

and investigated in accordance with §213.192.

(b) A written record of each complaint regarding a medical gas must be maintained. The record must include the name of the gas, the lot or 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. Where an investigation is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.

(c) Complaint files shall be maintained in a manner such that they are readily available for inspection by the firm or by FDA during an inspection. Complaint files shall be maintained for at least 1 year after the date the complaint was received or for at least 3 years after distribution of the medical gas, whichever is longer.

Subpart K—Returned and Salvaged Medical Gases

§213.204 Returned medical gases.

Returned medical gases shall be identified as such and held. If the conditions under which such returned gases have been held, stored, or shipped before or during their return, or if the condition of the gas, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality, or purity of the gas, the returned gas shall be destroyed unless examination, testing, or other investigations prove the gas meets appropriate standards of safety, identity, strength, quality, or purity. Records of returned medical gases shall be maintained and shall include the name, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned gas. If the reason for a medical gas being returned implicates associated batches, an appropriate investigation shall be conducted in accordance with the requirements of §213.192. Procedures for the holding, testing, and use of returned medical gases shall be in writing and shall be

followed. This section is not applicable to the routine refilling of cryogenic medical gas containers in the normal course of business unless the cryogenic medical gas container was returned due to a quality issue.

§213.208 Salvaging of medical gases.

Medical gases in containers that have been subjected to improper storage conditions may be salvaged unless their containers have been subjected to adverse conditions that impact the identity, strength, quality, and purity of the gas or integrity of the container closure. Whenever there is a question whether medical gases have been subjected to such conditions, salvaging operations may be conducted only if there is evidence from laboratory tests that such gases meet all applicable standards of identity, strength, quality, and purity, and the integrity of the container closure system is not compromised. Procedures for the holding, testing, and use of salvaged medical gases shall be in writing and shall be followed.

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.

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- 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.
- Dipyrrone*: All drug products containing dipyrrone.
- 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.

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- 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.
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- 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.

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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.
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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,