

initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action. After December 1, 1993, any such OTC drug product containing lobeline (in the form of lobeline sulfate or natural lobelia alkaloids or *Lobelia inflata* herb), povidone-silver nitrate, silver acetate, or any other ingredients initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

[58 FR 31241, June 1, 1993]

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

(a) A number of active ingredients have been present in OTC drug products for various uses, as described below. However, based on evidence currently available, there are inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses:

(1) *Topical acne drug products.*

Alcloxa
Alkyl isoquinolinium bromide
Aluminum chlorohydrate
Aluminum hydroxide
Benzocaine
Benzoic acid
Boric acid
Calcium polysulfide
Calcium thiosulfate
Camphor
Chloroxylenol
Cloxyquin
Coal tar
Dibenzothiophene
Estrone
Magnesium aluminum silicate
Magnesium sulfate
Phenol
Phenolate sodium
Phenyl salicylate
Povidone-iodine
Pyrilamine maleate
Resorcinol (as single ingredient)
Resorcinol monoacetate (as single ingredient)
Salicylic acid (over 2 up to 5 percent)
Sodium borate
Sodium thiosulfate
Tetracaine hydrochloride
Thymol
Vitamin E
Zinc oxide
Zinc stearate

Zinc sulfide

(2) *Anticaries drug products—(i) Approved as of May 7, 1991.*

Hydrogen fluoride
Sodium carbonate
Sodium monofluorophosphate (6 percent rinse)
Sodium phosphate

(ii) *Approved as of October 7, 1996.*

Calcium sucrose phosphate
Dicalcium phosphate dihydrate
Disodium hydrogen phosphate¹
Phosphoric acid¹
Sodium dihydrogen phosphate
Sodium dihydrogen phosphate monohydrate
Sodium phosphate, dibasic anhydrous reagent¹

(3) *Antidiarrheal drug products.*

Aluminum hydroxide
Atropine sulfate
Calcium carbonate
Carboxymethylcellulose sodium
Glycine
Homatropine methylbromide
Hyoscyamine sulfate
Lactobacillus acidophilus
Lactobacillus bulgaricus
Opium, powdered
Opium tincture
Paregoric
Phenyl salicylate
Scopolamine hydrobromide
Zinc phenolsulfonate

(4) *Antiperspirant drug products.*

Alum, potassium
Aluminum bromohydrate
Aluminum chloride (alcoholic solutions)
Aluminum chloride (aqueous solution) (aerosol only)
Aluminum sulfate
Aluminum sulfate, buffered (aerosol only)
Sodium aluminum chlorohydroxy lactate

(5) [Reserved]

(6) *Cold, cough, allergy, bronchodilator, and antiasthmatic drug products—(i) Antihistamine drug products—(A) Ingredients.*

Methapyrilene hydrochloride
Methapyrilene fumarate
Thenyldiamine hydrochloride

(B) *Ingredients.*

Phenyltoloxamine dihydrogen citrate
Methapyrilene hydrochloride

¹These ingredients are nonmonograph except when used to prepare acidulated phosphate fluoride treatment rinses identified in § 355.10(a)(3) of this chapter.

Methapyrilene fumarate
 Thenyldiamine hydrochloride

(ii) *Nasal decongestant drug products—*
 (A) *Approved as of May 7, 1991.*

Allyl isothiocyanate
 Camphor (lozenge)
 Creosote, beechwood (oral)
 Eucalyptol (lozenge)
 Eucalyptol (mouthwash)
 Eucalyptus oil (lozenge)
 Eucalyptus oil (mouthwash)
 Menthol (mouthwash)
 Peppermint oil (mouthwash)
 Thenyldiamine hydrochloride
 Thymol
 Thymol (lozenge)
 Thymol (mouthwash)
 Turpentine oil

(B) *Approved as of August 23, 1995.*

Bornyl acetate (topical)
 Cedar leaf oil (topical)
 Creosote, beechwood (topical)
 l-desoxyephedrine (topical)
 Ephedrine (oral)
 Ephedrine hydrochloride (oral)
 Ephedrine sulfate (oral)
 Rephedrine hydrochloride (oral/topical)

(iii) *Expectorant drug products.*

Ammonium chloride
 Antimony potassium tartrate
 Beechwood creosote
 Benzoin preparations (compound tincture of benzoin, tincture of benzoin)
 Camphor
 Chloroform
 Eucalyptol/eucalyptus oil
 Horehound
 Iodides (calcium iodide anhydrous, hydroidic acid syrup, iodized lime, potassium iodide)
 Ipecac
 Ipecac fluidextract
 Ipecac syrup
 Menthol/peppermint oil
 Pine tar preparations (extract white pine compound, pine tar, syrup of pine tar, compound white pine syrup, white pine)
 Potassium guaiacolsulfonate
 Sodium citrate
 Squill preparations (squill, squill extract)
 Terpin hydrate preparations (terpin hydrate, terpin hydrate elixir)
 Tolu preparations (tolu, tolu balsam, tolu balsam tincture)
 Turpentine oil (spirits of turpentine)

(iv) *Bronchodilator drug products—*(A)
Approved as of October 2, 1987.

Aminophylline
 Belladonna alkaloids
 Euphorbia pilulifera
 Metaproterenol sulfate
 Methoxyphenamine hydrochloride

Pseudoephedrine hydrochloride
 Pseudoephedrine sulfate
 Theophylline, anhydrous
 Theophylline calcium salicylate
 Theophylline sodium glycinate

(B) *Approved as of January 29, 1996.*
 Any combination drug product containing theophylline (e.g., theophylline and ephedrine, or theophylline and ephedrine and phenobarbital).

(C) *Approved as of June 19, 1996.* Any ingredient(s) in a pressurized metered-dose inhaler container.

(7) *Dandruff/seborrheic dermatitis/psoriasis drug products.*

Alkyl isoquinolinium bromide
 Allantoin
 Benzalkonium chloride
 Benzethonium chloride
 Boric acid
 Calcium undecylenate
 Captan
 Chloroxylenol
 Colloidal oatmeal
 Cresol, saponated
 Ethohexadiol
 Eucalyptol
 Juniper tar
 Lauryl isoquinolinium bromide
 Menthol
 Mercury oleate
 Methylbenzethonium chloride
 Methyl salicylate
 Phenol
 Phenolate sodium
 Pine tar
 Povidone-iodine
 Resorcinol
 Sodium borate
 Sodium salicylate
 Thymol
 Undecylenic acid

(8) *Digestive aid drug products—*(i) *Approved as of May 7, 1991.*

Bismuth sodium tartrate
 Calcium carbonate
 Cellulase
 Dehydrocholic acid
 Dihydroxyaluminum sodium carbonate
 Duodenal substance
 Garlic, dehydrated
 Glutamic acid hydrochloride
 Hemicellulase
 Homatropine methylbromide
 Magnesium hydroxide
 Magnesium trisilicate
 Ox bile extract
 Pancreatin
 Pancrelipase
 Papain
 Peppermint oil
 Pepsin
 Sodium bicarbonate

Sodium citrate
Sorbitol

(ii) *Approved as of November 10, 1993.*

Alcohol
Aluminum hydroxide
Amylase
Anise seed
Aromatic powder
Asafetida
Aspergillus oryza enzymes (except lactase enzyme derived from *Aspergillus oryzae*)
Bacillus acidophilus
Bean
Belladonna alkaloids
Belladonna leaves, powdered extract
Betaine hydrochloride
Bismuth subcarbonate
Bismuth subgallate
Black radish powder
Blessed thistle (*cnicus benedictus*)
Buckthorn
Calcium gluconate
Capsicum
Capsicum, fluid extract of
Carbon
Cascara sagrada extract
Catechu, tincture
Catnip
Chamomile flowers
Charcoal, wood
Chloroform
Cinnamon oil
Cinnamon tincture
Citrus pectin
Diastase
Diastase malt
Dog grass
Elecampane
Ether
Fennel acid
Galega
Ginger
Glycine
Hydrastis canadensis (golden seal)
Hectorite
Horsetail
Huckleberry
Hydrastis fluid extract
Hydrochloric acid
Iodine
Iron ox bile
Johnswort
Juniper
Kaolin, colloidal
Knotgrass
Lactic acid
Lactose
Lavender compound, tincture of
Linden
Lipase
Lysine hydrochloride
Mannitol
Mycozyme
Myrrh, fluid extract of
Nettle
Nickel-pectin

Nux vomica extract
Orthophosphoric acid
Papaya, natural
Pectin
Peppermint
Peppermint spirit
Phenacetin
Potassium bicarbonate
Potassium carbonate
Protease
Prolase
Rhubarb fluid extract
Senna
Sodium chloride
Sodium salicylate
Stem bromelain
Strawberry
Strychnine
Tannic acid
Trillium
Woodruff

(iii) Charcoal, activated

(9) [Reserved]

(10) *External analgesic drug products—*

(i) *Analgesic and anesthetic drug products.*

Aspirin
Chloral hydrate
Chlorobutanol
Cyclomethycaine sulfate
Eugenol
Hexylresorcinol
Methapyrilene hydrochloride
Salicylamide
Thymol

(ii) *Counterirritant drug products.*

Chloral hydrate
Eucalyptus oil

(iii) *Male genital desensitizer drug products.*

Benzyl alcohol
Camphorated metacresol
Ephedrine hydrochloride

(iv) *Diaper rash drug products.*

Any ingredient(s) labeled with claims or directions for use in the treatment and/or prevention of diaper rash.

(v) *Fever blister and cold sore treatment drug products.*

Allyl isothiocyanate
Aspirin
Bismuth sodium tartrate
Camphor (exceeding 3 percent)
Capsaicin
Capsicum
Capsicum oleoresin
Chloral hydrate
Chlorobutanol
Cyclomethycaine sulfate
Eucalyptus oil
Eugenol

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Glycol salicylate
 Hexylresorcinol
 Histamine dihydrochloride
 Menthol (exceeding 1 percent)
 Methapyrilene hydrochloride
 Methyl nicotinate
 Methyl salicylate
 Pectin
 Salicylamide
 Strong ammonia solution
 Tannic acid
 Thymol
 Tripeleennamine hydrochloride
 Trolamine salicylate
 Turpentine oil
 Zinc sulfate

(vi) *Insect bite and sting drug products.*

Alcohol
 Alcohol, ethoxylated alkyl
 Benzalkonium chloride
 Calamine
 Ergot fluidextract
 Ferric chloride
 Panthenol
 Peppermint oil
 Pyrilamine maleate
 Sodium borate
 Trolamine salicylate
 Turpentine oil
 Zinc oxide
 Zirconium oxide

(vii) *Poison ivy, poison oak, and poison sumac drug products.*

Alcohol
 Aspirin
 Benzethonium chloride
 Benzocaine (0.5 to 1.25 percent)
 Bithionol
 Calamine
 Cetalkonium chloride
 Chloral hydrate
 Chlorobutanol
 Chlorpheniramine maleate
 Creosote, beechwood
 Cyclomethycaine sulfate
 Dexpanthenol
 Dipiperodon hydrochloride
 Eucalyptus oil
 Eugenol
 Glycerin
 Glycol salicylate
 Hectorite
 Hexylresorcinol
 Hydrogen peroxide
 Impatiens biflora tincture
 Iron oxide
 Isopropyl alcohol
 Lanolin
 Lead acetate
 Merbromin
 Mercuric chloride
 Methapyrilene hydrochloride
 Panthenol
 Parethoxycaine hydrochloride

Phenyltoloxamine dihydrogen citrate
 Povidone-vinylacetate copolymers
 Pyrilamine maleate
 Salicylamide
 Salicylic acid
 Simethicone
 Sulfur
 Tannic acid
 Thymol
 Trolamine salicylate
 Turpentine oil
 Zirconium oxide
 Zyloxin

(11) [Reserved]
 (12) *Laxative drug products—(i) Bulk laxatives.*

Agar
 Carrageenan (degraded)
 Carrageenan (native)
 Guar gum

(ii) *Saline laxative.*

Tartaric acid

(iii) *Stool softener.*

Poloxamer 188

(iv) *Stimulant laxatives.*

Aloin
 Bile salts/acids
 Calcium pantothenate
 Calomel
 Colocynth
 Elaterin resin
 Frangula
 Gamboge
 Ipomea
 Jalap
 Ox bile
 Podophyllum resin
 Prune concentrate dehydrate
 Prune powder
 Rhubarb, Chinese
 Sodium Oleate

(13) [Reserved]
 (14) *Oral health care drug products (nonantimicrobial).*

Antipyrine
 Camphor
 Cresol
 Dibucaine
 Dibucaine hydrochloride
 Eucalyptol
 Lidocaine
 Lidocaine hydrochloride
 Methly salicylate
 Myrrh tincture
 Pyrilamine maleate
 Sorbitol
 Sugars
 Tetracaine
 Tetracaine hydrochloride
 Thymol

(15) *Topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears—(i) Approved as of May 7, 1991.*

Acetic acid

(ii) *Approved as of August 15, 1995.*

Glycerin and anhydrous glycerin
Isopropyl alcohol

(16) *Poison treatment drug products.*

Ipecac fluidextract
Ipecac tincture
Zinc sulfate

(17) *Skin bleaching drug products.*

Mercury, ammoniated

(18) *Skin protectant drug products. (i) Ingredients.*

Allantoin (wound healing claims only)
Sulfur
Tannic acid
Zinc acetate (wound healing claims only)

(ii) *Astringent drug products.*

Acetone
Alcohol
Alum, ammonium
Alum, potassium
Aluminum chlorhydroxy complex
Aromatics
Benzalkonium chloride
Benzethonium chloride
Benzocaine
Benzoic acid
Boric acid
Calcium acetate
Camphor gum
Clove oil
Colloidal oatmeal
Cresol
Cupric sulfate
Eucalyptus oil
Eugenol
Ferric subsulfate (Monsel's Solution)
Honey
Isopropyl alcohol
Menthol
Methyl salicylate
Oxyquinoline sulfate
P-t-butyl-m-cresol
Peppermint oil
Phenol
Polyoxyethylene laurate
Potassium ferrocyanide
Sage oil
Silver nitrate
Sodium borate
Sodium diacetate
Talc
Tannic acid glycerite
Thymol
Topical starch

Zinc chloride
Zinc oxide
Zinc phenolsulfonate
Zinc stearate
Zinc sulfate

(iii) *Diaper rash drug products.*

Aluminum hydroxide
Cocoa butter
Cysteine hydrochloride
Glycerin
Protein hydrolysate
Racemethionine
Sulfur
Tannic acid
Zinc acetate
Zinc carbonate

(iv) *Fever blister and cold sore treatment drug products.*

Bismuth subnitrate
Boric acid
Pyridoxine hydrochloride
Sulfur
Tannic acid
Topical starch
Trolamine
Zinc sulfate

(v) *Insect bite and sting drug products.*

Alcohol
Alcohol, ethoxylated alkyl
Ammonia solution, strong
Ammonium hydroxide
Benzalkonium chloride
Camphor
Ergot fluidextract
Ferric chloride
Menthol
Peppermint oil
Phenol
Pyrilamine maleate
Sodium borate
Trolamine
Turpentine oil
Zirconium oxide

(vi) *Poison ivy, poison oak, and poison sumac drug products.*

Alcohol
Anion and cation exchange resins buffered
Benzethonium chloride
Benzocaine
Benzyl alcohol
Bismuth subnitrate
Bithionol
Boric acid
Camphor
Cetalkonium chloride
Chloral hydrate
Chlorpheniramine maleate
Creosote
Diperodon hydrochloride
Diphenhydramine hydrochloride
Eucalyptus oil
Ferric chloride

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Glycerin
 Hectorite
 Hydrogen peroxide
 Impatiens biflora tincture
 Iron oxide
 Isopropyl alcohol
 Lanolin
 Lead acetate
 Lidocaine
 Menthol
 Merbromin
 Mercuric chloride
 Panthenol
 Parethoxycaine hydrochloride
 Phenol
 Phenyltoloxamine dihydrogen citrate
 Povidone-vinylacetate copolymers
 Salicylic acid
 Simethicone
 Tannic acid
 Topical starch
 Trolamine
 Turpentine oil
 Zirconium oxide
 Zyloxin

(19) [Reserved]

(20) *Weight control drug products.*

Alcohol
 Alfalfa
 Alginic acid
 Anise oil
 Arginine
 Ascorbic acid
 Bearberry
 Biotin
 Bone marrow, red
 Buchu
 Buchu, potassium extract
 Caffeine
 Caffeine citrate
 Calcium
 Calcium carbonate
 Calcium caseinate
 Calcium lactate
 Calcium pantothenate
 Carboxymethylcellulose sodium
 Carrageenan
 Cholecalciferol
 Choline
 Chondrus
 Citric acid
 Cnicus benedictus
 Copper
 Copper gluconate
 Corn oil
 Corn syrup
 Corn silk, potassium extract
 Cupric sulfate
 Cyanocobalamin (vitamin B₁₂)
 Cystine
 Dextrose
 Docusate sodium
 Ergocalciferol
 Ferric ammonium citrate
 Ferric pyrophosphate

Ferrous fumarate
 Ferrous gluconate
 Ferrous sulfate (iron)
 Flax seed
 Folic acid
 Fructose
 Guar gum
 Histidine
 Hydrastis canadensis
 Inositol
 Iodine
 Isoleucine
 Juniper, potassium extract
 Karaya gum
 Kelp
 Lactose
 Lecithin
 Leucine
 Liver concentrate
 Lysine
 Lysine hydrochloride
 Magnesium
 Magnesium oxide
 Malt
 Maltodextrin
 Manganese citrate
 Mannitol
 Methionine
 Methylcellulose
 Mono- and di-glycerides
 Niacinamide
 Organic vegetables
 Pancreatin
 Pantothenic acid
 Papain
 Papaya enzymes
 Pepsin
 Phenacetin
 Phenylalanine
 Phosphorus
 Phytolacca
 Pineapple enzymes
 Plantago seed
 Potassium citrate
 Pyridoxine hydrochloride (vitamin B₆)
 Riboflavin
 Rice polishings
 Saccharin
 Sea minerals
 Sesame seed
 Sodium
 Sodium bicarbonate
 Sodium caseinate
 Sodium chloride (salt)
 Soybean protein
 Soy meal
 Sucrose
 Thiamine hydrochloride (vitamin B₁)
 Thiamine mononitrate (vitamin B₁ mono-nitrate)
 Threonine
 Tricalcium phosphate
 Tryptophan
 Tyrosine
 Uva ursi, potassium extract
 Valine
 Vegetable

Vitamin A
 Vitamin A acetate
 Vitamin A palmitate
 Vitamin E
 Wheat germ
 Xanthan gum
 Yeast

(21) *Ophthalmic drug products.*(i) *Ophthalmic anesthetic drug products.*

Antipyrine
 Piperocaine hydrochloride

(ii) *Ophthalmic anti-infective drug products.*

Boric acid
 Mild silver protein
 Yellow mercuric oxide

(iii) *Ophthalmic astringent drug products.*

Infusion of rose petals

(iv) *Ophthalmic demulcent drug products.*

Polyethylene glycol 6000

(v) *Ophthalmic vasoconstrictor drug products.*

Phenylephrine hydrochloride (less than 0.08 percent)

(22) *Topical antifungal drug products.*

(i) *Diaper rash drug products.* Any ingredient(s) labeled with claims or directions for use in the treatment and/or prevention of diaper rash.

(ii) *Ingredients.*

Alcloxa
 Alum, potassium
 Aluminum sulfate
 Amyltripresols, secondary
 Basic fuchsin
 Benzethonium chloride
 Benzoic acid
 Benzoxiquine
 Boric acid
 Camphor
 Candicidin
 Chlorothymol
 Coal tar
 Dichlorophen
 Menthol
 Methylparaben
 Oxyquinoline
 Oxyquinoline sulfate
 Phenol
 Phenolate sodium
 Phenyl salicylate
 Propionic acid
 Propylparaben
 Resorcinol
 Salicylic acid

Sodium borate
 Sodium caprylate
 Sodium propionate
 Sulfur
 Tannic acid
 Thymol
 Tolindate
 Triacetin
 Zinc caprylate
 Zinc propionate

(iii) Any ingredient(s) labeled with claims or directions for use on the scalp or on the nails.

(iv) *Ingredients.*

Camphorated metacresol
 Chloroxylenol
m-cresol
 Nystatin

(23) *Internal analgesic drug products.*

Aminobenzoic acid
 Antipyrine
 Aspirin, aluminum
 Calcium salicylate
 Codeine
 Codeine phosphate
 Codeine sulfate
 Iodoantipyrine
 Lysine aspirin
 Methapyrilene fumarate
 Phenacetin
 Pheniramine maleate
 Pyrilamine maleate
 Quinine
 Salsalate
 Sodium aminobenzoate

(24) *Orally administered menstrual drug products.*

Alcohol
 Alfalfa leaves
 Aloes
 Asclepias tuberosa
 Asparagus
 Barosma
 Bearberry (extract of uva ursi)
 Bearberry fluidextract (extract of bearberry)
 Blessed thistle (cnicus benedictus)
 Buchu powdered extract (extract of buchu)
 Calcium lactate
 Calcium pantothenate
 Capsicum oleoresin
 Cascara fluidextract, aromatic (extract of cascara)
 Chlorprophenpyridamine maleate
 Cimicifuga racemosa
 Codeine
 Collinsonia (extract stone root)
 Corn silk
 Couch grass
 Dog grass extract
 Ethyl nitrite
 Ferric chloride
 Ferrous sulfate
 Gentiana lutea (gentian)

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Glycyrrhiza (licorice)
 Homatropine methylbromide
 Hydrangea, powdered extract (extract of hydrangea)
 Hydrastis canadensis (golden seal)
 Hyoscyamine sulfate
 Juniper oil (oil of juniper)
 Magnesium sulfate
 Methapyrilene hydrochloride
 Methenamine
 Methylene blue
 Natural estrogenic hormone
 Niacinamide
 Nutmeg oil (oil of nutmeg)
 Oil of erigeron
 Parsley
 Peppermint spirit
 Pepsin, essence
 Phenacetin
 Phenindamine tartrate
 Phenyl salicylate
 Piscidia erythrina
 Pipsissewa
 Potassium acetate
 Potassium nitrate
 Riboflavin
 Saw palmetto
 Senecio aureus
 Sodium benzoate
 Sodium nitrate
 Sucrose
 Sulfurated oils of turpentine
 Taraxacum officinale
 Theobromine sodium salicylate
 Theophylline
 Thiamine hydrochloride
 Triticum
 Turpentine, venice (venice turpentine)
 Urea

(25) *Pediculicide drug products*—(i) *Approved as of November 10, 1993.*

Benzocaine
 Benzyl alcohol
 Benzyl benzoate
 Chlorophenothane (dichlorodiphenyl trichloroethane)
 Coconut oil soap, aqueous
 Copper oleate
 Docusate sodium
 Formic acid
 Isobornyl thiocyanacetate
 Picrotoxin
 Propylene glycol
 Sabadilla alkaloids
 Sulfur, sublimed
 Thiocyanacetate

(ii) *Approved as of June 14, 1994.* The combination of pyrethrum extract (formerly named pyrethrins) and piperonyl butoxide in an aerosol dosage formulation.

(26) *Anorectal drug products*—(i) *Anticholinergic drug products.*

Atropine

Belladonna extract

(ii) *Antiseptic drug products.*

Boric acid
 Boroglycerin
 Hydrastis
 Phenol
 Resorcinol
 Sodium salicylic acid phenolate

(iii) *Astringent drug products.*

Tannic acid

(iv) *Counterirritant drug products.*

Camphor (greater than 3 to 11 percent)
 Hydrastis
 Menthol (1.25 to 16 percent)
 Turpentine oil (rectified) (6 to 50 percent)

(v) *Keratolytic drug products.*

Precipitated sulfur
 Sublimed sulfur

(vi) *Local anesthetic drug products.*

Diperodon
 Phenacaine hydrochloride

(vii) *Other drug products.*

Collinsonia extract
 Escherichia coli vaccines
 Lappa extract
 Leptandra extract
 Live yeast cell derivative
 Mullein

(viii) *Protectant drug products.*

Bismuth oxide
 Bismuth subcarbonate
 Bismuth subgallate
 Bismuth subnitrate
 Lanolin alcohols

(ix) *Vasoconstrictor drug products.*

Epinephrine undecylenate

(x) *Wound healing drug products.*

Cholecalciferol
 Cod liver oil
 Live yeast cell derivative
 Peruvian balsam
 Shark liver oil
 Vitamin A

(b) Any OTC drug product that is labeled, represented, or promoted for the uses specified and containing any active ingredient(s) as specified in paragraph (a) of this section is regarded as a new drug within the meaning of section 210(p) of the Federal Food, Drug, and Cosmetic Act (the Act), for which an approved new drug application under section 505 of the Act and part

314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the Act.

(c) Clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for the OTC uses and containing any active ingredient(s) as specified in paragraph (a) of this section is safe and effective for the purpose intended must comply with the requirements and procedures governing the use of investigational new drugs set forth in part 312 of this chapter.

(d) Any OTC drug product that is not in compliance with this section is subject to regulatory action if initially introduced or initially delivered for introduction into interstate commerce after the dates specified in paragraphs (d)(1) through (d)(25) of this section.

(1) May 7, 1991, for products subject to paragraphs (a)(1) through (a)(2)(i), (a)(3) through (a)(4), (a)(6)(i)(A), (a)(6)(ii)(A), (a)(7) (except as covered by paragraph (d)(3) of this section), (a)(8)(i), (a)(9) through (a)(10)(iii), (a)(12)(i) through (a)(12)(iv), (a)(14) through (a)(15)(i), and (a)(16) through (a)(18)(i) of this section.

(2) February 10, 1992, for products subject to paragraph (a)(20) of this section.

(3) December 4, 1992, for products subject to paragraph (a)(7) of this section that contain menthol as an antipruritic in combination with the antidandruff ingredient coal tar identified in § 358.710(a)(1) of this chapter.

(4) February 28, 1990, for products subject to paragraph (a)(6)(iii) of this section, except those that contain ipecac.

(5) September 14, 1993, for products subject to paragraph (a)(6)(iii) of this section that contain ipecac.

(6) December 9, 1993, for products subject to paragraph (a)(6)(i)(B) of this section.

(7) March 6, 1989, for products subject to paragraph (a)(21) of this section, except those that contain ophthalmic anti-infective ingredients listed in paragraph (a)(21)(ii).

(8) June 18, 1993, for products subject to paragraph (a)(21) of this section that

contain ophthalmic anti-infective ingredients.

(9) June 18, 1993, for products subject to paragraph (a)(10)(iv) of this section.

(10) June 18, 1993, for products subject to paragraph (a)(22)(i) of this section.

(11) November 10, 1993, for products subject to paragraph (a)(18)(ii) of this section, except products that contain ferric subsulfate.

(12) March 2, 1994, for products subject to paragraph (a)(22)(iii) of this section.

(13) August 5, 1991, for products subject to paragraphs (a)(26) of this section, except for those that contain live yeast cell derivative.

(14) September 2, 1994, for products subject to paragraph (a)(26)(vii) and (a)(26)(x) of this section that contain live yeast cell derivative.

(15) September 23, 1994, for products subject to paragraph (a)(22)(iv) of this section.

(16) June 14, 1994, for products subject to paragraph (a)(25)(ii) of this section.

(17) [Reserved]

(18) August 15, 1995, for products subject to paragraph (a)(15)(ii) of this section.

(19) October 2, 1987, for products subject to paragraph (a)(6)(iv)(A) of this section.

(20) January 29, 1996, for products subject to paragraph (a)(6)(iv)(B) of this section.

(21) April 21, 1994, for products subject to paragraph (a)(8)(iii) of this section.

(22) April 21, 1993, for products subject to paragraph (a)(18)(ii) of this section that contain ferric subsulfate.

(23) August 23, 1995, for products subject to paragraph (a)(6)(ii)(B) of this section.

(24) October 7, 1996, for products subject to paragraph (a)(2)(ii) of this section.

(25) June 19, 1996, for products subject to paragraph (a)(6)(iv)(C) of this section.

[55 FR 46919, Nov. 7, 1990]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 310.545, see the List of CFR Sections Affected in the Finding Aids section of this volume.

EFFECTIVE DATE NOTES: 1. At 60 FR 42436, Aug. 16, 1995, in § 310.545, paragraph (a)(15)(ii)

was stayed for topical otic drug products for the drying of water-clogged ears.

2. At 61 FR 9571, Mar. 8, 1996, in § 310.545 in paragraph (a)(6)(ii)(B), the entry for “1-desoxyephedrine (topical)” was stayed until further notice.

§ 310.546 Drug products containing active ingredients offered over-the-counter (OTC) for the treatment and/or prevention of nocturnal leg muscle cramps.

(a) Quinine sulfate alone or in combination with vitamin E has been present in over-the-counter (OTC) drug products for the treatment and/or prevention of nocturnal leg muscle cramps, i.e., a condition of localized pain in the lower extremities usually occurring in middle life and beyond with no regular pattern concerning time or severity. There is a lack of adequate data to establish general recognition of the safety and effectiveness of quinine sulfate, vitamin E, or any other ingredients for OTC use in the treatment and/or prevention of nocturnal leg muscle cramps. In the doses used to treat or prevent this condition, quinine sulfate has caused adverse events such as transient visual and auditory disturbances, dizziness, fever, nausea, vomiting, and diarrhea. Quinine sulfate may cause unpredictable serious and life-threatening hypersensitivity reactions requiring medical intervention and hospitalization; fatalities have been reported. The risk associated with use of quinine sulfate, in the absence of evidence of its effectiveness, outweighs any potential benefit in treating and/or preventing this benign, self-limiting condition. Based upon the adverse benefit-to-risk ratio, any drug product containing quinine or quinine sulfate cannot be considered generally recognized as safe for the treatment and/or prevention of nocturnal leg muscle cramps.

(b) Any OTC drug product that is labeled, represented, or promoted for the treatment and/or prevention of nocturnal leg muscle cramps is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act), for which an approved application or abbreviated application under section 505 of the act and part 314 of this chapter is required for marketing. In the absence of an ap-

proved new drug application or abbreviated new drug application, such product is also misbranded under section 502 of the act.

(c) Clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for OTC use for the treatment and/or prevention of nocturnal leg muscle cramps is safe and effective for the purpose intended must comply with the requirements and procedures governing the use of investigational new drugs set forth in part 312 of this chapter.

(d) After February 22, 1995, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

[59 FR 43252, Aug. 22, 1994]

§ 310.547 Drug products containing quinine offered over-the-counter (OTC) for the treatment and/or prevention of malaria.

(a) Quinine and quinine salts have been used OTC for the treatment and/or prevention of malaria, a serious and potentially life-threatening disease. Quinine is no longer the drug of choice for the treatment and/or prevention of most types of malaria. In addition, there are serious and complicating aspects of the disease itself and some potentially serious and life-threatening risks associated with the use of quinine at doses employed for the treatment of malaria. There is a lack of adequate data to establish general recognition of the safety of quinine drug products for OTC use in the treatment and/or prevention of malaria. Therefore, quinine or quinine salts cannot be safely and effectively used for the treatment and/or prevention of malaria except under the care and supervision of a doctor.

(b) Any OTC drug product containing quinine or quinine salts that is labeled, represented, or promoted for the treatment and/or prevention of malaria is regarded as a new drug within the meaning of section 201(p) of the act, for which an approved application or abbreviated application under section 505 of the act and part 314 of this chapter