

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Incorporation by reference, Safety.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends 14 CFR part 39 of the Federal Aviation Regulations as follows:

PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 continues to read as follows:

Authority: 49 U.S.C. App. 1354(a), 1421 and 1423; 49 U.S.C. 106(g); and 14 CFR 11.89.

§ 39.13 [Amended]

2. Section 39.13 is amended by adding the following new airworthiness directive:

93-01-10. **British Aerospace:** Amendment 39-8464. Docket 92-NM-90-AD.

Applicability: Model DH/HS/BAe 125 series airplanes equipped with Garrett engines; as listed in British Aerospace Service Bulletin SB.24-289-3267A, B, C, D, E, F & G, Revision 1, dated April 10, 1992; certificated in any category.

Compliance: Required as indicated, unless accomplished previously.

To prevent battery overheating and/or damage of voltage sensitive avionics equipment, accomplish the following:

(a) Within 180 days after the effective date of this AD, modify the Generator Control Circuit (GCU) circuitry in accordance with British Aerospace Service Bulletin SB.24-289-3267 A, B, C, D, E, F & G, Revision 1, dated April 10, 1992.

(b) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Standardization Branch, ANM-113, FAA, Transport Airplane Directorate. Operators shall submit their requests through an appropriate FAA Principal Maintenance Inspector, who may add comments and then send it to the Manager, Standardization Branch, ANM-113.

Note: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Standardization Branch, ANM-113.

(c) Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate the airplane to a location where the requirements of this AD can be accomplished.

(d) The modification shall be done in accordance with British Aerospace Service Bulletin SB.24-289-3267 A, B, C, D, E, F & G, Revision 1, dated April 10, 1992. (NOTE: The issue date of this British Aerospace Service Bulletin SB.24-289-3267 A, B, C, D, E, F & G is indicated only on "page 1 of 57";

no other page of this document is dated.)

This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR Part 51. Copies may be obtained from British Aerospace, PLC, Librarian for Service Bulletins, P.O. Box 17414, Dulles International Airport, Washington, DC. Copies may be inspected at the FAA, Transport Airplane Directorate, 1601 Lind Avenue, SW., Renton, Washington; or at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.

(e) This amendment becomes effective on March 2, 1993.

Issued in Renton, Washington, on January 8, 1993.

N.B. Martenson,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.

[FR Doc. 93-1813 Filed 1-25-93; 8:45 am]

BILLING CODE 4910-13-U

14 CFR Part 39

[Docket No. 92-NM-170-AD; Amendment 39-8460; AD 93-01-06]

Airworthiness Directives; Short Brothers Model SD3-60 Series Airplanes

AGENCY: Federal Aviation Administration, DOT.

ACTION: Final rule.

SUMMARY: This amendment supersedes an existing airworthiness directive (AD), applicable to certain Short Brothers Model SD3-60 series airplanes, that currently requires repetitive inspections of the horizontal stabilizer rear spar web fuselage attachment fitting area for defective rivets, and repair, if necessary. This amendment clarifies that the aft face of the front spar web need not be inspected. This amendment is prompted by a report that a requirement to inspect the aft face of the front spar web was inadvertently included in the existing AD. The actions specified by this AD are intended to ensure that only the appropriate area of the horizontal stabilizer is inspected.

DATES: Effective March 2, 1993.

The incorporation by reference of certain publications listed in the regulations is approved by the Director of the Federal Register as of March 2, 1993.

ADDRESSES: The service information referenced in this AD may be obtained from Short Brothers, PLC, 2011 Crystal Drive, suite 713, Arlington, Virginia 22202-3719. This information may be examined at the Federal Aviation Administration (FAA), Transport Airplane Directorate, Rules Docket, 1601 Lind Avenue, SW., Renton,

Washington; or at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.

FOR FURTHER INFORMATION CONTACT: Mr. Bud Schroeder, Aerospace Engineer, Standardization Branch, ANM-113, FAA, Transport Airplane Directorate, 1601 Lind Avenue, SW., Renton, Washington 98055-4056; telephone (206) 227-2148; fax (206) 227-1320.

SUPPLEMENTARY INFORMATION: A proposal to amend part 39 of the Federal Aviation Regulations by superseding AD 89-07-14, Amendment 39-6176 (54 FR 12588, March 28, 1989), which is applicable to certain Short Brothers Model SD3-60 series airplanes, was published in the Federal Register on October 15, 1992 (57 FR 47302). The action proposed to clarify that the aft face of the front spar web need not be inspected.

Interested persons have been afforded an opportunity to participate in the making of this amendment. Due consideration has been given to the single comment received.

The commenter supports the proposed rule.

After careful review of the available data, including the comment noted above, the FAA has determined that air safety and the public interest require the adoption of the rule as proposed.

The FAA estimates that 51 airplanes of U.S. registry will be affected by this AD, that it will take approximately 8 work hours per airplane to accomplish the required actions, and that the average labor rate is \$55 per work hour. Based on these figures, the total cost impact of the AD on U.S. operators is estimated to be \$22,440, or \$440 per airplane. This total cost figure assumes that no operator has yet accomplished the requirements of this AD.

The regulations adopted herein will not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 12612, it is determined that this final rule does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

For the reasons discussed above, I certify that this action (1) is not a "major rule" under Executive Order 12291; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) will not have a significant economic impact, positive or negative, on a substantial number of small entities under the criteria of the Regulatory

Flexibility Act. A final evaluation has been prepared for this action and it is contained in the Rules Docket. A copy of it may be obtained from the Rules Docket at the location provided under the caption "ADDRESSES."

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Incorporation by reference, Safety.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends 14 CFR part 39 of the Federal Aviation Regulations as follows:

PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 continues to read as follows:

Authority: 49 U.S.C. App. 1354(a), 1421 and 1423; 49 U.S.C. 106(g); and 14 CFR 11.89.

§ 39.13 [Amended]

2. Section 39.13 is amended by removing amendment 39-6176 (54 FR 12588, March 28, 1989), and by adding

a new airworthiness directive (AD), amendment 39-8460, to read as follows:

93-01-06. Short Brothers, PLC: Amendment 39-8460. Docket 92-NM-170-AD. Supersedes AD 89-07-14, Amendment 39-6176.

Applicability: Model SD3-60 series airplanes, serial numbers SH3601 through SH3691, inclusive, and SH3694; certificated in any category.

Compliance: Required as indicated, unless accomplished previously.

To prevent loss of the structural integrity of the horizontal stabilizer attachment to the fuselage, accomplish the following:

(a) Visually inspect, in accordance with the schedule listed below, the forward face of the rear spar web for defective rivets between fuselage attach fitting at 12.5" left and right of the airplane center line, in accordance with Shorts Service Bulletin SD360-55-16, dated April 1988.

(1) For airplane serial numbers SH3680 through SH3691, inclusive, and SH3694, and for airplanes affected by this AD that have used only a 15 degree takeoff flap setting since before or upon reaching 5,000 flights, inspection is required within the next 100 flights after April 28, 1989 (the effective date of AD 89-07-14, Amendment 39-6176), or prior to the total accumulation of 12,000 flights, whichever occurs later. Repeat the inspection at intervals not to exceed 1,500 flights.

(2) For all other airplanes affected by this AD, inspection is required within the next 100 flights after April 28, 1989, or prior to the accumulation of 8,000 flights, whichever occurs later. Repeat the inspection at intervals not to exceed 1,000 flights.

(b) If defective rivets are found, prior to further flight, repair in accordance with Part II of Shorts Service Bulletin SD360-55-16, dated April 1988. After repair, continue inspections in accordance with paragraph (a) of this AD.

(c) The repetitive inspections required by paragraph (a) of this AD may be terminated following completion of the modification of the horizontal stabilizer spar webs (Modification 7998), in accordance with Shorts Service Bulletin SD360-55-12, Revision 2, dated November 1986.

(d) An alternative method of compliance or adjustment of the compliance time that provides an acceptable level of safety may be used if approved by the Manager, Standardization Branch, ANM-113, FAA, Transport Airplane Directorate. Operators shall submit their requests through an appropriate FAA Principal Maintenance Inspector, who may add comments and then send it to the Manager, Standardization Branch, ANM-113.

Note: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Standardization Branch, ANM-113.

(e) Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate the airplane to a location where the requirements of this AD can be accomplished.

(f) The inspections, repair, and modification shall be done in accordance with the following Shorts service bulletins, which contain the specified effective pages:

Service bulletin referenced and date	Page No.	Revision level shown on page	Date shown on page
SD360-55-16, April 1988	1-7	Original	Apr. 1988.
SD360-55-12, Revision 2, November 1986	1, 4-5, 7-44	2	Nov. 1986.
	2-3, 6	Original	Apr. 1986.

This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR Part 51. Copies may be obtained from Short Brothers, PLC, 2011 Crystal Drive, Suite 713, Arlington, Virginia 22202-3719. Copies may be inspected at the FAA, Transport Airplane Directorate, 1601 Lind Avenue, SW., Renton, Washington; or at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC.

(g) This amendment becomes effective on March 2, 1993.

Issued in Renton, Washington, on December 29, 1992.

James V. Devany,

Acting Manager, Transport Airplane Directorate, Aircraft Certification Service.
[FR Doc. 93-1816 Filed 1-25-93; 8:45 am]

BILLING CODE 4910-13-U

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 2

[Docket No. 87P-0422/CP]

Chlorofluorocarbon Propellants in Self-Pressurized Containers; Addition to List of Essential Uses

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: This document codifies the Food and Drug Administration's (FDA's) decision to grant the petition of Fisons Corp. to add metered-dose nedocromil sodium for oral inhalation to the list of products containing a chlorofluorocarbon (CFC) propellant for an essential use. Essential use products,

which are listed in 21 CFR Part 2—General Administrative Rulings and Decisions, at § 2.125(e) (21 CFR 2.125(e)), are exempt from FDA's ban on the use of CFC propellants in FDA-regulated products. In the agency's decision that is now being codified, FDA concluded that the product provides a unique health benefit that would be unavailable without the use of a chlorofluorocarbon.

DATES: Effective January 26, 1993; written comments by March 29, 1993.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Philip L. Chao, Center for Drug Evaluation and Research (HFD-362), Food and Drug Administration, 7500

Standish Pl., Rockville, MD 20855, 301-295-8046.

SUPPLEMENTARY INFORMATION:

I. Background

Under § 2.125 Use of chlorofluorocarbon propellants in self-pressurized containers (21 CFR 2.125), any food, drug, device, or cosmetic in a self-pressurized container that contains a chlorofluorocarbon propellant for a nonessential use is adulterated or misbranded, or both, under the Federal Food, Drug, and Cosmetic Act (the act). This prohibition is based on scientific research indicating that chlorofluorocarbons may reduce the amount of ozone in the stratosphere and thereby increase the amount of ultraviolet radiation reaching the earth. An increase in ultraviolet radiation may increase the incidence of skin cancer, change the climate, and produce other adverse effects of unknown magnitude on humans, animals, and plants.

Section 2.125(d) exempts from the adulteration and misbranding provisions of § 2.125(c) certain products containing chlorofluorocarbon propellants that FDA determines provide a unique health benefit that would not be available without the use of a chlorofluorocarbon. These products are referred to in the regulation as essential uses of chlorofluorocarbon and are listed in § 2.125(e).

Under § 2.125(f), any person may petition the agency to request additions to the list of uses considered essential. To demonstrate that the use of a chlorofluorocarbon is essential, the petition must be supported by an adequate showing that: (1) There are no technically feasible alternatives to the use of a chlorofluorocarbon in the product; (2) the product provides a substantial health, environmental, or other public benefit unobtainable without the use of the chlorofluorocarbon; and (3) the use does not involve a significant release of chlorofluorocarbons into the atmosphere or, if it does, the release is warranted by the benefit conveyed.

II. Petition Received by FDA

Fisons Corp. submitted a petition under § 2.125(f) and part 10 (21 CFR part 10) requesting an addition to the list of chlorofluorocarbon uses considered essential. The petition is on file under the docket number appearing in the heading of this document and may be seen in the Dockets Management Branch (address above). The petition requested that metered-dose nedocromil sodium for oral inhalation be included in § 2.125(e) as an essential use of

chlorofluorocarbon. The petition contained a discussion supporting the position that there are no technically feasible alternatives to the use of chlorofluorocarbon in the product. It included information showing that no alternative delivery systems (e.g., the hand-operated pump) or other substitute propellants (e.g., compressed gases) can dispense the drug for effective inhalation therapy as safely and uniformly as chlorofluorocarbon propellants. Also, the petition stated that the product provided a substantial health benefit that would not be obtainable without the use of chlorofluorocarbon. In this regard, the petition contained information to support the use of this product as a bronchodilator. Further, the petition stated that, unlike a bulb nebulizer, the vial and the mouthpiece for the product are portable and can be easily carried in a purse or a pocket. The petition asserted that metered-dose nedocromil sodium would not result in a significant release of chlorofluorocarbon propellants into the atmosphere because the total daily amount released per product is estimated to be approximately 1.088 grams.

III. FDA's Review of the Petition

Because the agency agreed that, for some asthmatic patients, the use of metered-dose nedocromil sodium provides a special benefit that would be unavailable without the use of chlorofluorocarbons, FDA has granted the petition. FDA also agrees that the use of a metered-dose delivery system for this product does not involve a significant release of chlorofluorocarbons into the atmosphere. Therefore, FDA is including metered-dose nedocromil sodium administered by oral inhalation in the list of essential uses of chlorofluorocarbon propellants. The purpose of this document is to add the product to the list in § 2.125(e), for public information purposes.

IV. Effective Date

The petition was granted on December 12, 1992. This codification is effective January 26, 1993. FDA had previously allowed a period for public comment prior to exempting a product from the agency's ban on the use of CFC propellants. Upon further consideration, however, FDA has concluded that a comment period prior to granting an essential use exemption is not necessary. A decision to grant an essential use petition for a CFC propellant is not a rule but an informal decision. Therefore, additions to the list of essential use products (21 CFR

2.125(e)) differ from most material published in the *Code of Federal Regulations* in that the items listed in § 2.125(e) are not rules, but are listings in the *Code of Federal Regulations* to facilitate public availability of important information. Furthermore, because these products are considered essential, providing for a comment period prior to granting an exemption would be contrary to the public interest, particularly for those patients who gain important therapeutic benefits from these products, and would be adversely affected from any delay in their availability. Therefore, FDA will no longer provide for a comment period before granting an essential use exemption. However, FDA is providing a 60-day period for public comment for views on whether the exemption should be modified or revoked.

V. Request for Comments

Interested persons may, on or before March 29, 1993, submit to the Dockets Management Branch (address above) written comments regarding this rule. Two copies of any 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 office above between 9 a.m. and 4 p.m., Monday through Friday.

VI. Environmental Impact

The agency has carefully considered the potential environmental effects of this action under 21 CFR part 25 and has concluded that this action will not have a significant effect on the human environment and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 2

Administrative practice and procedure, Cosmetics, 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)(13) to read as follows:

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

* * * * *

(e) * * * * *

(13) Metered-dose nedocromil sodium human drugs administered by oral inhalation.

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Dated: January 15, 1993.

Michael R. Taylor,
Deputy Commissioner for Policy.
[FR Doc. 93-1792 Filed 1-25-93; 8:45 am]
BILLING CODE 4160-01-F

21 CFR Part 172

[Docket No. 90F-0446]

Food Additives Permitted for Direct Addition to Food for Human Consumption: Dimethyl Dicarbonate

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 dimethyl dicarbonate as a yeast inhibitor in dealcoholized and low alcohol wines. This action is in response to a petition filed by Miles, Inc. (formerly Mobay Corp.).

DATES: Effective January 26, 1993; written objections and requests for a hearing by February 25, 1993.

ADDRESSES: Written objections may be sent to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Rosalie M. Angeles, Center for Food Safety and Applied Nutrition (HFS-207), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-254-9515.

SUPPLEMENTARY INFORMATION: In a notice published in the Federal Register of November 20, 1990 (55 FR 48292), FDA announced that a food additive petition (FAP 0A4213) had been filed by Mobay Corp., 1575 I St. NW., Washington, DC 20005, proposing that § 172.133 *Dimethyl dicarbonate* (21 CFR 172.133) be amended to provide for the safe use of dimethyl dicarbonate as a yeast inhibitor in dealcoholized and low

alcohol wine. The petitioner currently operates under the name of Miles, Inc.

FDA has evaluated data in the petition and other relevant material and concludes that the proposed use of dimethyl dicarbonate in dealcoholized wine and low alcohol wine is safe. Dealcoholized wine and low alcohol wine will generally be consumed as substitutes for, rather than in addition to, wine. Thus, these uses will not increase consumer exposure to dimethyl dicarbonate or its decomposition products compared to that already deemed safe at the time § 172.133 was promulgated (53 FR 41325, October 21, 1988).

Dimethyl dicarbonate is unstable in aqueous solution and breaks down almost immediately after addition to beverages. In wine and other aqueous liquids, the principal breakdown products are methanol and carbon dioxide. Methyl ethyl carbonate, as well as carbomethoxy amino- and hydroxy-adducts of amines, sugars, and fruit acids, are also formed in minor amounts. Dimethyl carbonate is present as an impurity in dimethyl dicarbonate. Dimethyl dicarbonate also may react with traces of ammonia or ammonium ions in wines to form trace quantities of methyl carbamate, a compound that has been shown to cause cancer in laboratory animals (Ref. 1). In dealcoholized wine and low alcohol wine, the level of methyl carbamate formation is expected to be similar to that formed in standard wine because the critical parameters governing methyl carbamate formation, Ph and ammonium ion concentration, are not expected to be altered by the dealcoholization process (reverse osmosis) employed in the manufacture of dealcoholized wine and low alcohol wine (Ref. 2).

I. Determination of Safety

Under section 409(c)(3)(A) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(3)(A)), the so-called "general safety clause" of the statute, a food additive cannot be approved for a particular use unless a fair evaluation of the data available to FDA establishes that the additive is safe for that use. Under section 409(c)(5)(A) of the act (21 U.S.C. 348(c)(5)(A)), among the relevant factors to be considered in determining whether a proposed use of a food additive is safe is the probable consumption of the additive and of any substance formed in or on food because of the use of the additive. The concept of safety embodied in the Food Additives Amendment of 1958 is explained in the legislative history of the provision:

"Safety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstance." (H. Rept. 2284, 85th Cong., 2d sess. 4 (1958)). This definition of safety has been incorporated into FDA's food additive regulations (21 CFR 170.3(i)). The anticancer or Delaney clause of the Food Additives Amendment (section 409(c)(3)(A) of the act) provides further that no food additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal.

In the past, FDA has refused to approve the use of an additive that contained or was suspected of containing even minor amounts of a carcinogenic chemical, even though the additive as a whole had not been shown to cause cancer. The agency now believes, however, that developments in scientific technology and experience with risk assessment procedures make it possible for FDA to establish the safety of additives that contain carcinogenic chemicals but that have not themselves been shown to cause cancer.

In the preamble to the final rule permanently listing D&C Green No. 6 published in the Federal Register of April 2, 1982 (47 FR 14138), FDA explained the basis for approving the use of a color additive that had not been shown to cause cancer, even though it contained a carcinogenic impurity. Since that decision, FDA has approved the use of other color additives and food additives on the same basis.

An additive that has not been shown to cause cancer but that contains a carcinogenic impurity, or whose use will lead to the formation of trace amounts of a carcinogenic substance in or on food, may be properly evaluated under the general safety clause of the statute using risk assessment procedures to determine whether there is a reasonable certainty that no harm will result from the proposed use of the additive.

The agency's position is supported by *Scott v. FDA*, 728 F. 2d 322 (6th Cir. 1984). That case involved a challenge to FDA's decision to approve the use of D&C Green No. 5, which contains a carcinogenic chemical but has itself not been shown to cause cancer. Relying heavily on the reasoning in the agency's decision to list this color additive, the U.S. Court of Appeals for the Sixth Circuit rejected the challenge to FDA's action and affirmed the listing regulation.

II. Safety of the Petitioned Use

In evaluating the safety of the food additive, dimethyl dicarbonate, FDA reviewed the byproducts formed during hydrolysis and the reaction of the food additive with other constituents found in wines. The results of that evaluation were discussed in the preamble to the final rule establishing § 172.133 and are included in the discussion below.

FDA finds that the petitioned use level of 100 to 200 parts per million (ppm) of dimethyl dicarbonate will result in virtually no exposure of consumers to the additive itself. Dimethyl dicarbonate is unstable in aqueous solution and breaks down almost immediately after addition to the food (beverages) to form primarily carbon dioxide and methanol. The instability of dimethyl dicarbonate is confirmed by data submitted by the petitioner showing that dimethyl dicarbonate cannot be detected by analysis of food to which it has been added (Ref. 2).

To establish that dimethyl dicarbonate is safe for use as an inhibitor of yeast in wine, dealcoholized wine, and low alcohol wine, the petitioner submitted data from acute, subchronic, and chronic toxicity studies. In the subchronic and chronic toxicity studies, rats received either water, orange juice, or wine treated with 4,000 ppm of dimethyl dicarbonate (20 times the proposed use level in wine or wine substitutes) as the drinking fluid while the controls received water, orange juice, or wine. These studies showed no adverse effects from water, orange juice, or wine treated with dimethyl dicarbonate.

In another chronic toxicity study, dogs received either water or orange juice treated with 4,000 ppm of dimethyl dicarbonate as the drinking fluid. This study also revealed no adverse effects from the water or orange juice treated with dimethyl dicarbonate.

The petitioner also submitted a two-generation reproduction study in which rats received drinking fluids that were treated with dimethyl dicarbonate (4,000 ppm). This study revealed no treatment-related adverse effects. These chronic and other multigeneration (lifetime) studies of dimethyl dicarbonate also did not produce any evidence that dimethyl dicarbonate is a carcinogen.

III. Safety of Substances That May Be Present in Wine or Wine Substitutes Due to the Use of the Additive

Because dimethyl dicarbonate may contain impurities and decomposes into other chemical species when added to

aqueous solutions, such as wine, dealcoholized wine, and low alcohol wine, FDA has also evaluated the safety of the chemicals found in wine, dealcoholized wine, and low alcohol wine as a result of the use of dimethyl dicarbonate.

A. Minor Impurities and Reaction Products

The minor reaction products formed in wine, dealcoholized wine, and low alcohol wine from the use of dimethyl dicarbonate include methylethyl carbonate and carbomethoxy amino- and hydroxy-adducts of amines, sugars, and naturally occurring fruit acids such as lactic acid, citric acid, and ascorbic acid (vitamin C). Dimethyl carbonate, an impurity in dimethyl dicarbonate, is also present in minor amounts in wine, dealcoholized wine, and low alcohol wine, as a result of the use of the additive.

The petitioner presented data to show that the addition of 100 to 200 ppm of dimethyl dicarbonate to wine, dealcoholized wine, or low alcohol wine is effective in inhibiting the growth of most species of yeast found in such products. According to the U.S. Department of Agriculture Food Consumption Survey, 1977-1978, the 90th percentile consumption level for "drinkers only" of these products is 232 grams per person per day (g/person/day). Based upon a level of addition of dimethyl dicarbonate of 100-200 ppm, on consumption of 232 g of wine or wine substitutes, and on data submitted by the petitioner, the agency estimates that the maximum daily consumption of the minor reaction products resulting from the addition of dimethyl dicarbonate to wine or wine substitutes is from 2 to 5 milligrams per person per day (mg/person/day). Because these reaction products were formed in the dimethyl dicarbonate-treated fluids (water and wine) used in the subchronic and chronic rat and dog studies submitted by the petitioner, the safety of the reaction products is evidenced by the findings of no treatment-related adverse effects in these studies.

The safety of methylethyl carbonate was further evaluated in a subchronic toxicity study in rats in which the substance was added to the drinking water at levels of 0, 1,000, 3,000, and 10,000 ppm for 3 months. The average daily consumption of methylethyl carbonate ranged from approximately 0.1 mg/kilogram (kg) to 1 g/kg body weight/day. No adverse effects in rats from drinking the water treated with methylethyl carbonate were seen in this study.

A teratogenicity study was conducted with pregnant female rats of the Long-Evans FB30 strain. The animals were fed diets containing methylethyl carbonate at levels of 0, 100, 1,000, and 10,000 ppm. No signs of toxicity were noted. However, there was a dose-related reduction in fluid intake and a slight decrease in body weight gain in pregnant females receiving methylethyl carbonate throughout the gestational period. The reduced fluid intake appears to be attributable to the bad taste and smell of the water containing the methylethyl carbonate. All test and control females were sacrificed at day 20, Cesarean sections were performed, and the fetuses were examined. No embryotoxic or teratogenic effects were found in this examination.

To establish the safety of dimethyl carbonate, the petitioner submitted a subchronic study in rats in which dimethyl carbonate was incorporated into the drinking water at levels of 0, 1,000, 3,000 and 10,000 ppm. An increase in body weight gain was observed in male rats at all treatment levels. No adverse effects were found in this study at any level.

B. Carbon Dioxide

Carbon dioxide, one of the principal hydrolysis products of dimethyl dicarbonate, is a natural product of animal metabolism. Carbon dioxide is present in solution as the carbonate and bicarbonate anions, however, and is routinely used to carbonate beverages (Ref. 3). The levels of carbon dioxide present in wine or wine substitutes as a result of the use of dimethyl dicarbonate are well below the levels found in carbonated beverages. Thus, the agency has no evidence that carbon dioxide would be harmful under the intended conditions of use.

C. Methanol

Methanol is the principal reaction product of concern resulting from the addition of dimethyl dicarbonate to wine. Theoretically, complete hydrolysis of dimethyl dicarbonate would yield 2 moles of methanol and 2 moles of carbon dioxide from each mole of dimethyl dicarbonate added to wine or wine substitute. On a weight basis, this yield corresponds to approximately 48 mg of methanol for each 100 mg of the additive added to a liter (L) of wine or wine substitute. To estimate a worst-case exposure of consumers to methanol from the proposed use of the additive, the agency assumed complete hydrolysis of dimethyl dicarbonate to methanol and carbon dioxide. Based on the addition of 100 to 200 mg dimethyl dicarbonate to 1 L of wine or wine

substitute and on a beverage intake of 232 g/person/day (90th percentile consumption level), the agency estimates that the daily intake of methanol from this use of dimethyl dicarbonate would range from 11 to 22 mg/day (0.18 to 0.36 mg/kg body weight for a 60-kg person) (Ref. 4).

The agency considers the daily intake of methanol from the addition of dimethyl dicarbonate to wine or wine substitutes, even when added to the amount of methanol naturally present in other foods such as fresh fruits and vegetables and grain alcohol, to be safe. The no observed adverse effect level (NOAEL) in humans for methanol is 71 to 84 mg/kg body weight (Ref. 5). Because the NOAEL is derived from studies in humans, an acceptable daily intake (ADI) of 7.1 to 8.4 mg/kg body weight (426 to 500 mg/person for a 60-kg adult) is derived from the NOAEL by using a 10-fold safety factor (Ref. 5). The levels of methanol that occur naturally in fruit juices average 140 mg/L (140 ppm) and an additional 50 to 100 mg/L (50 to 100 ppm) may result from the use of dimethyl dicarbonate in wine (Ref. 4). Based upon consumption data from the U.S. Department of Agriculture Food Consumption Survey, 1977-1978, the total methanol exposure from these sources would be up to 50 to 60 mg/person/day (or one-tenth of ADI). There is, therefore, a large margin of safety between the methanol intake from the subject uses and the amount which can be safely ingested.

D. Methyl Carbamate

1. *Carcinogenicity.* Reaction of dimethyl dicarbonate with naturally occurring ammonia or ammonium ions in wine or wine substitutes may result in the formation of trace amounts of methyl carbamate, which has been shown to be carcinogenic in rats (Ref. 1). FDA has evaluated the safety of this reaction byproduct using risk assessment procedures to estimate the upper-bound limit of risk presented by the presence of this chemical as an impurity in wine treated with dimethyl dicarbonate. Based on this evaluation, the agency has concluded that under the proposed conditions of use, dimethyl dicarbonate is safe.

2. *Basis for evaluation.* The risk assessment procedures that FDA used in this evaluation are similar to the methods that it has used to examine the risk associated with the presence of minor carcinogenic impurities in various food and color additives (see e.g., 49 FR 13018, April 2, 1984). This evaluation of the risk from the use of dimethyl dicarbonate has two aspects: (1) Assessment of the probable exposure

to methyl carbamate produced in food from the use of dimethyl dicarbonate; and (2) extrapolation of the risk observed in the animal bioassay to the conditions of probable exposure to humans.

Based on an estimate of the level of methyl carbamate that may be produced from the addition of dimethyl dicarbonate to wine or wine substitutes as a yeast inhibitor, as well as the estimated average daily intake of wine over a lifetime, FDA estimated the worst-case exposure to methyl carbamate to be 2.4 micrograms per person per day ($\mu\text{g}/\text{person}/\text{day}$) (Refs. 4, 6, and 7).

The agency used data in a carcinogenesis bioassay report on methyl carbamate conducted by the National Toxicology Program (NTP) (Ref. 6) to estimate the upper-bound level of lifetime human risk from exposure to this chemical stemming from the proposed use of dimethyl dicarbonate. The bioassay report consisted of results from studies of methyl carbamate in both rats and mice. The bioassay in B6C3F1 mice was reported by NTP to be negative. The bioassay of methyl carbamate in F344/N rats consisted of a 2-year chronic study and a parallel study with sacrifices at 6, 12, and 18 months. The 2-year study employed a high dosage level of 200 mg/kg body weight. The parallel study employed one dosage level of 400 mg/kg body weight. In the 2-year chronic study, an increase in hepatocellular neoplasms was found at the high dose in female F344/N rats. In the parallel study, hepatocellular neoplasms were found at 6 months in both sexes, and the sacrifices at the later times revealed a classic progression from benign to highly malignant neoplasms dependent upon the length of time of exposure. The NTP concluded that "there was clear evidence of carcinogenic activity for male and female F344/N rats given methyl carbamate as indicated by incidences of hepatocellular neoplastic nodules and hepatocellular carcinoma" (Ref. 1).

3. *Results of evaluation.* Using the NTP bioassay report, the Center for Food Safety and Applied Nutrition's Quantitative Risk Assessment Committee (QRAC) estimated the human cancer risk from the potential exposure to methyl carbamate stemming from the proposed use of dimethyl dicarbonate as a yeast inhibitor in wine (Ref. 7).

The QRAC used a quantitative risk assessment procedure (linear proportional model) to extrapolate from the dose used in the animal experiment through zero to cover the very low doses

expected to be encountered under the proposed conditions of use of the additive. This procedure is not likely to underestimate the actual risk from the very low doses and may, in fact, exaggerate it because the extrapolation models used are designed to estimate the maximum risk consistent with the data. For this reason, the estimate can be used with confidence to determine to a reasonable certainty whether any harm will result from the proposed conditions and a maximum 200 ppm level of use of the food additive.

Based on a worst-case exposure to methyl carbamate (2.4 $\mu\text{g}/\text{person}/\text{day}$), FDA estimated, using the linear proportional model, that the upper-bound limit of individual lifetime risk from potential exposure to methyl carbamate is 2.4×10^{-8} or less than 1 in 42 million. Because of numerous conservatisms in the exposure estimate, lifetime averaged individual daily exposure to methyl carbamate is expected to be substantially less than the estimated daily intake, and, therefore, the calculated upper-bound risk would be less than 1 in 42 million. Thus, the agency concludes that there is a reasonable certainty of no harm from the exposure to methyl carbamate that may result from the use of up to 200 ppm of dimethyl dicarbonate in wine, dealcoholized wine, or low alcohol wine.

4. *Need for specifications.* The agency also has considered whether a specification is necessary to control the amount of methyl carbamate that may be formed in wine or wine substitutes treated with the additive. The agency finds that the amount of methyl carbamate formed in wine or wine substitutes may be controlled by limiting the amount of dimethyl dicarbonate that may be added to the wine or wine substitute to 200 ppm or less rather than setting a specification for the level of methyl carbamate impurity in the wine product. The petitioner submitted data to show that the maximum level of methyl carbamate impurity formed in commercial wine is less than 10 parts per billion for each 100 ppm of dimethyl dicarbonate added to wine. A 200 ppm level of dimethyl dicarbonate is sufficient to control the growth of all significant genera and species of yeast in wine and in wine substitutes that have been adequately pasteurized or ultra-filtered according to current good manufacturing practices to reduce the microbial count to 500 per milliliter or less.

E. Ethyl Carbamate

The agency is aware that ethyl carbamate, an animal carcinogen occurs

as a "natural" contaminant in wine. The agency is in the process of obtaining as much information as possible about the levels of such ethyl carbamate contamination. In addition, in cooperation with the wine industry, a program has been instituted to find and control the formation of ethyl carbamate so as to reduce its concentration to the lowest levels possible (Ref. 8).

The petitioner submitted studies in which gas chromatography/mass spectroscopy was used to measure the formation of ethyl carbamate (urethane) in dimethyl dicarbonate treated-wine and model wine solutions, in the presence of high concentrations of ammonium ions. These studies, conducted over a 12-month period, did not show formation of ethyl carbamate in excess of endogenous levels found in wine. These studies also did not show evidence of formation of ethyl carbamate by transesterification of methyl carbamate. Thus, there is no evidence that the use of dimethyl dicarbonate affects the level of ethyl carbamate in wine.

IV. Conclusion on Safety

FDA has evaluated all of the data in the petition pertaining to the use of dimethyl dicarbonate in dealcoholized wine and low alcohol wine and has determined that the additive is safe for its proposed use.

To ensure the safe use of the additive, FDA, under 21 U.S.C. 348(c)(1)(A) and in accordance with section 403 of the act (21 U.S.C. 343), finds that it is necessary to require that the label of the package containing the additive include, in addition to other information required by the act: (1) The name of the additive, "dimethyl dicarbonate," and (2) directions to provide that not more than 200 ppm of dimethyl dicarbonate will be added to the dealcoholized wine or low alcohol wine.

In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition (address above) by appointment with the information contact person listed above. As provided in 21 CFR 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

V. Environmental Impact

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact

on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

VI. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Methyl Carbamate in F344/N Rats and B6C3F1 Mice, NTP, U.S. Department of Health and Human Services, Report No. 328, 1986.
2. Memorandum from the Food and Color Additives Review Section to the Direct Additives Branch, "Dimethyl Dicarbonate (DMDC) in Dealcoholized and Low-alcohol Wines," dated October 4, 1990.
3. Mones, Martha, "Carbonated Beverages," in "Encyclopedia of Chemical Technology," 4:710-725, 1978.
4. Memorandum from the Regulatory Food Chemistry Branch to the GRAS Review Branch, "Dimethyl Dicarbonate in Wine. Submission of September 5, 1986; Exposure Estimate for Methyl Carbamate and Methanol in Wine," dated January 14, 1987.
5. Memorandum from the Standards and Monitoring Branch to the Division of Regulatory Guidance, "Methanol in Brandy," dated December 18, 1989.
6. Memorandum from QAC to the Office of Toxicological Sciences, "Methyl Carbamate in Wine," dated October 28, 1986.
7. Memorandum from QAC to the Office of Toxicological Sciences, "Methyl Carbamate in Wine," dated November 20, 1987.
8. "Ethyl Carbamate Voluntary Program," Final Agreement Between the Wine Institute, the Association of American Vintners, and FDA, January 7, 1988.

VII. Objections

Any person who will be adversely affected by this regulation may at any time on or before February 25, 1993, file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and

analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation 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 172

Food additives, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 172 is amended as follows:

PART 172—FOOD ADDITIVES PERMITTED FOR DIRECT ADDITION TO FOOD FOR HUMAN CONSUMPTION

1. The authority citation for 21 CFR part 172 continues to read as follows:

- Authority:** Secs. 201, 401, 402, 409, 701, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 348, 371, 376).
2. Section 172.133 is amended by revising the introductory text and paragraphs (b) and (c)(2) to read as follows:

§ 172.133 Dimethyl dicarbonate.

Dimethyl dicarbonate (CAS Reg. No. 4525-33-1) may be safely used in wine, dealcoholized wine, and low alcohol wine, in accordance with the following prescribed conditions:

- * * * * *
- (b) The additive is used or intended for use as an inhibitor of yeast in wine, dealcoholized wine, and low alcohol wine under normal circumstances of bottling where the viable yeast count has been reduced to 500 per milliliter or less by current good manufacturing practices such as flash pasteurization or filtration. The additive may be added to wine, dealcoholized wine, or low alcohol wine in an amount not to exceed 200 parts per million (ppm).

(c) * * *

(2) Directions to provide that not more than 200 ppm of dimethyl dicarbonate will be added to the wine, dealcoholized wine, or low alcohol wine.

* * * * *

Dated: January 15, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 93-1795 Filed 1-25-93; 8:45 am]

BILLING CODE 4160-01-F

21 CFR Part 520

Oral Dosage Form New Animal Drugs; Sulfadimethoxine Oral Solution and Soluble Powder

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations to reflect approval of an abbreviated new animal drug application (ANADA) filed by Agri Laboratories, Ltd. The ANADA provides for the use of a generic sulfadimethoxine oral solution as an antibacterial in drinking water for the treatment of broiler and replacement chickens for coccidiosis, fowl cholera, and infectious coryza; meat-producing turkeys for coccidiosis and fowl cholera; and in drinking water and as a drench for the treatment of dairy calves, dairy heifers, and beef cattle for shipping fever complex, bacterial pneumonia, calf diphtheria, and foot rot.

EFFECTIVE DATE: January 26, 1993.

FOR FURTHER INFORMATION CONTACT:

Steven D. Vaughn, Center for Veterinary Medicine (HFV-135), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-295-8648.

SUPPLEMENTARY INFORMATION: Agri Laboratories, Ltd., P.O. Box 3103, St. Joseph, MO 64503, is the sponsor of ANADA 200-030, which provides for the use of a generic sulfadimethoxine oral solution as an antibacterial in drinking water for the treatment of broiler and replacement chickens for coccidiosis, fowl cholera, and infectious coryza; meat-producing turkeys for coccidiosis and fowl cholera; and in drinking water and as a drench for the treatment of dairy calves, dairy heifers, and beef cattle for shipping fever complex, bacterial pneumonia, calf diphtheria, and foot rot.

Approval of ANADA 200-030 for Agri Laboratories, Ltd.'s sulfadimethoxine 12.5 percent oral solution is as a generic copy of Hoffmann-La Roche's NADA 031-205 for Albon® 12.5 percent drinking water solution (sulfadimethoxine). The ANADA is approved as of December 31, 1992, and 21 CFR 520.2220a is amended to reflect the approval. The basis for approval is discussed in the freedom of information summary.

In accordance with the freedom of information provisions of part 20 (21 CFR part 20) and § 514.11(e)(2)(ii) (21 CFR 514.11(e)(2)(ii)), a summary of safety and effectiveness data and information submitted to support approval of this application may be seen in the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857, between 9 a.m. and 4 p.m., Monday through Friday.

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 520

Animal drugs.

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 520 is amended as follows:

PART 520—ORAL DOSAGE FORM NEW ANIMAL DRUGS

1. The authority citation for 21 CFR part 520 continues to read as follows:

Authority: Sec. 512 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b).

2. Section 520.2220a is amended by revising the section heading and paragraphs (a), (b), and the introductory text of paragraph (e) to read as follows:

§ 520.2220a Sulfadimethoxine oral solution and soluble powder.

(a) *Specifications.* (1) The oral solution contains 12.5 percent (3.75 grams per ounce) sulfadimethoxine.

(2) Each packet of powder contains the equivalent of 94.6 grams of sulfadimethoxine (as the sodium salt).

(b) *Sponsors.* See Nos. 000004 and 057561 in § 510.600(c) of this chapter.

* * * * *

(e) *Conditions of use.* The oral solution is administered as a cattle drench or diluted as directed to prepare drinking water. The powder is used to prepare a drench or drinking water. The concentrations and uses of the various solutions are as follows:

* * * * *

Dated: January 14, 1993.

Gerald B. Guest,

Director, Center for Veterinary Medicine.

[FR Doc. 93-1794 Filed 1-25-93; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of the Assistant Secretary for Public and Indian Housing

24 CFR Parts 905 and 906

[Docket No. R-93-1529; FR-2810-N-04]

RIN 2577-AA90

Extension of Section 5(h) Homeownership Program for Public and Indian Housing

AGENCY: Office of the Assistant Secretary for Public and Indian Housing, HUD.

ACTION: Notice.

SUMMARY: This notice extends the period that the interim rule for the Section 5(h) Homeownership Program will be in effect, from January 20, 1993 until the effective date of final rule.

EFFECTIVE DATE: January 20, 1993.

FOR FURTHER INFORMATION CONTACT:

C. Wayne Hunter, Senior Homeownership Programs Advisor, Office of Public and Indian Housing, Department of Housing and Urban Development, 451 Seventh Street SW., room 4118, Washington, DC 20410. Telephone number (202) 708-4233, TDD (202) 708-0850. (These are not toll-free numbers.)

SUPPLEMENTARY INFORMATION: A regulatory codification of the requirements of the Section 5(h) Homeownership Program for public (24 CFR part 906) and Indian (24 CFR part 905) housing was published as an interim rule in the Federal Register on September 20, 1991 (56 FR 47852). The primary statutory mandate for this program is section 5(h) of the United States Housing Act of 1937 (Act). Secondary authority is found in section 6(c)(4)(D) of the Act.

As the primary statutory mandate, section 5(h) authorizes PHAs to sell public housing to residents "on such terms and conditions as the [PHA] may determine." That emphasis on local initiative and discretion is reinforced by section 6(c)(4)(D), which speaks of "the development by local housing authority managements of viable homeownership opportunity programs." These two complementary portions of the Act constitute what is essentially one provision that established the statutory