexpected adverse drug experience. Any adverse drug experience that is not listed in the current labeling for the drug product. This includes events that may be symptomatically and pathophysiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the labeling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the labeling only listed cerebral vascular accidents. ''Unexpected,'' as used in this definition, refers to an adverse drug experience that has not been previously observed (*i.e.*, included in the labeling) rather than from the perspective of such experience

not being anticipated from the pharmacological properties of the pharmaceutical product.

(c) *Reporting requirements.* Each person identified in paragraph (c)(1)(i) of this section must submit to FDA adverse drug experience information as described in this section. Except as provided in paragraph (e)(2) of this section, 15-day ''Alert reports'' and followup reports, including ICSRs and any ICSR attachments, must be submitted to the Agency in electronic format as described in paragraph (e)(1) of this section.

(1) *Postmarketing 15-day ''Alert reports''.* (i) Any person whose name appears on the label of a marketed prescription drug product as its manufacturer, packer, or distributor must report to FDA each adverse drug experience received or otherwise obtained that is both serious and unexpected as soon as possible, but no later than 15 calendar days from initial receipt of the information by the person whose name appears on the label. Each report must be accompanied by the current content of labeling in electronic format as an ICSR attachment unless it is already on file at FDA.

(ii) A person identified in paragraph (c)(1)(i) of this section is not required to submit a 15-day ''Alert report'' for an adverse drug experience obtained from a postmarketing study (whether or not conducted under an investigational new drug application) unless the applicant concludes that there is a reasonable possibility that the drug caused the adverse experience.

(2) *Postmarketing 15-day ''Alert reports''—followup.* Each person identified in paragraph (c)(1)(i) of this section must promptly investigate all serious, unexpected adverse drug experiences that are the subject of these postmarketing 15-day Alert reports and must submit followup reports within 15 calendar days of receipt of new information or as requested by FDA. If additional information is not obtainable, records should be maintained of the unsuccessful steps taken to seek additional information.

(3) *Submission of reports.* To avoid unnecessary duplication in the submission of, and followup to, reports required in this section, a packer's or distributor's obligations may be met by submission of all reports of serious adverse drug experiences to the manufacturer of the drug product. If a packer or distributor elects to submit these adverse drug experience reports to the manufacturer rather than to FDA, it must submit, by any appropriate means, each report to the manufacturer within 5 calendar days of its receipt by the packer or distributor, and the manufacturer must then comply with the requirements of this section even if its name does not appear on the label of the drug product. Under this circumstance, the packer or distributor must maintain a record of this action which must include:

(i) A copy of each adverse drug experience report;

(ii) The date the report was received by the packer or distributor;

(iii) The date the report was submitted to the manufacturer; and

(iv) The name and address of the manufacturer.

(4) [Reserved]

(5) A person identified in paragraph (c)(1)(i) of this section is not required to resubmit to FDA adverse drug experience reports forwarded to that person by FDA; however, the person must submit all *followup* information on such reports to FDA.

(d) *Information reported on ICSRs.* ICSRs include the following information:

(1) *Patient information.*

(i) Patient identification code;

(ii) Patient age at the time of adverse drug experience, or date of birth;

(iii) Patient gender; and

(iv) Patient weight.

(2) *Adverse drug experience.*

(i) Outcome attributed to adverse drug experience;

(ii) Date of adverse drug experience;

(iii) Date of ICSR submission;

(iv) Description of adverse drug experience (including a concise medical narrative);

(v) Adverse drug experience term(s);

(vi) Description of relevant tests, including dates and laboratory data; and

(vii) Other relevant patient history, including preexisting medical conditions.

(3) *Suspect medical product(s).*

(i) Name;

(ii) Dose, frequency, and route of administration used;

(iii) Therapy dates;

(iv) Diagnosis for use (indication);

(v) Whether the product is a combination product as defined in § 3.2(e) of this chapter;

(vi) Whether the product is a prescription or nonprescription product;

(vii) Whether adverse drug experience abated after drug use stopped or dose reduced;

(viii) Whether adverse drug experience reappeared after reintroduction of drug;

(ix) Lot number;

(x) Expiration date;

(xi) National Drug Code (NDC) number; and

(xii) Concomitant medical products and therapy dates.

(4) *Initial reporter information.*

(i) Name, address, and telephone number;

(ii) Whether the initial reporter is a health care professional; and

(iii) Occupation, if a health care professional.

(5) *Manufacturer, packer, or distributor information.*

(i) Manufacturer, packer, or distributor name and contact office address;

(ii) Telephone number;

(iii) Report source, such as spontaneous, literature, or study;

(iv) Date the report was received by manufacturer, packer, or distributor;

(v) Whether the ICSR is a 15-day ''Alert report'';

(vi) Whether the ICSR is an initial report or followup report; and

(vii) Unique case identification number, which must be the same in the initial report and any subsequent followup report(s).

(e) *Electronic format for submissions.* (1) Each report required to be submitted to FDA under this section, including the ICSR and any ICSR attachments, must be submitted in an electronic format that FDA can process, review, and archive. FDA will issue guidance on how to provide the electronic submission (e.g., method of transmission, media, file formats, preparation and organization of files).

(2) Each person identified in paragraph (c)(1)(i) of this section may request, in writing, a temporary waiver of the requirements in paragraph (e)(1) of this section. These waivers will be granted on a limited basis for good cause shown. FDA will issue guidance on requesting a waiver of the requirements in paragraph (e)(1) of this section.

(f) *Patient privacy.* Manufacturers, packers, and distributors should not include in reports under this section the names and addresses of individual patients; instead, the manufacturer, packer, and distributor should assign a unique code for identification of the patient. The manufacturer, packer, and distributor should include the name of the reporter from whom the information was received as part of the initial reporter information, even when the reporter is the patient. The names of patients, individual reporters, health care professionals, hospitals, and geographical identifiers in adverse drug experience reports are not releasable to the public under FDA's public information regulations in part 20 of this chapter.

(g) *Recordkeeping.* (1) Each manufacturer, packer, and distributor must maintain for a period of 10 years records of all adverse drug experiences required under this section to be reported, including raw data and any correspondence relating to the adverse drug experiences, and the records required to be maintained under paragraph (c)(3) of this section.

(2) Manufacturers and packers may retain the records required in paragraph (f)(1) of this section as part of its complaint files maintained under § 211.198 of this chapter.

(3) Manufacturers, packers, and distributors must permit any authorized FDA employee, at all reasonable times, to have access to and copy and verify the records established and maintained under this section.

(h) *Disclaimer.* A report or information submitted by a manufacturer, packer, or distributor under this section (and any release by FDA of that report or information) does not necessarily reflect a conclusion by the manufacturer, packer, or distributor, or by FDA, that the report or information constitutes an admission that the

drug caused or contributed to an adverse effect. The manufacturer, packer, or distributor need not admit, and may deny, that the report or information submitted under this section constitutes an admission that the drug caused or contributed to an adverse effect.

[51 FR 24479, July 3, 1986, as amended at 52 FR 37936, Oct. 13, 1987; 55 FR 11578, Mar. 29, 1990; 57 FR 17980, Apr. 28, 1992; 62 FR 34167, June 25, 1997; 62 FR 52249, Oct. 7, 1997; 67 FR 9585, Mar. 4, 2002; 74 FR 13113, Mar. 26, 2009; 79 FR 33087, June 10, 2014]

§ 310.306 Notification of a permanent discontinuance or an interruption in manufacturing of marketed prescription drugs for human use without approved new drug applications.

(a) *Applicability.* Marketed prescription drug products that are not the subject of an approved new drug or abbreviated new drug application are subject to this section.

(b) *Notification of a permanent discontinuance or an interruption in manufacturing.* The manufacturer of each product subject to this section must make the notifications required under § 314.81(b)(3)(iii) of this chapter and otherwise comply with § 314.81(b)(3)(iii) of this chapter. If the manufacturer of a product subject to this section fails to provide notification as required under § 314.81(b)(3)(iii), FDA will send a letter to the manufacturer and otherwise follow the procedures set forth under § 314.81(b)(3)(iii)(*e*).

(c) *Drug shortages list.* FDA will include on the drug shortages list required by § 314.81(b)(3)(iii)(*d*) drug products that are subject to this section that it determines to be in shortage. For such drug products, FDA will provide the names of each manufacturer rather than the names of each applicant. With respect to information collected under this paragraph, FDA will observe the confidentiality and disclosure provisions set forth in § 314.81(b)(3)(iii)(*d*)(*2*).

[80 FR 38938, July 8, 2015]

Subpart E—Requirements for Specific New Drugs or Devices

§ 310.501 Patient package inserts for oral contraceptives.

(a) *Requirement for a patient package insert.* The safe and effective use of oral contraceptive drug products requires that patients be fully informed of the benefits and the risks involved in their use. An oral contraceptive drug product that does not comply with the requirements of this section is misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act. Each dispenser of an oral contraceptive drug product shall provide a patient package insert to each patient (or to an agent of the patient) to whom the product is dispensed, except that the dispenser may provide the insert to the parent or legal guardian of a legally incompetent patient (or to the agent of either). The patient package insert is required to be placed in or accompany each package dispensed to the patient.

(b) *Distribution requirements.* (1) For oral contraceptive drug products, the manufacturer and distributor shall provide a patient package insert in or with each package of the drug product that the manufacturer or distributor intends to be dispensed to a patient.

(2) Patient package inserts for oral contraceptives dispensed in acute-care hospitals or long-term care facilities will be considered to have been provided in accordance with this section if provided to the patient before administration of the first oral contraceptive and every 30 days thereafter, as long as the therapy continues.

(c) *Contents of patient package insert.* A patient package insert for an oral contraceptive drug product is required to contain the following:

(1) The name of the drug.

(2) A summary including a statement concerning the effectiveness of oral contraceptives in preventing pregnancy, the contraindications to the drug's use, and a statement of the risks and benefits associated with the drug's use.

(3) A statement comparing the effectiveness of oral contraceptives to other methods of contraception.