and that the use of the drugs in combination has the potential to reduce the amount of CFC's released into the atmosphere. In this regard, FDA notes that albuterol sulfate and ipratropium bromide are currently listed separately (i.e., not in combination) in 1A2.125(e) as essential uses of CFC's. Based on the evidence currently before it, FDA also agrees that the use of a metered-dose delivery system for this product does not involve asignificant release of CFC's into the atmosphere. Therefore, FDA is amending 1A2.125(e) to include metered-dose albuterol sulfate and ipratropium bromide in combination for oral inhalation in the list of essential uses of CFC propellants.

A copy of the proposed rule was provided to the Administrator.

III. Comments on the Proposed Rule

Interested persons were given 30 days to comment on the proposed rule. FDA received one comment regarding the proposed rule. The comment pointed out that CFC-free MDI's for albuterol sulfate and other drugs are generally expected to be developed and marketed in the near future, and that the availability of alternative propellants will undercut the factual basis for FDA's determination that the use of CFC's in MDI's is medically necessary. The comment suggested that FDA's determination be made conditionally, and that FDA reexamine the "medical essentiality" of the MDI if and when a CFC-free albuterol sulfate MDI is approved. The comment also suggested that future rulemaking may be necessary to provide for the transition between MDI's containing CFC's and CFC-free MDI's.

FDA is aware of the development of CFC-free MDI's and shares the comment's concerns that proper provision should be made for the transition between MDI's containing CFC's and CFC-free MDI's. FDA, working with EPA, is developing a policy on this matter at this time, and anticipates that a rulemaking procedure may be necessary to implement that policy. Section 2.125 does not provide for a "conditional" listing as an essential use and to provide for such a "conditional" listing in this rule would be beyond the scope of the proposal. Any phase-out or reformulation requirement for MDI's containing albuterol sulfate and ipratropium bromide in combination undertaken because of the availability of alternative propellants will be undertaken as part of a properly implemented general policy on the elimination of CFC's from MDI's and other similar products.

IV. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). 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 final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under 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 the agency is not aware of any adverse impact this final rule will have on any small entities, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

List of Subjects in 21 CFR Part 2

Administrative practice and procedure, Cosmetics, Devices, Drugs, Foods.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 2 is amended as follows:

PART 2—GENERAL ADMINISTRATIVE RULINGS AND DECISIONS

1. The authority citation for 21 CFR part 2 continues to read as follows:

Authority: Secs. 201, 301, 305, 402, 408, 409, 501, 502, 505, 507, 512, 601, 701, 702, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 335, 342, 346a, 348, 351, 352, 355, 357, 360b, 361, 371, 372, 374); 15 U.S.C. 402, 409.

2. Section 2.125 is amended by adding new paragraph (e)(14) to read as follows:

§ 2.125 Use of chlorofluorocarbon propellants in self-pressurized containers.

* * * * *

(e) * * *

(14) Metered-dose ipratropium bromide and albuterol sulfate, in combination, administered by oral inhalation for human use.

* * * * *

Dated: March 29, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–8826 Filed 4–8–96; 8:45 am]

BILLING CODE 4160–01–F

---

21 CFR Part 341

[Docket No. 76N–052G]

RIN 0910–AA01

Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Products Containing Diphenhydramine Citrate or Diphenhydramine Hydrochloride; Enforcement Policy

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; enforcement policy.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule, and a statement of its enforcement policy, providing for the use of diphenhydramine citrate or diphenhydramine hydrochloride as an antitussive and an antihistamine for treating concurrent symptoms in either single-ingredient or combination drug products. The agency will include the permitted combination products that may include diphenhydramine citrate or diphenhydramine hydrochloride in the final monograph for over-the-counter (OTC) cold, cough, allergy, bronchodilator, and antiasthmatic (cough-cold) combination drug products. The OTC marketing of combination drug products containing diphenhydramine citrate or diphenhydramine hydrochloride is being permitted pending completion under the OTC drug review of the final monograph for OTC cough-cold combination drug products. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: April 9, 1996.

ADDRESSES: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–105), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2304.

SUPPLEMENTARY INFORMATION:

I. Background

In the Federal Register of February 23, 1995 (60 FR 10286), FDA proposed to amend the tentative final monograph for OTC cough-cold combination drug products to classify combination drug products containing the ingredients diphenhydramine citrate or diphenhydramine hydrochloride. As part of that proposal, FDA discussed the use of a single dose of diphenhydramine citrate or diphenhydramine hydrochloride as an antitussive and antihistamine for treating concurrent symptoms either in an OTC cough-cold single-ingredient or combination drug product. The agency proposed specific labeling for drug products containing diphenhydramine citrate or diphenhydramine hydrochloride for concurrent antitussive and antihistamine use. At that time, the agency did not allow marketing to occur because this was a new concept. The agency stated that it wanted to receive public comment on the proposed new concept and on the proposed labeling approach before marketing of such products began. The agency added that it would issue a notice of enforcement policy at a later date to state whether marketing may begin prior to the issuance of the final monograph for OTC cough-cold combination drug products.

In response to the proposed amendment, two drug manufacturers submitted comments. Copies of the comments received are on public display in the Dockets Management Branch (address above).

After carefully reviewing the comments received, the agency is issuing a final rule containing the required labeling of drug products containing diphenhydramine citrate or diphenhydramine hydrochloride for concurrent antitussive and antihistamine use either as a single ingredient product or as a single ingredient in combination with other active ingredients. The agency is allowing the marketing of combination products prior to the completion of the final monograph for OTC cough-cold combination drug products, subject to the risk that the agency may in the final monograph adopt a different position that could require relabeling, recall, or other regulatory action. Marketing of any such product with labeling not in accord with the final monograph may result in regulatory action against the product, the manufacturer, or both.

II. The Agency's Conclusions on the Comments

1. One comment requested that the agency allow a broader dosage range for a single-ingredient drug product containing diphenhydramine hydrochloride for concurrent use as both an antitussive and an antihistamine. The comment requested a dose of 25 milligrams (mg) every 4 to 6 hours (h), not to exceed 150 mg in 24 h, instead of restricting the dose to every 4 h. The comment stated that the shorter antitussive dosing interval (every 4 h) would limit other ingredients in a combination product with a broader dosing interval (every 4 to 6 h). The comment questioned whether restricting these combination products to a 4-h dosing interval would increase the number of consumer exposures to diphenhydramine over a 24-h period. The comment added that a dosing regimen of 25 mg every 4 to 6 h, not to exceed 150 in 24 h, would reduce exposure to both diphenhydramine and other ingredients in the combination on a faster timing that may be consistent with a safe yet satisfactory level of effectiveness.

When the agency included diphenhydramine citrate and diphenhydramine hydrochloride in the OTC antitussive drug products monograph (59 FR 29172 at 29174, June 3, 1994), the agency concluded that diphenhydramine hydrochloride is generally recognized as safe and effective in an antitussive dosage of 25 mg every 4 h, not to exceed 150 mg in 24 h. The agency stated that the available clinical data and marketing history of products containing diphenhydramine citrate or diphenhydramine hydrochloride for antitussive use do not support a broader dosage range (4 to 6 h). The comment did not submit any data to show that 25 mg diphenhydramine hydrochloride is effective over a 6-h period. Without any supporting data, the agency has no basis to establish such a dosage. While the proposed every 4 to 6 h dosage may potentially be safer, there is no evidence that it is effective. Therefore, in this final rule, the agency is including the following adult dosage for diphenhydramine hydrochloride drug products for concurrent antitussive and antihistamine use: 25 mg every 4 h, not to exceed 150 mg in 24 h.

2. Both comments requested that marketing of diphenhydramine in the same product as both an antitussive and antihistamine be allowed prior to the issuance of the final monograph for OTC cough-cold combination drug products. One comment noted that an OTC drug product in which diphenhydramine citrate or diphenhydramine hydrochloride serves both as the antitussive and antihistamine component for treating concurrent symptoms would reduce the number of ingredients in the product. The comment stated that allowing marketing of such a product would be consistent with FDA's policy to expose the user of OTC drug products to the smallest number of ingredients possible at the lowest possible dosage consistent with a satisfactory level of effectiveness. The comment added that permitting an antitussive indication on currently marketed OTC drug products labeled with an antihistamine-only indication would not be a safety concern.

The agency agrees with the comments and is permitting the OTC marketing of such products pending completion under the OTC drug review of a final monograph covering OTC cough-cold combination drug products. The labeling required for these products appears in new § 341.70 (21 CFR 341.70) of the cough-cold drug products monograph.

Specifically, when diphenhydramine citrate or diphenhydramine hydrochloride is labeled for concurrent use, the statement of identity is "antihistamine/cough suppressant" or "antihistamine/antitussive (cough suppressant)." The indications are combined from §§ 341.72(b) and 341.74(b) (21 CFR 341.72(b) and 341.74(b)). The warnings are combined from § 341.72(c)(1), (c)(2), (c)(4), and (c)(6) and § 341.74(c)(1), (c)(2), (c)(3), and (c)(4). The warnings for diphenhydramine for antitussive use in § 341.74(c)(4) encompass all of the same warnings for diphenhydramine for antihistamine use in § 341.72(c)(1), (c)(2), (c)(4), and (c)(6). In addition, the labeling must include the required warnings for antitussive use in § 341.74(c)(1), (c)(2), and (c)(3), as applicable (depending on the ages for which the product is labeled). Thus, when diphenhydramine citrate or diphenhydramine hydrochloride as a single ingredient is labeled for both antihistamine and antitussive use, all of the warnings in § 341.74 of the antitussive monograph must be used. At this time, diphenhydramine citrate or diphenhydramine hydrochloride may only be marketed for concurrent antitussive and antihistamine use in the permitted combinations of active ingredients proposed in § 341.40(d), (e), and (f). (See 60 FR 10286 at 10292.) The agency will discuss the other permitted combinations proposed in § 341.40 in the final rule for OTC cough-cold combination drug products.

The agency recognizes there are other ingredients such as menthol in the final monograph for OTC antitussive drug products (52 FR 30042, August 12, 1987), and in the proposed rule for OTC oral health care drug products (56 FR 48302, September 24, 1991), that may be used for treating concurrent symptoms. The agency will address menthol for treating concurrent symptoms in either a single-ingredient or combination drug product in the final monograph for OTC cough-cold combination drug products in a future issue of the **Federal Register** and is reserving § 341.70(b) for this ingredient at this time.

The agency proposed new combinations as well as single ingredients with diphenhydramine labeled as both an antihistamine and antitussive (60 FR 10286). The agency added § 341.70 for labeling for diphenhydramine-containing drug products for concurrent antitussive and antihistamine use under the heading: *Labeling of drug products containing diphenhydramine citrate or diphenhydramine hydrochloride for concurrent antitussive and antihistamine use either as a single ingredient or as a single ingredient in combination with other active ingredients.* In order to provide a general heading for diphenhydramine, menthol, and other OTC cough-cold ingredients that may be used for treating concurrent symptoms (in either a single-ingredient or combination drug product), the agency is revising the heading proposed in § 341.70 to read: *Labeling of OTC drug products containing ingredients that are used for treating concurrent symptoms (in either a single-ingredient or combination drug product).* The agency is placing the labeling information for diphenhydramine citrate and diphenhydramine hydrochloride in § 341.70(a) and is reserving § 341.70(b) for menthol.

3. One comment requested monograph status for the combination of a drug recognized as both an antitussive and an antihistamine (such as diphenhydramine) with another oral antitussive (such as dextromethorphan) and antihistamine when there is some advantage over the active ingredients alone. The agency intends to address this matter in the final monograph for OTC cough-cold combination drug products.

No comments were received in response to the agency's request for specific comment on the economic impact of the proposed rule.

III. Analysis of Impacts

FDA has examined the impacts of this final rule and notice of enforcement policy under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). 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 the final rule for OTC cough-cold combination products containing diphenhydramine citrate or diphenhydramine hydrochloride for concurrent antitussive and antihistamine use is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the rule is not a significant regulatory action as defined by the Executive Order and, thus, is not subject to review under 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. This final rule and notice of enforcement policy allow the use of diphenhydramine citrate or diphenhydramine hydrochloride as an active ingredient for concurrent antitussive and antihistamine use in OTC cough-cold drug products.

The agency's enforcement policy, which is set out in § 330.13 (21 CFR 330.13), relating to OTC marketing of drug products containing certain ingredients that are under consideration in FDA's review of OTC drug products, makes it clear that FDA may by notice in the **Federal Register** permit interim marketing of these products. Manufacturers may choose to market such products at their option. Accordingly, the agency certifies that this final rule and notice of enforcement policy will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

IV. Paperwork Reduction Act of 1995

FDA concludes that the labeling requirements in this document are not subject to review by the Office of Management and Budget because they do not constitute a "collection of information" under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the labeling is a "public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

V. Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) 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.

VI. Enforcement Status

The agency advises that any OTC drug product containing diphenhydramine citrate or diphenhydramine hydrochloride intended for concurrent use as an antitussive and antihistamine in either a single-ingredient or combination drug product may be marketed pending completion of the final monograph, subject to the risk that the agency may, in the final monograph, adopt a different position that could require relabeling, recall, or other regulatory action. Marketing of such products with labeling not in accord with the labeling required by § 341.70 may result in regulatory action against the product, the marketer, or both.

VII. Opportunity for Comments

Interested persons may submit written comments to the Dockets Management Branch (address above). Such comments will be considered in determining whether further amendments to or revisions of this enforcement policy are warranted. Three copies of all comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 341

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 341 is amended as follows:

PART 341—COLD, COUGH, ALLERGY, BRONCHODILATOR, AND ANTIASTHMATIC DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

1. The authority citation for 21 CFR part 341 continues to read as follows:

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

2. New § 341.70 is added to subpart C to read as follows:

§ 341.70 Labeling of OTC drug products containing ingredients that are used for treating concurrent symptoms (in either a single-ingredient or combination drug product).

The statements of identity, indications, warnings, and directions for use, respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) *For products containing diphenhydramine citrate and diphenhydramine hydrochloride identified in § 341.14(a)(5) and (a)(6).* The labeling of the product contains the established name of the drug, if any, and identifies the product as an "antihistamine/cough suppressant" or "antihistamine/antitussive (cough suppressant)." The indications shall be combined from §§ 341.72(b) and 341.74(b). The warnings shall be combined from §§ 341.72(c)(1), (c)(2), (c)(4), and (c)(6) and 341.74(c)(1), (c)(2), (c)(3), and (c)(4). Alternatively, all of the warnings in § 341.74(c) shall be used. The directions for OTC labeling shall follow §§ 341.74(d)(1)(iv) or (d)(1)(v), as applicable. The directions for professional labeling shall follow § 341.90(j) or (k), as applicable.

(b) (Reserved)

Dated: March 28, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–8761 Filed 4–8–96; 8:45 am]

BILLING CODE 4160–01–F

21 CFR Part 510

New Animal Drugs; Change of Sponsor Name

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations to reflect a change of sponsor name from A. L. Pharma, Inc., to ALPHARMA INC.

EFFECTIVE DATE: April 9, 1996.

FOR FURTHER INFORMATION CONTACT: Thomas J. McKay, Center for Veterinary Medicine (HFV–102), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–0213.

SUPPLEMENTARY INFORMATION: A. L. Pharma, Inc., One Executive Dr., Fort Lee, NJ 07024, has informed FDA of a change of sponsor name to ALPHARMA INC. Accordingly, FDA is amending the regulations in 21 CFR 510.600(c)(1) and (c)(2) to reflect the change of sponsor name.

List of Subjects in 21 CFR Part 510

Administrative practice and procedure, Animal drugs, Labeling, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Center for Veterinary Medicine, 21 CFR part 510 is amended as follows:

PART 510—NEW ANIMAL DRUGS

1. The authority citation for 21 CFR part 510 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 512, 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 360b, 371, 379e).

§ 510.600 [Amended]

2. Section 510.600 *Names, addresses, and drug labeler codes of sponsors of approved applications* is amended in the table in paragraph (c)(1) by removing the entry for "A. L. Pharma, Inc." and by alphabetically adding a new entry for "ALPHARMA INC." and in the table in paragraph (c)(2) in the entry "046573" by removing the sponsor name "A. L. Pharma, Inc." and adding in its place "ALPHARMA INC."

Dated: March 28, 1996.

Robert C. Livingston,

Director, Office of New Animal Drug Evaluation, Center for Veterinary Medicine.

[FR Doc. 96–8762 Filed 4–8–96; 8:45 am]

BILLING CODE 4160–01–F

21 CFR Part 573

[Docket No. 90F–0297]

Food Additives Permitted in Feed and Drinking Water of Animals; Formaldehyde

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of formaldehyde (37 percent aqueous solution), at the rate of 5.4 pounds per ton (2.5 kilograms per ton) (lb/t) (kg/t) as an antimicrobial food additive for maintaining complete poultry feeds salmonella negative for up to 14 days. This action is in response to a food additive petition filed by Anitox Corp.

DATES: Effective April 9, 1996; written objections and requests for hearing by May 9, 1996.

ADDRESSES: Submit written objections and requests for hearing to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Daniel G. McChesney, Center for Veterinary Medicine (HFV–222), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–1728.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of October 18, 1990 (55 FR 42272), FDA announced that a food additive petition (FAP 2215) had been filed by Anitox Corp., P.O. Box 1929, Buford, GA 30518. The petition proposed to amend the food additive regulations in § 573.460 *Formaldehyde* (21 CFR 573.460) to provide for the safe use of formaldehyde as an antimicrobial agent against bacteria, mold, and yeast in feed, at a level of 1.65 to 2.65 pounds per ton for fishmeal and animal byproduct meals, and at a level of 0.66 to 1.32 pounds per ton for complete feeds or feed ingredients. The notice of filing of FAP 2215 provided for a 60-day comment period. No comments have been received.

The sponsor amended the petition since it was originally filed. The amended petition proposed that § 573.460 be amended to provide for the safe use of formaldehyde (37 percent aqueous solution), at the rate of 5.4 lb/t (2.5 kg/t), as an antimicrobial food additive for maintaining complete poultry feeds salmonella negative for up to 14 days.

FDA has evaluated data in the petition and other relevant material. FDA concludes that the proposed food additive use of formaldehyde (37 percent aqueous solution) as an antimicrobial for maintaining complete poultry feeds salmonella negative for up to 14 days is safe. Therefore, the food additive regulations in § 573.460 is amended.

Formaldehyde can be life threatening if improperly handled. The proposed label for formaldehyde (37 percent aqueous solution) acknowledges this fact and identifies the product as a poison. The label provides for worker safety and further minimizes safety concerns for persons handling formaldehyde by containing adequate directions for use, strong cautionary statements about potential adverse respiratory effects, information about emergency aid in case of inhalation,