

DEPARTMENT OF HEALTH AND HUMAN SERVICES**Food and Drug Administration****21 CFR Part 73****[Docket No. FDA-2012-C-0224]****Listing of Color Additives Exempt From Certification; Mica-Based Pearlescent Pigments****AGENCY:** Food and Drug Administration, HHS.**ACTION:** Final rule.

SUMMARY: The Food and Drug Administration (FDA or we) is amending the color additive regulations to provide for the safe use of mica-based pearlescent pigments prepared from titanium dioxide and mica as color additives in distilled spirits containing not less than 18 percent and not more than 23 percent alcohol by volume but not including distilled spirits mixtures containing more than 5 percent wine on a proof gallon basis. This action is in response to a petition filed by E. & J. Gallo Winery.

DATES: This rule is effective July 15, 2013. See section VIII for further information on the filing of objections. Submit either electronic or written objections and requests for a hearing by July 12, 2013.

ADDRESSES: You may submit either electronic or written objections and requests for a hearing identified by Docket No. FDA-2012-C-0224, by any of the following methods:

Electronic Submissions

Submit electronic objections in the following way:

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

Written Submissions

Submit written objections in the following ways:

- *Mail/Hand delivery/Courier (for paper or CD-ROM submissions):* Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Agency name and Docket No. FDA-2012-C-0224 for this rulemaking. All objections received will be posted without change to <http://www.regulations.gov>, including any personal information provided. For detailed instructions on submitting objections, see the "Objections" heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or objections received, go to <http://www.regulations.gov> and insert the docket number(s), found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Raphael A. Davy, Center for Food Safety and Applied Nutrition (HFS-265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835, 240-402-1272.

SUPPLEMENTARY INFORMATION:**I. Background**

In a document published in the **Federal Register** of March 22, 2012 (77 FR 16784), FDA announced that a color additive petition (CAP 2C0294) had been filed by E. & J. Gallo Winery, c/o Keller and Heckman LLP, One Embarcadero Center, Suite 2110, San Francisco, CA 94111. The petition proposed to amend the color additive regulations in § 73.350 (21 CFR 73.350) *Mica-based pearlescent pigments*, to provide for the safe use of mica-based pearlescent pigments prepared from titanium dioxide and mica in distilled spirits containing not less than 18 percent and not more than 23 percent alcohol by volume but not including distilled spirits mixtures containing more than 5 percent wine on a proof gallon basis. The maximum use level of the pigments proposed by the petitioner is 0.07 percent by weight in the distilled spirits. Mica-based pearlescent pigments prepared from titanium dioxide and mica are currently permitted under § 73.350 for use as color additives in amounts up to 1.25 percent by weight in cereals, confections and frostings, gelatin deserts, hard and soft candies (including lozenges), nutritional supplement tablets and gelatin capsules, and chewing gum. Mica-based pearlescent pigments prepared from titanium dioxide, iron oxide, and mica are permitted for use as color additives in ingested drugs under § 73.1350 (21 CFR 73.1350) and in contact lenses under 21 CFR 73.3128.

II. Safety Evaluation**A. Determination of Safety**

Under section 721(b)(4) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 379e(b)(4)), a color additive cannot be listed for a particular use unless a fair evaluation of the data and information available to FDA establishes that the color additive is safe for that use. FDA's color additive

regulations in 21 CFR 70.3(i) define "safe" as the existence of "convincing evidence that establishes with reasonable certainty that no harm will result from the intended use of the color additive."

To establish with reasonable certainty that a color additive intended for use in food is safe under its intended conditions of use, we consider the projected human dietary intake of the additive, toxicological data on the additive, and other relevant information available to us. We compare an individual's estimated daily intake (EDI) of the additive from all sources for both the mean and high-intake consumer to an acceptable daily intake (ADI) level established by toxicological data. The EDI is determined by projections based on the amount of the additive proposed for use in particular foods and on data regarding the amount consumed from all sources of the additive.

B. Safety of the Petitioned Use of the Color Additive

During our review of the safety of the petitioned use of mica-based pearlescent pigments in distilled spirits, we considered the exposure to the color additive from both its petitioned use and from the uses for which it is currently permitted in food and ingested drugs under §§ 73.350 and 73.1350, respectively. In estimating the cumulative exposure to these pigments, we also considered the exposure to these pigments from their uses in contact lenses and determined that such exposure would be negligible.

For those consuming mica-based pearlescent pigments from the petitioned use in distilled spirits, we have estimated the exposure to mica-based pearlescent pigments at the mean and at the 90th percentile to be 0.12 grams/person/day (g/p/d) and 0.25 g/p/d, respectively, for persons aged 2 years or more (Ref. 1).

Previously, in the issuance of § 73.350 we calculated a cumulative EDI (CEDI) for the use of mica-based pearlescent pigments in food (§ 73.350) and ingested drugs (§ 73.1350) (71 FR 31927, June 2, 2006). For those exposed to mica-based pearlescent pigments from their use in food and ingested drugs, the CEDI was estimated to be 0.24 g/p/d and 0.48 g/p/d at the mean and at the 90th percentile, respectively, for persons aged 2 years or more, and to be 0.26 g/p/d and 0.52 g/p/d at the mean and at the 90th percentile, respectively, for the subgroup of children aged 2 to 5 years (71 FR 31927). This exposure estimate used food consumption data from the 1994 to 1996 and 1998 Continuing Survey of Food Intakes by Individuals

(CSFII) survey, which was integrated into the National Health and Nutrition Examination Survey (NHANES) in 2002.

In our current safety assessment, we updated the previous exposure to mica-based pearlescent pigments from all regulated uses in foods using the latest publicly available NHANES food consumption data (2003 to 2008). In estimating the exposure from the use of mica-based pearlescent pigments in ingested drugs, we relied on the estimates used in the issuance of § 73.350 (71 FR 31927). The current CEDI of mica-based pearlescent pigments from the petitioned use in distilled spirits and its regulated uses in food and ingested drugs is 0.26 g/p/d at the mean and 0.52 g/p/d at the 90th percentile for persons aged 2 years or more, and also for the subgroup of children aged 2 to 5 years (Ref. 1). The current CEDIs of mica-based pearlescent pigments are not significantly different from the previous CEDIs, as the percent of the population consuming distilled spirits from the petitioned use is low compared to the percent of the population consuming foods and ingested drugs formulated with mica-based pearlescent pigments. Further, our estimate assumes no contribution from the petitioned use of mica-based pearlescent pigments to the CEDI for the subgroup of children aged 2 to 5 years because they do not typically consume distilled spirits (Ref. 1).

In our previous safety evaluation of mica-based pearlescent pigments in food, which the petitioner referenced, we established an ADI level for mica-based pearlescent pigments to be 1.8 g/p/d based on a 2-year rat carcinogenicity bioassay that tested a 1:1 blend of mica and titanium dioxide (71 FR 31927 at 31928). Since the CEDI is less than the ADI, we conclude that the proposed expanded use of mica-based pearlescent pigments as color additives at a level of up to 0.07 percent by weight in distilled spirits is safe (Ref. 2).

III. Conclusion

Based on the data and information in the petition and other relevant material, FDA concludes that the petitioned use of mica-based pearlescent pigments prepared from titanium dioxide and mica as a color additive at a level of up to 0.07 percent by weight in distilled spirits containing not less than 18 percent and not more than 23 percent alcohol by volume but not including distilled spirits mixtures containing more than 5 percent wine on a proof gallon basis is safe. We further conclude that the additive will achieve its intended technical effect and is suitable for use in coloring food. Therefore, we

conclude that the color additive regulations should be amended as set forth in this document. In addition, based upon the factors listed in 21 CFR 71.20(b), we conclude that certification of titanium dioxide-coated mica-based pearlescent pigments is not necessary for the protection of the public health.

IV. Public Availability of Documents

In accordance with § 71.15 (21 CFR 71.15), the petition and the documents that we considered and relied upon in reaching our decision to approve the petition will be made available for public disclosure (see **FOR FURTHER INFORMATION CONTACT**). As provided in § 71.15, we will delete from the documents any materials that are not available for public disclosure.

V. Environmental Impact

We have previously considered the environmental effects of this rule as announced in the notice of filing for CAP 2C0294 (77 FR 16784, March 22, 2012). No new information or comments have been received that would affect our previous determination that there is no significant impact on the human environment and that an environmental impact statement is not required.

VI. Paperwork Reduction Act of 1995

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

VII. Section 301(ll) of the FD&C Act

FDA's review of this petition was limited to section 721 of the FD&C Act. This final rule is not a statement regarding compliance with other sections of the FD&C Act. For example, the Food and Drug Administration Amendments Act of 2007, which was signed into law on September 27, 2007, amended the FD&C Act to, among other things, add section 301(ll) of the FD&C Act (21 U.S.C. 331(ll)). Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act (21 U.S.C. 355), a biological product licensed under section 351 of the Public Health Service Act (42 U.S.C. 262), or a drug or biological product for which substantial clinical investigations have been instituted and their existence has been made public, unless one of the exemptions in section 301(ll)(1)–(4) of the FD&C Act applies. In our review of this petition, we did not consider whether section 301(ll) of the FD&C Act or any of its exemptions apply to food

containing this color additive. Accordingly, this final rule should not be construed to be a statement that a food containing this color additive, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll) of the FD&C Act. Furthermore, this language is included in all color additive final rules that pertain to food and therefore should not be construed to be a statement of the likelihood that section 301(ll) of the FD&C Act applies.

VIII. Objections

This rule is effective as shown in the **DATES** section of this document; except as to any provisions that may be stayed by the filing of proper objections. Any person who will be adversely affected by this regulation may file with the Division of Dockets Management (see **ADDRESSES**) either electronic or written objections regarding this document. 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. It is only necessary to send one set of documents. Identify documents 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 Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>. FDA will publish notice of the objections that the Agency has received or lack thereof in the **Federal Register**.

IX. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at <http://www.regulations.gov>.

1. Memorandum from Hyoungh S. Lee, Division of Petition Review, Chemistry Review Team, to Raphael Davy, Division of Petition Review, Regulatory Group I, May 30, 2012.

2. Memorandum from Tina W. Walker, Division of Petition Review, Toxicology Team, to Raphael Davy, Division of Petition Review, Regulatory Group I, October 3, 2012.

List of Subjects in 21 CFR Part 73

Color additives, Cosmetics, Drugs, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, and redelegated to the Director, Center for Food Safety and Applied Nutrition, 21 CFR part 73 is amended as follows:

PART 73—LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

■ 1. The authority citation for 21 CFR part 73 continues to read as follows:

Authority: 21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e.

■ 2. Section 73.350 is amended by revising paragraph (c)(1) to read as follows:

§ 73.350 Mica-based pearlescent pigments.

* * * * *

(c) * * *

(1) The substance listed in paragraph (a) of this section may be safely used as a color additive in food as follows:

(i) In amounts up to 1.25 percent, by weight, in the following foods: Cereals, confections and frostings, gelatin desserts, hard and soft candies (including lozenges), nutritional supplement tablets and gelatin capsules, and chewing gum.

(ii) In amounts up to 0.07 percent, by weight, in distilled spirits containing not less than 18 percent and not more than 23 percent alcohol by volume but not including distilled spirits mixtures containing more than 5 percent wine on a proof gallon basis.

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Dated: June 6, 2013.

Susan M. Bernard,

Director, Office of Regulations, Policy and Social Sciences, Center for Food Safety and Applied Nutrition.

[FR Doc. 2013-13857 Filed 6-11-13; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 316

[Docket No. FDA-2011-N-0583]

RIN 0910-AG72

Orphan Drug Regulations

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing final regulations amending the 1992 Orphan Drug Regulations issued to implement the Orphan Drug Act. These amendments are intended to clarify regulatory provisions and make minor improvements to address issues that have arisen since those regulations were issued.

DATES: This rule is effective August 12, 2013.

FOR FURTHER INFORMATION CONTACT:

Erica K. McNeilly, Office of Orphan Products Development, Food and Drug Administration, Bldg. 32, rm. 5271, 10903 New Hampshire Ave., Silver Spring, MD 20993, 301-796-8660.

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I. Background

In the **Federal Register** of October 19, 2011 (76 FR 64868), FDA issued a proposed rule to amend the Orphan Drug Regulations (part 316 (21 CFR part 316)), to clarify certain regulatory language and propose areas of minor improvement regarding orphan-drug designation and orphan-drug exclusivity. The proposed rule addressed the following aspects of the Orphan Drug Regulations: (1) Demonstration of an appropriate "orphan subset" of persons with a particular disease or condition that otherwise affects 200,000 or more persons in the United States ("non-rare disease or condition"), for the purpose of designating a drug for use in that subset; (2) eligibility for designation of a drug that is otherwise the same drug for the same use as a previously approved drug; (3) eligibility for multiple orphan-drug exclusive approvals when a drug is designated for use in a rare disease or condition,¹ but is then separately approved for different indication(s) or use(s) within that particular rare disease or condition; (4) requirement for demonstrating clinical superiority for the purpose of orphan-drug exclusive approval when the drug is otherwise the same as a previously approved drug for the same use or indication; (5) requirement for submitting the name of the drug in a designation request; (6) required drug description and scientific rationale in a designation request; (7) required information in a designation request relating to the sponsor's interest in the drug; (8) timing of a request for orphan-drug designation; (9) responding to a deficiency letter from FDA on an orphan-drug designation request; (10) FDA publication of information regarding orphan-drug designations; (11) FDA recognition of orphan-drug exclusive approval; (12) miscellaneous terminology changes; and (13) an address change.

FDA received comments on the proposed rule from 14 entities, mainly from companies and trade associations of companies that are marketing or hope to market orphan drugs. On the whole, the comments were strongly supportive of the orphan drug program and recognized the need for clarity in FDA requirements, though many comments raised objections to and questions about certain aspects of the proposed rule.

¹ Section 526(a) of the Federal Food, Drug and Cosmetic Act (FD&C Act) defines a "rare disease or condition" to include any disease or condition that affects fewer than 200,000 persons in the United States.