DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. FDA–2008–N–0297]

RIN 0910–AF95

Status of Certain Additional Over-the-Counter Drug Category II Active Ingredients

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing that certain ingredients in over-the-counter (OTC) drug products are not generally recognized as safe and effective (GRASE) or are misbranded. FDA is issuing this proposed rule because we did not receive any data and information on these ingredients in response to our request on December 31, 2003 (68 FR 75585). This proposed rule is part of FDA's ongoing review of OTC drug products.

DATES: Submit written or electronic comments on the proposed rule and on FDA's economic impact determination by [*insert date 90 days after date of publication in the* **Federal Register**]. Please see section IV of this document for the proposed effective date of any final rule that may publish based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. FDA–2008–N–0297 and RIN number 0910–AF95, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301–827–6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]: Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal, as described previously, in the **ADDRESSES** portion of this document under *Electronic Submissions*.

Instructions: All submissions received must include the agency name, docket number, and Regulatory Information Number (RIN) for this rulemaking and may be accompanied by a supporting memorandum or brief. All comments received may be posted without change to *http://www.regulations.gov*, including any personal information provided.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson or Gerald M. Rachanow, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, MS5411, Silver Spring, MD 20993, 301–796–2090.

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I. What is the Purpose of This Document?

In this rule, FDA proposes to add to § 310.545 (21 CFR 310.545) certain ingredients and categories of OTC drug products that are not GRASE and are misbranded in the absence of an approved new drug application (NDA):

Ingredients

- Any external analgesic drug products containing aloe vera or urea

- Any topical antimicrobial drug products containing aloe vera
- Any drug products containing urea for any labeled claims
- Ammonia as a reflex stimulant

Drug Categories

- All skin protectant blister guard drug products
- Any skin protectant drug products labeled with claims or directions for use as a nipple protectant (previously referred to as breast creams for use when nursing), except lanolin
- Any drug products formulated as a wet dressing other than skin protectant and astringent drug products formulated and labeled in accordance with 21 CFR part 347
- Any drug products labeled with claims or directions for the following uses:
    - Bed-wetting deterrent
    - Blemish remedy other than topical acne drug products formulated and labeled in accordance with 21 CFR part 333, subpart D
    - Bunion remedy
    - Drawing salve (for drawing or removing splinters, slivers, or similar items), except ichthammol
    - Foot balm, bath, or other topical dosage forms for any ''foot'' claims (including relieving foot muscle strains and soreness from working out), other than topical antifungal drug products formulated and labeled in accordance with 21 CFR part 333, subpart C and external analgesic drug products formulated and labeled in accordance with the tentative final monograph (proposed 21 CFR part 348) published on February 8, 1983 (48 FR 5852)
    - Impotency cure

- Medicated bath preparation
- Nonantimicrobial skin wound cleanser (previously listed as ‘‘detergents’’ in call-for-data notices
- Topical products for treatment or prevention of male urethral problems
- Treatment or prevention of prickly heat
- Urinary acidifier
- Urinary alkalinizer
- Weight control drug products with ingredients formulated as an impregnated body wrap
- Wound wash saline

FDA notes that the names of several active ingredients have changed from the way they appeared in the December 31, 2003, call-for-data notice. FDA is using the new names in the proposed amendments to § 310.545. Table 1 lists the old and new ingredient names:

TABLE 1.—ACTIVE INGREDIENTS WITH NAME CHANGES

Old name	Current name	Category
Aromatic spirits of ammonia	Ammonia spirit, aromatic	Ammonia as a reflex stimulant
Benzophenone-3	Oxybenzone	Medicated bath
Carbolic acid	Phenol	Foot balm, bath
Formalin	Formaldehyde solution	Foot balm, bath
Natural pine needle oil	Pine needle oil	Foot balm, bath
Oil of eucalyptus	Eucalyptus oil	Foot balm, bath
Oil of peppermint	Peppermint oil	Foot balm, bath
Peru balsam	Peruvian balsam	Medicated bath
Phenol sodium	Phenolate sodium	Nonantimicrobial skin wound cleanser
Trisodium phosphate	Sodium phosphate, tribasic	Foot balm, bath

FDA is proposing that any OTC drug product containing any of these ingredients that are not considered GRASE for the uses discussed in this document must first be the subject of an approved NDA before it may be

initially introduced (or initially delivered for introduction) into interstate commerce.

The following product categories, for which data were submitted in response to the December 31, 2003, call-for-data notice, will be discussed in future issues of the **Federal Register**: Lubricants and vaginal moisturizers, nasal moisturizers, urinary analgesics/antiseptics, wrinkle removers, lanolin as a nipple protectant, and ichthammol as a drawing salve. FDA is not discussing those product categories, or specific active ingredients in those categories, in this document.

II. What Past FDA Actions Are Relevant to This Proposed Rule?

A. What Categories of Products Were Included in the Call-for-Data Notice?

In the **Federal Register** of December 31, 2003, FDA published a call for data for certain categories of ingredients in OTC drug products that FDA had not reviewed to date. We listed the following 22 categories (68 FR 75585 at 75589 to 75590): Ammonia as a reflex stimulant; bed-wetting deterrents; blemish remedies (excluding topical acne active ingredients in § 310.545(a)(1) and § 333.310 (21 CFR 333.310)); breast creams (for use when nursing) (now called ''nipple protectants''); bunion remedies; drawing salves (excluding products labeled for the treatment of boils in 21 CFR 310.531 and including products labeled for the drawing or removal of splinters, slivers, or similar items); foot balms, baths, and creams (excluding topical antifungal active ingredients in § 310.545(a)(22) and § 333.210 (21 CFR 333.210) and including claims for relieving foot muscle strains and soreness from working out); impotency cures; impregnated body wraps for weight reduction; lubricants and vaginal moisturizers; medicated bath preparations; nasal moisturizers; nonantimicrobial skin wound cleansers; prickly heat products; skin protectant

blister guard; urethral creams for males; urinary acidifiers; urinary alkalinizers; urinary analgesics/antiseptics; wet dressings (excluding astringent active ingredients in § 310.545(a)(18)(ii) and § 347.10 (21 CFR 347.10)); wound wash saline; and wrinkle removers. Most categories identified in the call for data included a list of specific active ingredients for review.

FDA also requested the submission of data and information (68 FR 75585 at 75588) on:

- Aloe vera as an active ingredient in OTC topical antimicrobial and external analgesic drug products
- Urea as an active ingredient in OTC external analgesic drug products, or for any other OTC drug use

FDA invited interested persons to submit data and information on these categories and ingredients by June 28, 2004.

B. What Data Were Submitted in Response to the Call-for-Data Notice?

Data were submitted for the following product categories: Nipple protectants (for use when nursing); drawing salves labeled for the drawing or removal of splinters, slivers, or similar items; lubricants and vaginal moisturizers; nasal moisturizers; urinary analgesics/antiseptics; and wrinkle removers. For two of the product categories, FDA received data and information on only one ingredient in each category. In the category of nipple protectants, FDA received data on a product containing lanolin. FDA did not receive any data or information on the following ingredients that were listed for the nipple protectant category in the call-for-data notice: Cetyl alcohol, cocoa butter, cod liver oil, dimethicone, glycerin, glyceryl monostearate, hard fat, mineral oil, petrolatum, and white petrolatum. In the category of drawing salves, FDA received data on a product containing ichthammol. FDA did not

receive any data or information on the following ingredients that were listed for the drawing salves category in the call-for-data notice: Ergot fluid extract, juniper tar (oil of cade), magnesium sulfate, pine tar, rosin, rosin cerate, and sulfur. Based on the submissions received, the following products are not included in this proposed rule and will be discussed in a future issue of the **Federal Register**: Lubricants and vaginal moisturizers, nasal moisturizers, urinary analgesics/antiseptics, wrinkle removers, lanolin for use as a nipple protectant, and ichthammol for use in drawing salves.

FDA did not receive any data or information on products or active ingredients in the following product categories: Ammonia as a reflex stimulant; bed-wetting deterrents; blemish remedies (excluding topical acne active ingredients in § § 310.545(a)(1) and 333.310); bunion remedies; foot balms, baths, and creams (excluding topical antifungal active ingredients in § § 310.545(a)(22) and 333.210 and including claims for relieving foot muscle strains and soreness from working out); impotency cures; impregnated body wraps for weight reduction; medicated bath preparations; nonantimicrobial skin wound cleansers; prickly heat products; skin protectant blister guard; urethral creams for males; urinary acidifiers; urinary alkalinizers; wet dressings (excluding astringent active ingredients in § § 310.545(a)(18)(ii) and 347.10); and wound wash saline. FDA also did not receive any data or information on aloe vera and urea for topical uses. Therefore, FDA has no data and information to review to determine if any of these products or ingredients are GRASE and not misbranded for OTC use.

III. What Is the Regulatory Process When No Data Are Submitted to Support Ingredients?

Under the procedures for classifying OTC drugs as GRASE and not misbranded and for establishing OTC drug monographs (§ 330.10 (21 CFR 330.10)):

- An advisory review panel reviews the data and information submitted in response to a call for data and then submits a report with its recommendations to the Commissioner of Food and Drugs (the Commissioner) (§ 330.10(a)(2), (a)(3), and (a)(5)).
- After reviewing the advisory review panel's report and recommendations, the Commissioner publishes a proposed order with the panel's report and a monograph listing proposed GRASE conditions and a statement of the proposed nonmonograph conditions (§ 330.10(a)(6)).
- After reviewing comments and new data submitted in response to the publication of the advisory review panel's report, the Commissioner publishes a tentative final monograph (TFM) proposing conditions under which a category of drugs or specific OTC drugs are GRASE and not misbranded (§ 330.10(a)(7)(i)).
- The Commissioner may also publish a separate tentative order, such as this document, containing a statement of those active ingredients reviewed and proposed to be excluded from the monograph because they would result in a drug product not being GRASE or would result in misbranding. This order may be published when FDA receives no substantive comments in opposition to the advisory review panel's report or no new data and information (§ 330.10(a)(7)(ii)).
- After reviewing the entire administrative record, the Commissioner publishes a final order containing a monograph establishing conditions under

which a category of OTC drugs or a specific or specific OTC drugs are GRASE and not misbranded (§ 330.10(a)(9)). If there are no GRASE conditions, the Commissioner includes the category or the specific OTC drugs in § 310.545, which lists active ingredients for which the data are inadequate to establish GRASE status (i.e., identifies nonmonograph ingredients and uses).

FDA did not receive any data and information on most of the ingredients and drug categories in the call-for-data notice for an advisory review panel to evaluate and upon which a panel could issue a report. Thus, for those ingredients and drug categories, there is no data or report for the Commissioner to evaluate and no basis for FDA to publish a TFM. Therefore, the Commissioner is publishing a tentative order (proposed rule) listing these ingredients and drug categories as nonmonograph conditions.

IV. What Is FDA's Proposed Effective Date?

FDA is proposing that any final rule that may issue based on this proposal be implemented 180 days after its publication in order to provide for safe and effective use of OTC drug products at the earliest possible time. Manufacturers are encouraged to comply voluntarily at the earliest possible date.

FDA points out that publication of a final rule under this proceeding would not preclude a manufacturer from testing an ingredient to support future use. Where a manufacturer believes it has adequate data to establish that an active ingredient is GRASE when used for a specific indication, such data may be submitted in an appropriate citizen petition to amend or to establish an OTC drug monograph, as appropriate (see 21 CFR 10.30). Data to support safety and effectiveness can be developed under an investigational new drug (IND) application to support submission and review of an NDA. An NDA, if approved, would make the drug eligible for prescription or OTC marketing

status. For ingredients subject to a final monograph, an NDA may be submitted for a deviation from the monograph (see 21 CFR 330.11 describing an NDA deviation). A product cannot continue to be marketed legally while FDA reviews a petition or NDA.

V. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because few products will likely be affected and those effects would probably be small, FDA does not believe that this proposed rule would have a significant economic impact on a substantial number of small entities. FDA requests comment on this issue.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ‘‘any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year. ’’The current threshold after

adjustment for inflation is $127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

The purpose of this proposed rule is to classify OTC drug products containing certain active ingredients as not GRASE (i.e., nonmonograph) for certain uses for which FDA did not receive any safety and effectiveness data and information. This proposed rule amends § 310.545 to include these product categories and ingredients.

We are not able to identify the number of products that would be affected by this proposed rule, but the number is probably low. Based on our experience, when no data are received after a **Federal Register** request, it often indicates that manufacturers have little or no interest in those ingredients, have phased out or are in the process of phasing out those ingredients, or in some cases are removing the drug claims at issue from the product label. Without actually reading the label for each and every manufacturer's product, we cannot distinguish the numbers of products containing the proposed nonmonograph ingredients from those with monograph ingredients. In addition, some of the affected products are sold alongside cosmetics and drug-cosmetic combination products and we would need to read the actual labels to determine their classifications.

Many of the products affected could still be marketed as OTC drugs if they were reformulated with an active ingredient that is contained in a monograph and complied with that monograph's labeling conditions. For example, blemish remedies covered by this proposal could be reformulated to contain a topical acne active ingredient included in § 333.310. Other products could

be marketed as cosmetics, some with a simple label change and no reformulation. For example, some foot balms and baths covered by this proposal might be able to be marketed as cosmetic products with certain label changes (i.e., deletion of any drug claims). For a few of the product categories, such as bed wetting deterrents and impotency cures, there are currently no OTC drug substitute products on the market, but there are prescription drugs approved for the conditions.

A. What Are the Costs and Benefits Associated With This Proposed Rule?

For products that cannot be reformulated or relabeled to remain on the market, the cost of the rule is the short-run loss of economic profits from the lost sales of those goods once they are removed from the market. Over the long-run, however, manufacturers will be able to produce alternative goods on their existing equipment to partly or fully offset these losses. For the products that remain on the market, the costs include one-time costs to reformulate or relabel the product. We do not know the number of manufacturers that would be affected or the number of products and stockkeeping units (SKUs) (individual products, packages, and sizes) that might need to be relabeled. Many of the products in these categories were probably discontinued some time ago but a few manufacturers will continue to market them until a final rule prohibits such marketing.

The one-time costs to relabel a product include designing the new carton and the inventory loss of any unused current labeling. FDA assumes the same weighted average cost to relabel, inflated to reflect current (2006) dollars, that it estimated for the final rule requiring uniform label formats of OTC drug products (64 FR 13254 at 13279 to 13281, March 17, 1999) (i.e., $3,600 x 1.22),

$4,392 per SKU.[1] We also have estimated inventory loss using data from a study of the costs of the uniform label format rule. With a 6-month implementation period, we have estimated the inventory loss to be between $610 and $3,660 per SKU, depending on product sales, for an estimated weighted average inventory loss of $1,220.[2] For example, if there were 100 SKUs that needed to be relabeled, the total one-time incremental costs would be about $561,200 (100 x ($4,392 + $1,220)).

The cost to reformulate an OTC drug product varies greatly depending on the nature of the product, dosage form, availability of alternative active ingredients, and size of company. If there are monograph ingredients available in the affected product category, the reformulation costs for another product (such as product validation, stability testing, and change in master production documents) would range from $100,000 to $500,000.[3] The decision to reformulate would depend on the manufacturer's product portfolio and projected sales for the reformulated product. Using the midpoint of the range, $300,000, if there were 50 products reformulated the total incremental costs would be about $15 million ($300,000 x 50).

We are not able to estimate the total foregone economic profit from the lost sale of products that would be discontinued by the manufacturers, but sales of the products affected by the proposed rule were never large relative to other OTC drug products. The loss would be largely a short-run loss because other products, including OTC drugs, cosmetics, and dietary supplements,

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[1] The annual Producer Price Index (PPI) for pulp, paper, and allied products, series Id: WPU09 (the major cost driver for labeling) rose by 22 percent between 1998 and 2006 (from 174.1 to 209.8) *http://data.bls.gov*.

[2] The original values from the uniform label formats rule (64 FR 13254), inventory loss between $500 and $3,000 and a weighted average of $1,000, were inflated by 22 percent. The weighting ratio for calculating the average was 80 percent small and private label firms to 20 percent large firms.

[3] Value based on previously published estimations (70 FR 75988 at 75995, December 22, 2005 and 67 FR 78158 at 78167, December 23, 2002).

could be manufactured on the same equipment as the replaced products. In addition, manufacturers could increase production of some of their other existing products or conduct contract manufacturing for other products.

FDA cannot quantify the benefits associated with this proposed rule. Potential benefits include removal from the market of OTC drug products or ingredients that have not been shown to be safe and effective. For the classes of products affected by this proposed rule, consumers would have substitute products available, either OTC or by prescription. The potential benefits from the rule would result from those substitute products having been shown to be safe and effective.

B. What Regulatory Alternatives Has FDA Considered?

We have few alternatives available to us when we determine there are no data or qualitative information available to demonstrate a product's safety and effectiveness. Even without evidence of harm caused by the use of these products, they cannot remain on the market because there is no evidence that they are safe and effective. The two most plausible regulatory alternatives to this proposed rule are a shorter and a longer implementation period. With a shorter implementation period, the products at issue would be removed from the market sooner, but the labeling costs for 100 SKUs would rise to $622,000 with a 3-month compliance period.[4] We could allow a longer implementation period so manufacturers could reduce their inventory of cartons and labels. Costs for relabeling 100 SKUs would fall to $500,200 with a 12-month compliance period, but consumers would be exposed to these products that have not been shown to be safe and effective for a longer period of time.

[4] The weighted average inventory loss would increase to $1,830 per SKU with a 3-month compliance period, but decrease to the irreducible (label inventory can never be used up entirely so whenever there are label changes, there is always some portion of inventory that is scraped) inventory loss of $610 per SKU with a compliance period of 12 months or longer.

Furthermore, it is probable that few products will, in fact, bear substantial labeling costs. Manufacturers have been aware of the status of these ingredients since the December 31, 2003, call-for-data notice and have had sufficient notice and time to adjust their supply of labels to limit the impact in the event this rule becomes final. The 6-month implementation period used in the cost model probably understates the actual average time that manufacturers will have to change labels.

C. What is the Small Business Impact?

The Small Business Administration defines an entity as small in the pharmaceutical manufacturing industry if it has fewer than 750 employees. Over 90 percent of firms in the pharmaceutical industry are classified as small. We assume that 90 to 100 percent of the entities that would be affected by this proposed rule are also small.

The economic impact on individual firms will vary based on the number of affected products they manufacture, and how they respond to the rule. Their response could be to withdraw, relabel, or reformulate the product. If a small entity withdraws the product, its production line could be used for alternative OTC drug, dietary supplement, and cosmetic products, or for contract manufacturing in those industries, thereby limiting economic losses. Labeling costs due to the proposed rule, as explained in this section, would likely be small. The largest potential cost would be reformulation. However, we do not know if a sufficient number of small entities would reformulate a large enough number of products to constitute a significant economic impact on a substantial number of small entities. FDA requests comment on this issue.

VI. Paperwork Reduction Act of 1995

This proposed rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VII. Environmental Impact

FDA has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule, if finalized as proposed, would have a preemptive effect on State law. Section 4(a) of the Executive order requires agencies to ''construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute.'' Section 751 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 379r) is an express preemption provision. Section 751(a) of the act (21 U.S.C. 379r(a)) provides that '' * * * no State or political subdivision of a State may establish or continue in effect any requirement— * * * (1) that relates to the regulation of a drug that is not subject to the requirements of section 503(b)(1) or 503(f)(1)(A); and (2) that is different from or in addition to, or that is otherwise not identical with, a requirement under this Act, the Poison Prevention Packaging Act of 1970 (15 U.S.C. 1471 *et seq.*), or the Fair Packaging and Labeling Act (15 U.S.C. 1451 *et seq.*).''

Currently, this provision operates to preempt States from imposing requirements related to the regulation of nonprescription drug products. (See Section 751(b) through (e) of the act for the scope of the express preemption provision, the exemption procedures, and the exceptions to the provision.) This proposed rule, if finalized as proposed, would classify as not GRASE all of the ingredients in the product categories listed in the December 31, 2003, request for data and information for which FDA did not receive any data and information. Although any final rule would have a preemptive effect, in that it would preclude States from issuing requirements related to these OTC drug products that are different from or in addition to, or not otherwise identical with a requirement in the final rule, this preemptive effect is consistent with what Congress set forth in section 751 of the act. Section 751(a) of the act displaces both State legislative requirements and State common law duties. We also note that even where the express preemption provision is not applicable, implied preemption may arise. *See Geier v. American Honda Co.,* 529 US 861 (2000).

FDA believes that the preemptive effect of the proposed rule, if finalized as proposed, would be consistent with Executive Order 13132. Section 4(e) of the Executive order provides that ''when an agency proposes to act through adjudication or rulemaking to preempt State law, the agency shall provide all affected State and local officials notice and an opportunity for appropriate participation in the proceedings.'' FDA is providing an opportunity for State and local officials to comment on this rulemaking.

List of Subjects in 21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 310 be amended as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360b–360f, 360j, 361(a), 371, 374, 375, 379e; 42 U.S.C. 216, 241, 242(a), 262, 263b–263n.

2. Section 310.545 is amended by redesignating the text of paragraph (a)(20) as paragraph (a)(20)(i), by adding new paragraph (a)(20)(i) heading, by adding and reserving paragraph (a)(20)(ii), by adding paragraphs (a)(10)(viii), (a)(18)(vii), (a)(18)(viii), (a)(20)(iii), (a)(27)(iii), (a)(30) through (a)(45), and (d)(52), and by revising paragraph (d) introductory text and paragraph (d)(2) to read as follows:

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

(a) * * *

(10) * * *

(viii) *Aloe vera and urea drug products*. Any product labeled with claims or directions for use as an external analgesic.

* * * * *

(18) * * *

(vii) *Blister guard drug products—Approved as of* (date 180 days after publication of a final rule in the **Federal Register**).

Beta-hydroxyquinolone

Eugenol

Pyroxylin solution

Any other ingredient labeled with claims or directions for use as a skin protectant blister guard

(viii) *Nipple protectant drug products (in association with breast feeding)—Approved as of* (date 180 days after publication of a final rule in the **Federal Register**).

Cetyl alcohol

Cocoa butter

Cod liver oil

Dimethicone

Glycerin

Glyceryl monostearate

Hard fat

Mineral Oil

Petrolatum

White petrolatum

* * * * *

(20) *Weight control drug products*.—(i) *Ingredients—Approved as of February 10, 1992*.

* * * * *

(iii) *Impregnated body wraps—Approved as of* (date 180 days after publication of a final rule in the **Federal Register**).

Amino acids

Collagen

Magnesium sulfate

Any other ingredient labeled with claims or directions for use for weight control

* * * * *

(27) * * *

(iii) *Aloe vera drug products*. Any product labeled with claims or directions for use as a topical antimicrobial.

* * * * *

(30) *Ammonia as a reflex stimulant*.

Ammonia inhalants

Ammonia spirit, aromatic

Any other ammonia ingredient labeled with claims or directions for use as a reflex stimulant

(31) *Bed-wetting deterrents*.

Belladonna

Any other ingredient labeled with claims or directions for use as a bed-wetting deterrent

(32) *Blemish remedies (excluding topical acne active ingredients in paragraph (a)(1) of this section and § 333.310 of this chapter)*.

Allantoin

Aloe vera gel

Calamine

Ethyl alcohol

Eugenol

Menthol

Oil of eucalyptus

Oil of peppermint

Propylene glycol

Sodium alkylarylpolyether sulfonate

Titanium dioxide

Triclocarban

Triclosan

Any other ingredient labeled with claims or directions for use as a blemish remedy

(33) *Bunion remedies*. Any ingredient(s) labeled with claims or directions for use to treat and/or prevent bunions.

(34) *Drawing salves (excluding products labeled for the treatment of boils in § 310.531 of this chapter)—includes products labeled for the drawing or removing of splinters, slivers, or similar items*.

Ergot fluid extract

Juniper tar (oil of cade)

Magnesium sulfate

Pine tar

Rosin

Rosin cerate

Sulfur

(35) *Foot balms, baths, and other topical dosage forms for any ''foot'' claims (including relieving foot muscle strains and soreness from working out), excluding topical antifungal active ingredients in paragraph (a)(22) of this section and § 333.210 of this chapter and excluding external analgesic active ingredients in paragraphs (a)(10)(i) and (a)(10)(ii) of this section and §§ 348.10*

and 348.12 of the external analgesic drug products tentative final monograph published on February 8, 1983 (48 FR 5852).

Amyl salicylate

Benzalkonium chloride

Cajeput oil

Di-isobutyl phenoxy ethoxy ethyldimethyl benzyl ammonium chloride

Essential oils

Eucalyptus oil

Formaldehyde solution

Glyceryl monostearate

8-Hydroxyquinoline

Iodized botanical oil

Iron sulfate

Isopropyl alcohol

Lanolin

Lithium chloride

Magnesium sulfate

O-benzyl-p-chlorophenol

Oil of thyme

Peppermint oil

Pine needle oil

Potassium iodide

Propylene glycol

Sodium bicarbonate

Sodium chloride

Sodium hypochloride

Sodium lauryl sulfate

Sodium phosphate, tribasic

Sodium sesquicarbonate

Sodium sulfate

Talc

Tragacanth mucilage

Water soluble chlorophyllins

Witch hazel

Zinc oxide

Any other ingredient labeled with claims or directions for use as a foot balm, bath, or other topical dosage form *for any ''foot'' claims (including relieving foot muscle strains and soreness from working out*)

(36) *Impotency cures*.

Yohimbine

Yohimbine hydrochloride

Any other ingredient labeled with claims or directions for use as an impotency cure

(37) *Medicated bath preparations*.

Acetylated lanolin

Alkyl aryl polyether alcohol

Colloidal sulfur

Cottonseed oil

Di-isopropyl sebacate

Drometrizole

Iron sulfate

Isopropyl myristate

Isopropyl palmitate

Isostearic acid

Lanolin alcohols extract

Lanolin oil

Liquid petrolatum

Lithium chloride

Magnesium sulfate

Mineral oil

Natural and essential oils

Nonoxynol-5

Octoxynol-3

Oxybenzone

PEG–4 dilaurate

PEG–8 dioleate

PEG–40 sorbitan peroleate

PEG–200 dilaurate

Peruvian balsam

PPG–15

Pine needle oil

Potassium iodide

Stearyl ether oleth-2

Sodium bicarbonate

Sodium carbonate

Sodium chloride

Sodium hyposulfate

Sodium lauryl sulfate

Sodium sesquicarbonate

Sodium sulfate

Tar distillate

Vitamin E

Water soluble chlorophyllins

Any other ingredient labeled with claims or directions for use as a medicated bath preparation

(38) *Nonantimicrobial skin wound cleansers* (previously listed as ''detergents'' in call-for-data notices).

Tincture of Green Soap

Phenolate sodium

Poloxamer 188

Any other ingredient labeled with claims or directions for use as a nonantimicrobial skin wound cleanser

(39) *Prickly heat products*.

Aluminum hydroxide gel

Zinc carbonate

Zinc oxide

Any other ingredient labeled with claims or directions for use for prickly heat

(40) *Urethral topical products for males*. Any product labeled with claims or directions for use to treat and/or prevent male urethral problems.

(41) *Urinary acidifiers*.

Ammonium chloride

Ascorbic acid

Any other ingredient labeled with claims or directions for use as an urinary acidifier

(42) *Urinary alkalinizers*.

Sodium bicarbonate

Any other ingredient labeled with claims or directions for use as an urinary alkalinizer

(43) Wet *dressings (excluding astringent active ingredients in paragraph (a)(18)(ii) of this section and skin protectant and astringent active ingredients in §§ 347.10 and 347.12 of this chapter*).

Aloe vera

Calcium polysulfide

Calcium thiosulfate

Oxyquinoline sulfate

Sodium propionate

Any other ingredient labeled with claims or directions for use as a wet dressing

(44) *Wound wash saline*.

Sodium chloride solution

Sterile sodium chloride solution

Any other ingredient labeled with claims or directions for use as wound wash saline

(45) *Urea*. Any product containing urea for any labeled claims.

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(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)(52) of this section.

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

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(52) [Date 180 days after date of publication of a final rule in the **Federal Register**], for products subject to paragraphs (a)(10)(viii), (a)(18)(vii), (a)(18)(viii), (a)(20)(iii), (a)(27)(iii), and (a)(30) through (a)(45) of this section.

Dated: June 9, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

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