DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 74

[Docket No. 98C–0158]

Listing of Color Additives For Coloring Meniscal Tacks; D&C Violet No. 2; Confirmation of Effective Date

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; confirmation of effective date.

SUMMARY: The Food and Drug Administration (FDA) is confirming the effective date of July 20, 1999, for the final rule that appeared in the **Federal Register** of June 18, 1999 (64 FR 32803), and that amended the color additive regulations to provide for the safe use of D&C Violet No. 2 to color absorbable meniscal tacks made from poly(L-lactic acid).

DATES: Effective date confirmed: July 20, 1999.

FOR FURTHER INFORMATION CONTACT: Ellen M. Waldron, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3089.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 18, 1999 (64 FR 32803), FDA amended the color additive regulations in § 74.3602 *D&C Violet No. 2* (21 CFR 74.3602) to provide for the safe use of D&C Violet No. 2 to color absorbable meniscal tacks made from poly(L-lactic acid).

FDA gave interested persons until July 19, 1999, to file objections or requests for a hearing. The agency received no objections or requests for a hearing on the final rule. Therefore, FDA finds that the effective date of the final rule that published in the **Federal Register** of June 18, 1999, should be confirmed.

List of Subjects in 21 CFR Part 74

Color additives, Cosmetics, Drugs, Foods, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10), notice is given that no objections or requests for a hearing were filed in response to the June 18, 1999, final rule. Accordingly, the amendments issued thereby became effective July 20, 1999.

Dated: October 21, 1999.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation

[FR Doc. 99–28108 Filed 10–27–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 172

[Docket No. 84F–0050]

Food Additives Permitted for Direct Addition to Food for Human Consumption; Polysorbate 60

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 polysorbate 60 as an emulsifier in ice cream, frozen custard, fruit sherbet, and nonstandardized frozen desserts. This action is in response to a petition filed by ICI Americas, Inc.

DATES: This regulation is effective October 28, 1999; written objections and requests for a hearing by November 29, 1999.

ADDRESSES: Submit written objections to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Andrew D. Laumbach, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3071.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of March 20, 1984 (49 FR 10364), FDA announced that a food additive petition (FAP 4A3774) had been filed by ICI Americas, Inc., Wilmington, DE 19897 (now, Wilmington, DE 19850–5391). The petition proposed to amend the food additive regulations to provide for the safe use of polysorbate 60 (polyoxyethylene (20) sorbitan monostearate) as an emulsifier in ice cream, frozen custard, ice milk, fruit sherbet, and nonstandardized frozen desserts when used alone or in combination with polysorbate 65 and/or polysorbate 80. The agency notes that the standard of identity for ice milk was removed from the Code of Federal Regulations in the final rule published in the **Federal Register** of September 14, 1994 (59 FR 47080). Therefore, the amendment to provide for the use of polysorbate 60 in ice milk will be included under the provisions for nonstandardized desserts in the regulation set forth below.

In its evaluation of the safety of this additive, FDA has reviewed the safety of the additive itself and the chemical impurities that may be present in the additive resulting from its manufacturing process. Although the additive itself has not been shown to cause cancer, it has been found to contain minute amounts of unreacted 1,4-dioxane and ethylene oxide, which are carcinogenic impurities resulting from the manufacture of the additive. Residual amounts of reactants, and manufacturing aids, such as 1,4-dioxane and ethylene oxide are commonly found as contaminants in chemical products, including food additives.

I. Determination of Safety

Under the general safety standard of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(3)(A)), 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. FDA's food additive regulations (21 CFR 170.3(i)) define safe as ''a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.''

The food additives anticancer, or Delaney, clause of the act (21 U.S.C. 348(c)(3)(A)) provides that no food additive shall be deemed safe if it is found to induce cancer when ingested by man or animal. Importantly, however, the Delaney clause applies to the additive itself and not to impurities in the additive. That is, where an additive itself has not been shown to cause cancer, but contains a carcinogenic impurity, the additive is properly evaluated under the general safety standard using risk assessment procedures to determine whether there is a reasonable certainty that no harm will result from the intended use of the additive (*Scott* v. *FDA*, 728 F. 2d 322 (6th Cir. 1984)).

II. Safety of Petitioned Use of the Additive

FDA estimates that the petitioned use of the additive will result in an estimated mean daily intake of 39 milligrams per person per day (mg/p/d). The cumulative exposure to all ethoxylated direct additives from previously regulated uses is estimated to be 166 mg/p/d (Ref. 1).

The agency has reviewed the available toxicological data on the additive and concludes that the estimated dietary exposure resulting from the petitioned use of the additive is safe. The calculated cumulative intake of ethoxylated direct food additives (166 mg/p/d) when added to the estimated intake of polysorbate 60 for use in frozen dairy desserts (39 mg/p/d) (i.e., 205 mg/p/d) is much lower than the current estimated acceptable daily intake of 1,500 mg/p/d for all regulated polysorbates, thus supporting the safety of the petitioned use (Ref. 2).

FDA has evaluated the safety of this additive under the general safety standard, considering all available data and using risk assessment procedures to estimate the upper-bound limit of lifetime human risk presented by 1,4-dioxane and ethylene oxide, the carcinogenic chemicals that may be present as impurities in the additive. The risk evaluation of 1,4-dioxane and ethylene oxide has two aspects as follows: (1) Assessment of exposure to the impurities from the petitioned use of the additive; and (2) extrapolation of the risk observed in the animal bioassays to the conditions of exposure to humans.

A. 1,4-Dioxane

FDA has estimated that exposure to 1,4-dioxane from the petitioned uses of the additive in frozen dairy desserts would not exceed 19 nanograms (ng)/p/d (Ref. 1). The agency used data from a carcinogenesis bioassay on 1,4-dioxane, conducted by the National Cancer Institute (Ref. 3), to estimate the upper-bound limit of lifetime human risk from exposure to this chemical resulting from the petitioned use of the additive. The results of the bioassay on 1,4-dioxane demonstrated that the material was carcinogenic for female rats under the conditions of the study. The authors reported that the test material caused significantly increased incidence of squamous cell carcinomas and hepatocellular tumors in female rats.

Based on the agency's estimate that exposure to 1,4-dioxane from the use of the additive in frozen dairy desserts will not exceed 19 ng/p/d, FDA estimates that the upper-bound limit of lifetime human risk from the petitioned use of the subject additive in frozen dairy desserts is 6.7×10^{-10} or 6.7 in 10 billion (Ref. 4). Because of the numerous conservative assumptions used in calculating the exposure estimate, the actual lifetime-averaged individual exposure to 1,4-dioxane is likely to be substantially less than the estimated exposure, and therefore, the probable lifetime human risk would be less than the upper-bound limit of lifetime human risk. Thus, the agency concludes that there is reasonable certainty that no harm from exposure to 1,4-dioxane would result from the petitioned use of the additive.

B. Ethylene oxide

FDA has estimated that exposure to ethylene oxide from the petitioned use of the additive in the manufacture of frozen dairy desserts would not exceed 7.7 ng/p/d (Ref. 1). The agency used data from a carcinogenesis bioassay on ethylene oxide conducted by the Institute of Hygiene, University of Mainz, Germany (Ref. 5), to estimate the upper-bound limit of lifetime human risk from exposure to this chemical resulting from the petitioned use of the additive. The results of the bioassay on ethylene oxide demonstrated that ethylene oxide was carcinogenic for female rats under the conditions of the study. The author reported that the test material caused significantly increased incidence of squamous cell carcinomas of the forestomach and carcinomas *in situ* of the glandular stomach.

Based on the agency's estimate that the exposure to ethylene oxide will not exceed 7.7 ng/p/d, FDA estimates that the upper-bound limit of lifetime human risk from the petitioned use of the subject additive in frozen dairy desserts is 1.5×10^{-8} or 1.5 in 100 million (Ref. 4). Because of the numerous conservative assumptions used in calculating the exposure estimate, the actual lifetime-averaged individual exposure to ethylene oxide is likely to be substantially less than the estimated exposure, and therefore, the probable lifetime human risk would be less than the upper-bound limit of lifetime human risk. Thus, the agency concludes that there is reasonable certainty that no harm from exposure to ethylene oxide would result from the petitioned use of the additive.

C. Need for Specifications

The agency also has considered whether specifications are necessary to control the amount of 1,4-dioxane and ethylene oxide as impurities in polysorbate 60 for use in frozen dairy desserts (Ref. 6). The agency finds that specifications are not necessary for the following reasons: (1) Because of the low levels at which 1,4-dioxane and ethylene oxide may be expected to remain as impurities following production of the additive, the agency would not expect the impurities to become components of food at other than extremely low levels; and (2) the upper-bound limits of lifetime human risk from exposure to 1,4-dioxane and ethylene oxide are very low, 6.7 in 10 billion and 1.5 in 100 million, respectively.

III. Conclusion

FDA has evaluated data in the petition and other relevant material. Based on this information, the agency concludes that the proposed use of the additive is safe, and that the additive will achieve its intended technical effect as an emulsifier in frozen dairy desserts. Therefore, the agency concludes that the regulations in 21 CFR 172.836 should be amended as set forth below.

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 by appointment with the information contact person listed above. As provided in § 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.

IV. 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.

V. Paperwork Reduction Act of 1995

This final 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.

VI. Objections

Any person who will be adversely affected by this regulation may at any time on or before November 29, 1999, 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.

VII. 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. Memorandum from CFSAN's Chemistry Review Branch (HFS–247) to CFSAN's Direct Additives Branch (HFS–217) concerning ''FAP 4A3774 & FAP 4A3824: Ethylene Oxide and 1,4-dioxane Residues in Polysorbate 60, Direct Additives Branch Request of 9/3/93,'' dated September 28, 1993.

2. Memorandum from CFSAN's Additives Evaluation Branch No. 1 (HFS–226) to CFSAN's Direct Additives Branch (HFS-217) concerning ''Chemistry Review Branch (HFS–247) Memorandum of March 1, 1996, EDI's for Polyoxyethylene (20) Sorbitan Monostearate (Polysorbate 60) in Frozen Dairy Desserts and Coconut Milk Drinks, and Risks Estimates for Residual Ethylene Oxide and 1,4-dioxane,'' dated March 13, 1996.

3. ''Bioassay of 1,4-Dioxane for Possible Carcinogenicity,'' National Cancer Institute, NCI–CG–TR–80, 1978.

4. Memorandum from CFSAN's Division of Petition Control (HFS–215) to the Executive Secretary, Quantitative Risk Assessment Committee (HFS–308) concerning ''Estimation of Upper-bound Lifetime Risk from Ethylene Oxide (EO) and 1,4-dioxane (DX) Residues in Polysorbate 60: Subject of Food Additive Petition 4A3774 (ICI Americas, Inc.),'' dated December 14, 1998.

5. Dunkelberg, H., ''Carcinogenicity of Ethylene Oxide and 1,2-Propylene Oxide Upon Intragastric Administration to Rats,'' *British Journal of Cancer*, 46: pp. 924–933, 1982.

6. Memorandum to the Record from CFSAN's Division of Petition Control (HFS–215) concerning ''FAP 4A3774—Consideration of a Need for Specification for 1,4-dioxane in a Regulation for Polysorbate 60 use in Frozen Dairy Desserts,'' dated December 14, 1998.

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: 21 U.S.C. 321, 341, 342, 348, 371, 379e.

2. Section 172.836 is amended by adding new paragraph (c)(16) to read as follows:

§ 172.836 Polysorbate 60.

* * * * *

(c) * * *

(16) As an emulsifier in ice cream, frozen custard, fruit sherbet, and nonstandardized frozen desserts when used alone or in combination with polysorbate 65 and/or polysorbate 80, whereby the maximum amount of the additives, alone or in combination, does not exceed 0.1 percent of the finished frozen dessert.

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Dated: October 19, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99–28113 Filed 10–27–99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 177

[Docket No. 99F–0345]

Indirect Food Additives: Polymers

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 mono- and bis-(octadecyldiethylene oxide)phosphates as components of coatings on cellophane intended for use in contact with food. This action is in response to a petition filed by UCB Films PLC.

DATES: The regulation is effective October 28, 1999; written objections and requests for a hearing by November 29, 1999.

ADDRESSES: Submit written objections to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Vir D. Anand, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3081.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of March 18, 1999 (64 FR 13431), FDA announced that a food additive petition (FAP 9B4642) had been filed by UCB Films PLC, c/o Keller and Heckman LLP, 1001 G St. NW., suite 500 West, Washington, DC 20001. The petition proposed to amend the food additive regulations in § 177.1200 *Cellophane* (21 CFR 177.1200) to provide for the safe use of mono- and bis-(octadecyldiethylene oxide)phosphates as component of coatings on cellophane intended for use in contact with food.

In its evaluation of the safety of this additive, FDA has reviewed the safety of the additive itself and the chemical impurities that may be present in the additive resulting from its manufacturing process. Although the additive itself has not been shown to cause cancer, it has been found to contain minute amounts of unreacted 1,4-dioxane and ethylene oxide, carcinogenic impurities resulting from the manufacture of the additive. Residual amounts of reactants and manufacturing aids, such as 1,4-dioxane and ethylene oxide, are commonly found as contaminants in chemical products, including food additives.

I. Determination of Safety

Under the general safety standard of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348(c)(3)(A)), 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. FDA's food additive regulations (21 CFR 170.3(i)) define safe as ''a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.''

The food additives anticancer, or Delaney, clause of the act (21 U.S.C. 348(c)(3)(A)) provides that no food additive shall be deemed safe if it is found to induce cancer when ingested by man or animal. Importantly, however, the Delaney clause applies to the additive itself and not to impurities in the additive. That is, where an additive itself has not been shown to cause cancer, but contains a carcinogenic impurity, the additive is properly evaluated under the general safety standard using risk assessment