

### Subpart J—Distribution

#### §212.90 What actions must I take to control the distribution of PET drug products?

(a) *Written distribution procedures.* You must establish, maintain, and follow written procedures for the control of distribution of PET drug products shipped from the PET drug production facility to ensure that the method of shipping chosen will not adversely affect the identity, purity, or quality of the PET drug product.

(b) *Distribution records.* You must maintain distribution records for each PET drug product that include or refer to the following:

- (1) The name, address, and telephone number of the receiving facility that received each batch of a PET drug product;
- (2) The name and quantity of the PET drug product shipped;
- (3) The lot number, control number, or batch number for the PET drug product shipped; and
- (4) The date and time you shipped the PET drug product.

### Subpart K—Complaint Handling

#### §212.100 What do I do if I receive a complaint about a PET drug product produced at my facility?

(a) *Written complaint procedures.* You must develop and follow written procedures for the receipt and handling of all complaints concerning the quality or purity of, or possible adverse reactions to, a PET drug product.

(b) *Complaint review.* The procedures must include review by a designated person of any complaint involving the possible failure of a PET drug product to meet any of its specifications and an investigation to determine the cause of the failure.

(c) *Complaint records.* A written record of each complaint must be maintained in a file designated for PET drug product complaints. The record must include the name and strength of the PET drug product, the batch number, the name of the complainant, the date the complaint was received, the nature of the complaint, and the response to the complaint. It must also

include the findings of any investigation and followup.

(d) *Returned products.* A PET drug product that is returned because of a complaint or for any other reason may not be reprocessed and must be destroyed in accordance with applicable Federal and State law.

### Subpart L—Records

#### §212.110 How must I maintain records of my production of PET drugs?

(a) *Record availability.* Records must be maintained at the PET drug production facility or another location that is reasonably accessible to responsible officials of the production facility and to employees of FDA designated to perform inspections.

(b) *Record quality.* All records, including those not stored at the inspected establishment, must be legible, stored to prevent deterioration or loss, and readily available for review and copying by FDA employees.

(c) *Record retention period.* You must maintain all records and documentation referenced in this part for a period of at least 1 year from the date of final release, including conditional final release, of a PET drug product.

## PART 216—HUMAN DRUG COMPOUNDING

### Subpart A—General Provisions [Reserved]

#### Subpart B—Compounded Drug Products

Sec.

216.23 Bulk drug substances that can be used to compound drug products in accordance with section 503A of the Federal Food, Drug, and Cosmetic Act.

216.24 Drug products withdrawn or removed from the market for reasons of safety or effectiveness.

AUTHORITY: 21 U.S.C. 351, 352, 353a, 353b, 355, and 371.

SOURCE: 64 FR 10944, Mar. 8, 1999, unless otherwise noted.

### Subpart A—General Provisions [Reserved]

### Subpart B—Compounded Drug Products

#### § 216.23 Bulk drug substances that can be used to compound drug products in accordance with section 503A of the Federal Food, Drug, and Cosmetic Act.

(a) The following bulk drug substances can be used in compounding under section 503A(b)(1)(A)(i)(III) of the Federal Food, Drug, and Cosmetic Act.

- (1) Brilliant Blue G, also known as Coomassie Brilliant Blue G-250.
- (2) Cantharidin (for topical use only).
- (3) Diphenylcyclopropanone (for topical use only).
- (4) N-acetyl-D-glucosamine (for topical use only).
- (5) Squaric acid dibutyl ester (for topical use only).
- (6) Thymol iodide (for topical use only).

(b) After balancing the criteria set forth in paragraph (c) of this section, FDA has determined that the following bulk drug substances will not be included on the list of substances that can be used in compounding set forth in paragraph (a) of this section:

- (1) Oxitriptan.
- (2) Piracetam.
- (3) Silver Protein Mild.
- (4) Tranilast.

(c) FDA will use the following criteria in evaluating substances considered for inclusion on the list set forth in paragraph (a) of this section:

- (1) The physical and chemical characterization of the substance;
  - (2) Any safety issues raised by the use of the substance in compounded drug products;
  - (3) The available evidence of the effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists; and
  - (4) Historical use of the substance in compounded drug products, including information about the medical condition(s) the substance has been used to treat and any references in peer-reviewed medical literature.
- (d) Based on evidence currently available, there are inadequate data to demonstrate the safety or efficacy of any drug product compounded using any of the drug substances listed in paragraph (a) of this section, or to es-

tablish general recognition of the safety or effectiveness of any such drug product. Any person who represents that a compounded drug made with a bulk drug substance that appears on this list is FDA approved, or otherwise endorsed by FDA generally or for a particular indication, will cause the drug to be misbranded under section 502(a) and/or 502(bb) of the Federal Food, Drug, and Cosmetic Act.

[84 FR 4710, Feb. 19, 2019]

#### § 216.24 Drug products withdrawn or removed from the market for reasons of safety or effectiveness.

The following drug products were withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective. The following drug products may not be compounded under the exemptions provided by section 503A(a) or section 503B(a) of the Federal Food, Drug, and Cosmetic Act:

- Adenosine phosphate*: All drug products containing adenosine phosphate.
- Adrenal cortex*: All drug products containing adrenal cortex.
- Alatrofloxacin mesylate*: All drug products containing alatrofloxacin mesylate.
- Aminopyrine*: All drug products containing aminopyrine.
- Astemizole*: All drug products containing astemizole.
- Azaribine*: All drug products containing azaribine.
- Benoxaprofen*: All drug products containing benoxaprofen.
- Bithionol*: All drug products containing bithionol.
- Bromfenac sodium*: All drug products containing bromfenac sodium (except ophthalmic solutions).
- Bromocriptine mesylate*: All drug products containing bromocriptine mesylate for prevention of physiological lactation.
- Butamben*: All parenteral drug products containing butamben.
- Camphorated oil*: All drug products containing camphorated oil.
- Carbetapentane citrate*: All oral gel drug products containing carbetapentane citrate.
- Casein, iodinated*: All drug products containing iodinated casein.
- Cerivastatin sodium*: All drug products containing cerivastatin sodium.
- Chloramphenicol*: All oral drug products containing chloramphenicol.
- Chlorhexidine gluconate*: All tinctures of chlorhexidine gluconate formulated for use as a patient preoperative skin preparation.

## Food and Drug Administration, HHS

§ 216.24

- Chlormadinone acetate*: All drug products containing chlormadinone acetate.
- Chloroform*: All drug products containing chloroform.
- Cisapride*: All drug products containing cisapride.
- Cobalt*: All drug products containing cobalt salts (except radioactive forms of cobalt and its salts and cobalamin and its derivatives).
- Dexfenfluramine hydrochloride*: All drug products containing dexfenfluramine hydrochloride.
- Diamthazole dihydrochloride*: All drug products containing diamthazole dihydrochloride.
- Dibromsalan*: All drug products containing dibromsalan.
- Diethylstilbestrol*: All oral and parenteral drug products containing 25 milligrams or more of diethylstilbestrol per unit dose.
- Dihydrostreptomycin sulfate*: All drug products containing dihydrostreptomycin sulfate.
- Dipyrone*: All drug products containing dipyrone.
- Encainide hydrochloride*: All drug products containing encainide hydrochloride.
- Esmolol hydrochloride*: All parenteral dosage form drug products containing esmolol hydrochloride that supply 250 milligrams/milliliter of concentrated esmolol per 10-milliliter ampule.
- Etretinate*: All drug products containing etretinate.
- Fenfluramine hydrochloride*: All drug products containing fenfluramine hydrochloride.
- Flosequinan*: All drug products containing flosequinan.
- Gatifloxacin*: All drug products containing gatifloxacin (except ophthalmic solutions).
- Gelatin*: All intravenous drug products containing gelatin.
- Glycerol, iodinated*: All drug products containing iodinated glycerol.
- Gonadotropin, chorionic*: All drug products containing chorionic gonadotropins of animal origin.
- Grepafloxacin*: All drug products containing grepafloxacin.
- Mepazine*: All drug products containing mepazine hydrochloride or mepazine acetate.
- Metabromsalan*: All drug products containing metabromsalan.
- Methamphetamine hydrochloride*: All parenteral drug products containing methamphetamine hydrochloride.
- Methapyrilene*: All drug products containing methapyrilene.
- Methopholine*: All drug products containing methopholine.
- Methoxyflurane*: All drug products containing methoxyflurane.
- Mibefradil dihydrochloride*: All drug products containing mibefradil dihydrochloride.
- Nitrofurazone*: All drug products containing nitrofurazone (except topical drug products formulated for dermatologic application).
- Nomifensine maleate*: All drug products containing nomifensine maleate.
- Novobiocin sodium*: All drug products containing novobiocin sodium.
- Ondansetron hydrochloride*: All intravenous drug products containing greater than a 16 milligram single dose of ondansetron hydrochloride.
- Oxyphenisatin*: All drug products containing oxyphenisatin.
- Oxyphenisatin acetate*: All drug products containing oxyphenisatin acetate.
- Pemoline*: All drug products containing pemoline.
- Pergolide mesylate*: All drug products containing pergolide mesylate.
- Phenacetin*: All drug products containing phenacetin.
- Phenformin hydrochloride*: All drug products containing phenformin hydrochloride.
- Phenylpropanolamine*: All drug products containing phenylpropanolamine.
- Pipamazine*: All drug products containing pipamazine.
- Polyethylene glycol 3350, sodium chloride, sodium bicarbonate, potassium chloride, and bisacodyl*: All drug products containing polyethylene glycol 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and 10 milligrams or more of bisacodyl delayed-release tablets.
- Potassium arsenite*: All drug products containing potassium arsenite.
- Potassium chloride*: All solid oral dosage form drug products containing potassium chloride that supply 100 milligrams or more of potassium per dosage unit (except for controlled-release dosage forms and those products formulated for preparation of solution prior to ingestion).
- Povidone*: All intravenous drug products containing povidone.
- Propoxyphene*: All drug products containing propoxyphene.
- Rapacuronium bromide*: All drug products containing rapacuronium bromide.
- Reserpine*: All oral dosage form drug products containing more than 1 milligram of reserpine.
- Rofecoxib*: All drug products containing rofecoxib.
- Sibutramine hydrochloride*: All drug products containing sibutramine hydrochloride.
- Sparteine sulfate*: All drug products containing sparteine sulfate.
- Sulfadimethoxine*: All drug products containing sulfadimethoxine.
- Sulfathiazole*: All drug products containing sulfathiazole (except for those formulated for vaginal use).
- Suprofen*: All drug products containing suprofen (except ophthalmic solutions).
- Sweet spirits of nitre*: All drug products containing sweet spirits of nitre.

## Pt. 225

*Tegaserod maleate*: All drug products containing tegaserod maleate.  
*Temafloxacin hydrochloride*: All drug products containing temafloxacin hydrochloride.  
*Terfenadine*: All drug products containing terfenadine.  
*3,3',4',5-tetrachlorosalicylanilide*: All drug products containing 3,3',4',5-tetrachlorosalicylanilide.  
*Tetracycline*: All liquid oral drug products formulated for pediatric use containing tetracycline in a concentration greater than 25 milligrams/milliliter.  
*Ticrynafen*: All drug products containing ticrynafen.  
*Tribromsalan*: All drug products containing tribromsalan.  
*Trichloroethane*: All aerosol drug products intended for inhalation containing trichloroethane.  
*Troglitazone*: All drug products containing troglitazone.  
*Trovafloxacin mesylate*: All drug products containing trovafloxacin mesylate.  
*Urethane*: All drug products containing urethane.  
*Valdecoxib*: All drug products containing valdecoxib.  
*Vinyl chloride*: All aerosol drug products containing vinyl chloride.  
*Zirconium*: All aerosol drug products containing zirconium.  
*Zomepirac sodium*: All drug products containing zomepirac sodium.

[81 FR 69676, Oct. 7, 2016, as amended at 83 FR 63573, Dec. 11, 2018]

## PART 225—CURRENT GOOD MANUFACTURING PRACTICE FOR MEDICATED FEEDS

### Subpart A—General Provisions

Sec.  
225.1 Current good manufacturing practice.  
225.10 Personnel.

### Subpart B—Construction and Maintenance of Facilities and Equipment

225.20 Buildings.  
225.30 Equipment.  
225.35 Use of work areas, equipment, and storage areas for other manufacturing and storage purpose.

### Subpart C—Product Quality Control

225.42 Components.  
225.58 Laboratory controls.  
225.65 Equipment cleanout procedures.

### Subpart D—Packaging and Labeling

225.80 Labeling.

## 21 CFR Ch. I (4–1–24 Edition)

### Subpart E—Records and Reports

225.102 Master record file and production records.  
225.110 Distribution records.  
225.115 Complaint files.

### Subpart F—Facilities and Equipment

225.120 Buildings and grounds.  
225.130 Equipment.  
225.135 Work and storage areas.

### Subpart G—Product Quality Assurance

225.142 Components.  
225.158 Laboratory assays.  
225.165 Equipment cleanout procedures.

### Subpart H—Labeling

225.180 Labeling.

### Subpart I—Records

225.202 Formula, production, and distribution records.

AUTHORITY: 21 U.S.C. 351, 352, 360b, 371, 374.

SOURCE: 41 FR 52618, Nov. 30, 1976, unless otherwise noted.

## Subpart A—General Provisions

### § 225.1 Current good manufacturing practice.

(a) Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act provides that a drug (including a drug contained in a medicated feed) shall be deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirement of the act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.

(b)(1) The provisions of this part set forth the criteria for determining whether the manufacture of a medicated feed is in compliance with current good manufacturing practice. These regulations shall apply to all types of facilities and equipment used in the production of medicated feeds, and they shall also govern those instances in which failure to adhere to the regulations has caused nonmedicated feeds that are manufactured,