

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 approved 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 as a smoking deterrent 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 May 7, 1991, any such OTC drug product containing cloves, coriander, eucalyptus oil, ginger (Jamaica), lemon oil (terpeneless), licorice root extract, menthol, methyl salicylate, quinine ascorbate, silver nitrate, and/or thymol initially introduced or 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
Pyrimidine 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—(i) Approved as of May 7, 1991.*

Aluminum hydroxide
Atropine sulfate
Calcium carbonate
Carboxymethylcellulose sodium
Glycine
Homatropine methylbromide
Hyoscyamine sulfate
Lactobacillus acidophilus
Lactobacillus bulgaricus

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

§ 310.545

21 CFR Ch. I (4–1–08 Edition)

Opium, powdered
Opium tincture
Paregoric
Phenyl salicylate
Scopolamine hydrobromide
Zinc phenolsulfonate

(ii) *Approved as of April 19, 2004; April 18, 2005, for products with annual sales less than \$25,000.*

Attapulgate, activated
Bismuth subnitrate
Calcium hydroxide
Calcium polycarboxophil
Charcoal (activated)
Pectin
Polycarboxophil
Potassium carbonate
Rhubarb fluidextract

(4) *Antiperspirant drug products—(i) Ingredients—Approved as of May 7, 1991.*

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

(ii) *Approved as of December 9, 2004; June 9, 2005, for products with annual sales less than \$25,000.*

Aluminum sulfate buffered with sodium aluminum 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
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)
Ephedrine (oral)
Ephedrine hydrochloride (oral)
Ephedrine sulfate (oral)
Racephedrine hydrochloride (oral/topical)

(C) *Approved as of April 11, 2007; October 11, 2007, for products with annual sales less than \$25,000. Any ingredient(s) labeled with claims or directions for use for sinusitis or for relief of nasal congestion associated with sinusitis.*

(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, hydriodic 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*

Food and Drug Administration, HHS

§ 310.545

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.

(D) Approved as of October 29, 2001. Any oral bronchodilator active ingredient (e.g., ephedrine, ephedrine hydrochloride, ephedrine sulfate, racephedrine hydrochloride, or any other ephedrine salt) in combination with any analgesic(s) or analgesic-antipyretic(s), anticholinergic, antihistamine, oral antitussive, or stimulant active ingredient.

(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

§ 310.545

21 CFR Ch. I (4-1-08 Edition)

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
Glycol salicylate
Hexylresorcinol
Histamine dihydrochloride
Menthol (exceeding 1 percent)
Methapyrilene hydrochloride
Methyl nicotinate
Methyl salicylate
Pectin
Salicylamide
Strong ammonia solution
Tannic acid
Thymol
Tripeleminamine 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
Dexpantenol
Diperodon 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

Food and Drug Administration, HHS

§ 310.545

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)(A) Bulk laxatives.*

Agar
Carrageenan (degraded)
Carrageenan (native)
Guar gum

(i)(B) *Bulk laxatives—Approved as of March 29, 2007.*

Granular dosage forms containing psyllium (hemicellulose), psyllium hydrophilic mucilloid, psyllium seed, psyllium seed (blond), psyllium seed husks, plantago husks, or plantago seed including, but not limited to, any granules that are:

- (1) Swallowed dry prior to drinking liquid,
- (2) Dispersed, suspended, or partially dissolved in liquid prior to swallowing,
- (3) Chewed, partially chewed, or unchewed, and then washed down (or swallowed) with liquid, or
- (4) Sprinkled over food.

(ii) *Saline laxative.*

Tartaric acid

(iii) *Stool softener.*

Poloxamer 188

(iv)(A) *Stimulant laxatives—Approved as of May 7, 1991.*

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

(iv)(B) *Stimulant laxatives—Approved as of January 29, 1999.*

Danthron
Phenolphthalein

(C) *Stimulant laxatives—Approved as of November 5, 2002.*

Aloe ingredients (aloe, aloe extract, aloe flower extract)

Cascara sagrada ingredients (casanthranol, cascara fluidextract aromatic, cascara sagrada bark, cascara sagrada extract, cascara sagrada fluidextract).

(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—(i) For the prevention of swimmer's ear and for the drying of water-clogged ears, approved as of May 7, 1991.*

Acetic acid

(ii) *For the prevention of swimmer's ear, 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)(A) Ingredients—Approved as of May 7, 1991.*

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

§ 310.545

21 CFR Ch. I (4–1–08 Edition)

(B) *Ingredients—Approved as of June 4, 2004; June 6, 2005, for products with annual sales less than \$25,000.*

Beeswax
Bismuth subnitrate
Boric acid
Cetyl alcohol
Glyceryl stearate
Isopropyl palmitate
Live yeast cell derivative
Shark liver oil
Stearyl alcohol

(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—(A) Ingredients—Approved as of November 10, 1993.*

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

(B) *Ingredients—Approved as of June 4, 2004; June 6, 2005, for products with annual sales less than \$25,000.*

Beeswax
Bismuth subnitrate
Boric acid
Cetyl alcohol
Glyceryl stearate
Isopropyl palmitate
Live yeast cell derivative
Shark liver oil
Stearyl alcohol

(vi) *Poison ivy, poison oak, and poison sumac drug products—(A) Ingredients—Approved as of November 10, 1993.*

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

Food and Drug Administration, HHS

§ 310.545

Diperodon hydrochloride
 Diphenhydramine hydrochloride
 Eucalyptus oil
 Ferric chloride
 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

(B) *Ingredients—Approved as of June 4, 2004; June 6, 2005, for products with annual sales less than \$25,000.*

Beeswax
 Bismuth subnitrate
 Boric acid
 Cetyl alcohol
 Glyceryl stearate
 Isopropyl palmitate
 Live yeast cell derivative
 Shark liver oil
 Stearyl alcohol

(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

§ 310.545

21 CFR Ch. I (4–1–08 Edition)

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
Amyltriols, 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—*
(i) *Approved as of November 10, 1993.*

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

(ii) *Approved as of February 22, 1999.*

Any atropine ingredient
Any ephedrine ingredient

(24) *Orally administered menstrual drug products—*(i) *Approved as of November 10, 1993.*

Alcohol
Alfalfa leaves
Aloes

Food and Drug Administration, HHS

§ 310.545

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)
 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
 Sulfaterated oils of turpentine
 Taraxacum officinale
 Theobromine sodium salicylate
 Theophylline
 Thiamine hydrochloride
 Triticum
 Turpentine, venice (venice turpentine)
 Urea

(ii) *Approved as of February 22, 1999.*

Any atropine ingredient
 Any ephedrine ingredient

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

Benzocaine
 Benzyl alcohol
 Benzyl benzoate
 Chlorophenothane (dichlorodiphenyl tri-chloroethane)
 Coconut oil soap, aqueous
 Copper oleate
 Docusate sodium
 Formic acid
 Isobornyl thiocynoacetate
 Picrotoxin
 Propylene glycol
 Sabadilla alkaloids
 Sulfur, sublimed
 Thiocynoacetate

(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

§ 310.545

21 CFR Ch. I (4-1-08 Edition)

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

(xi) *Combination drug products.* Any combination drug product containing hydrocortisone and pramoxine hydrochloride.

(27) *Topical antimicrobial drug products—(i) First aid antiseptic drug products.*

Ammoniated mercury
Calomel (mercurous chloride)
Merbromin (mercurochrome)
Mercufenol chloride (ortho-chloromercuriphenol, ortho-hydroxyphenylmercuric chloride)
Mercuric chloride (bichloride of mercury, mercury chloride)
Mercuric oxide, yellow
Mercuric salicylate
Mercuric sulfide, red
Mercury
Mercury oleate
Mercury sulfide
Nitromersol
Para-chloromercuriphenol
Phenylmercuric nitrate
Thimerosal
Vitromersol
Zyloxin

(ii) *Diaper rash drug products.*

Para-chloromercuriphenol
Any other ingredient containing mercury

(28) *Vaginal contraceptive drug products—(i) Approved as of October 22, 1998.*

Dodecaethylene glycol monolaurate (polyethylene glycol 600 monolaurate)
Laureth 10S
Methoxypolyoxyethyleneglycol 550 laurate
Phenylmercuric acetate
Phenylmercuric nitrate
Any other ingredient containing mercury

(ii) *Approved as of November 5, 2002.*

Octoxynol 9

(29) *Sunscreen drug products.*

Diethanolamine methoxycinnamate
Digalloyl trioleate
Ethyl 4-[bis(hydroxypropyl)] aminobenzoate

Glyceryl aminobenzoate
Lawsone with dihydroxyacetone
Red petrolatum

(30) [Reserved]

(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)(38) of this section.

(1) May 7, 1991, for products subject to paragraphs (a)(1) through (a)(2)(i), (a)(3)(i), (a)(4)(i), (a)(6)(i)(A), (a)(6)(ii)(A), (a)(7) (except as covered by paragraph (d)(3) of this section), (a)(8)(i), (a)(10)(i) through (a)(10)(iii), (a)(12)(i)(A), (a)(12)(ii) through (a)(12)(iv)(A), (a)(14) through (a)(15)(i), (a)(16) through (a)(18)(i)(A), (a)(18)(ii) (except as covered by paragraph (d)(22) of this section), (a)(18)(iii), (a)(18)(iv), (a)(18)(v)(A), and (a)(18)(vi)(A) 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 anti-pruritic in combination with the antidandruff ingredient coal tar identified in §358.710(a)(1) of this chapter. This

section does not apply to products allowed by §358.720(b) of this chapter after April 5, 2007.

(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 paragraphs (a)(8)(ii), (a)(10)(v) through (a)(10)(vii), (a)(18)(ii) (except products that contain ferric subsulfate as covered by paragraph (d)(22) of this section) through (a)(18)(v)(A), (a)(18)(vi)(A), (a)(22)(ii), (a)(23)(i), (a)(24)(i), and (a)(25) of this section.

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

(13) August 5, 1991, for products subject to paragraph (a)(26) of this section, except for those that contain live yeast cell derivative and a combination of hydrocortisone and pramoxine hydrochloride.

(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) April 19, 2004, for products subject to paragraph (a)(3)(ii) of this section. April 18, 2005, for products with annual sales less than \$25,000.

(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.

(26) February 22, 1999, for products subject to paragraphs (a)(23)(ii) and (a)(24)(ii) of this section.

(27) [Reserved]

(28) October 22, 1998, for products subject to paragraphs (a)(27) and (a)(28)(i) of this section.

(29) January 29, 1999, for products subject to paragraph (a)(12)(iv)(B) of this section.

(30) November 5, 2002, for products subject to paragraph (a)(12)(iv)(C) of this section.

(31) December 31, 2002, for products subject to paragraph (a)(29) of this section.

(32) June 4, 2004, for products subject to paragraphs (a)(18)(i)(B), (a)(18)(v)(B), and (a)(18)(vi)(B) of this section. June 6, 2005, for products with annual sales less than \$25,000.

(33) October 29, 2001, for products subject to paragraph (a)(6)(iv)(D) of this section.

(34) December 9, 2004, for products subject to paragraph (a)(4)(ii) of this section. June 9, 2005, for products with annual sales less than \$25,000.

(35) [Reserved]

(36) November 5, 2002, for products subject to paragraph (a)(28)(ii) of this section.

(37) September 25, 2003, for products subject to paragraph (a)(26)(xi) of this section.

§ 310.546

(38) October 1, 2007, for products subject to paragraph (a)(12)(i)(B) 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, which appears in the Finding Aids section of the printed volume and on GPO Access.

EFFECTIVE DATE NOTE: 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 noc-

21 CFR Ch. I (4-1-08 Edition)

turnal 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 approved 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