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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 73

[Docket No. FDA-2023-C-5679]

Color Additive Petition from Environmental Defense Fund et al.; Request to Amend the Color Additive Regulations to Remove the Solvents Ethylene Dichloride, Methylene Chloride, and Trichloroethylene

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; order; notification of partial denial of petition.

SUMMARY: The Food and Drug Administration (FDA or we) is partially granting a color additive petition submitted by Environmental Defense Fund et al. (petitioners), by amending our color additive regulations, on the basis of the Delaney Clause, to remove the authorized use of methylene chloride as a diluent in color additive mixtures in inks for marking fruit and vegetables. The petitioners provided data demonstrating that this additive induces cancer in laboratory animals. We are denying the remaining petition requests to remove ethylene dichloride, methylene chloride, and trichloroethylene from the list of authorized extraction solvents for annatto extract, paprika oleoresin, and turmeric oleoresin, because any residue of the solvent would be an impurity in the color additive and such impurities are not subject to the Delaney Clause.

DATES: This order is effective [**INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER***]. If any provisions are delayed or stayed by the filing of proper objections, FDA will publish such notification in the *Federal Register*. Submit either electronic or written objections and requests for a hearing on the order by [**INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER***]. See section X for further information on the filing of objections.

ADDRESSES: You may submit objections and requests for a hearing as follows. Please note that late, untimely filed objections will not be considered. The https://www.regulations.gov electronic filing system will accept objections until 11:59 p.m. Eastern Time at the end of [**INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER***]. Objections received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic objections in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Objections submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your objection will be made public, you are solely responsible for ensuring that your objection does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your objection, that information will be posted on https://www.regulations.gov.
- If you want to submit an objection with confidential information that you do not wish to be made available to the public, submit the objection as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper instructions as follows:

- Mail/Hand Delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper objections submitted to the Dockets Management Staff, FDA will post your objection, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2023-C-5679 for "Color Additive Petition from Environmental Defense Fund et al.; Request to Amend the Color Additive Regulations to Remove the Solvents Ethylene Dichloride, Methylene Chloride, and Trichloroethylene." Received objections, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit an objection with confidential information that you do not wish to be made publicly available, submit your objection only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." We will review this copy, including the claimed confidential information, in our consideration of objections. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your objections and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Paulette M. Gaynor, Office of Pre-Market Additive Safety, Human Foods Program, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240-402-1192; or Alexandra Beliveau, Office of Regulations and International Programs, Human Foods Program, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240-402-2378.

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I. Introduction

In the *Federal Register* of January 11, 2024 (89 FR 1856), we announced that we filed a color additive petition (CAP 4C0327) submitted by Environmental Defense Fund, Breast Cancer Prevention Partners, Center for Environmental Health, Environmental Working Group, and Lisa Lefferts, c/o Lisa Lefferts, Nellysford, VA 22958 (currently c/o Liora Fiksel, 1875 Connecticut Ave. NW, Washington, DC 20009).

The petition proposed that we amend §§ 73.1 (21 CFR 73.1, "Diluents in color additive mixtures for food use exempt from certification"), 73.30 (21 CFR 73.30, "Annatto extract"), 73.345 (21 CFR 73.345, "Paprika oleoresin"), and 73.615 (21 CFR 73.615, "Turmeric oleoresin") to remove the use of three specified solvents.

The three solvents that are the subject of this petition are:

1. Ethylene dichloride (Chemical Abstract Service (CAS) No. 107-06-2);
2. Methylene chloride (CAS No. 75-09-2); and
3. Trichloroethylene (CAS No. 79-01-6).

Specifically, the petitioners state these substances have been found to induce cancer in animals and, therefore, are not safe pursuant to section 721(b)(5)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 379e(b)(5)(B)).

The notification of petition gave interested parties until March 11, 2024, to submit comments on the filed color additive petition. The petition was made available in the docket. In the *Federal Register* of May 28, 2026 (91 FR 31680), we reopened the comment period for 30

days to allow for the submission of any updated data and other information over the last two years.

This order grants the petition's request to amend the regulations to no longer provide for the use of methylene chloride as a diluent in color additive mixtures in inks for marking fruit and vegetables. This order denies the petition's remaining requests. However, as noted in section VI of this document, FDA is taking action on these remaining requests in response to a separate petition based on industry's abandonment of these uses.

II. Background

A. Statutory and Regulatory Background of Color Additive Regulation

The FD&C Act authorizes us to regulate "color additives" (see section 721(b) of the FD&C Act). The FD&C Act defines "color additive" as a material which is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and that when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with another substance) of imparting color ("color" includes black, white, and intermediate grays) thereto (see section 201(t) of the FD&C Act (21 U.S.C. 321(t))). Color additives used in or on a food, drug, cosmetic, or certain medical devices are deemed unsafe and prohibited except to the extent that we approve their use (see section 721(a) of the FD&C Act). Certain color additives must be certified by FDA (see section 721(c) of the FD&C Act).

The FD&C Act provides a process through which any person who wishes to use a color additive in or on food, drugs, certain devices, or cosmetics may submit a petition proposing the issuance of a color additive regulation listing such use with supporting information. A color additive petition may also be submitted to propose the amendment or repeal of any existing color additive regulation (see section 721(b)(5)(C) and (d) of the FD&C Act). In response to a color additive petition, FDA may issue a regulation listing a color additive for use in or on food, drugs,

devices, or cosmetics only if it determines that the additive is suitable and safe for such use (see section 721(b)(1) of the FD&C Act).

Under section 721(b) of the FD&C Act, we will not establish a regulation for the use of a color additive if a fair evaluation of the data fails to establish that the proposed use of the color additive, under the conditions of use to be specified in the regulation, will be safe. To determine whether a color additive is safe, the FD&C Act requires FDA to consider, among other relevant factors: (1) probable consumption of, or other relevant exposure from, the additive and of any substance formed in or on food, drugs or devices, or cosmetics because of the use of the additive; (2) cumulative effect, if any, of such additive "in the diet of man or animals," taking into account the same or any chemically or pharmacologically related substance or substances in such diet; and (3) safety factors recognized by experts "as appropriate for the use of animal experimentation data" (see section 721(b)(5)(A) of the FD&C Act) (referred to as the "general safety clause"). FDA's determination that a color additive is safe means that there is convincing evidence that establishes with reasonable certainty that no harm will result from the intended condition of use of the color additive (§ 70.3(i) (21 CFR 70.3(i))). We refer to this safety standard as "a reasonable certainty of no harm."

In addition, section 721(b)(5)(B) of the FD&C Act, often referred to as the Delaney Clause, deems a color additive unsafe under certain circumstances. The Delaney Clause for color additives consists of two parts. The first part (section 721(b)(5)(B)(i) of the FD&C Act) pertains specifically to ingested color additives. The second part (section 721(b)(5)(B)(ii) of the FD&C Act) applies to non-ingested color additives. For purposes of our review of this petition, we reviewed these uses of the solvents ethylene dichloride, methylene chloride, and trichloroethylene under the first part because these uses result in ingestion. Section 721(b)(5)(B)(i) of the FD&C Act states that a color additive shall be deemed unsafe for any use which will or may result in ingestion of all or part of such additive if the additive is found by the Secretary to induce cancer when ingested by man or animal, or if it is found by the Secretary,

after tests which are appropriate for the evaluation of the safety of additives for use in food, to induce cancer in man or animal. Courts have concluded that the Delaney Clause is to be interpreted very rigidly. In *Public Citizen v. Young*, 831 F.2d 1108, 1122 (D.C. Cir. 1987), the court held that Congress intended for the Delaney Clause to be "extraordinarily rigid," to protect the public from cancer-causing substances without exception, rejecting FDA's argument that a particular color additive should be approved because it did not pose more than a de minimis cancer risk; see also *Les v. Reilly*, 968 F.2d 985, 986 (9th Cir. 1992) (holding that the U.S. Environmental Protection Agency's (EPA) refusal to revoke regulations permitting the use of certain pesticides, which were regulated as food additives at the time of the court decision and subject to a similarly worded Delaney Clause for food additives, on the grounds that they pose a de minimis cancer risk, is contrary to the provisions of the Delaney Clause). Importantly, however, the Delaney Clause applies to the additive itself and not to constituents (such as nonfunctional chemicals present in the additive) or impurities in the additive. That is, where an additive itself has not been shown to cause cancer but contains a carcinogenic constituent or impurity, the additive is properly evaluated under the general safety clause 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)).

There is a similar Delaney Clause provision for food additives under section 409(c)(3) of the FD&C Act (21 U.S.C. 348(c)(3)), which states that no food additive shall be deemed safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal. In revoking certain authorizations for food additives under the Delaney Clause, FDA stated that the Delaney Clause limits FDA's discretion to determine the safety of food additives. FDA stated that the Delaney Clause prevents FDA from finding a food additive to be safe if it has been found to induce cancer when ingested by humans or animals, "regardless of the probability, or risk, of cancer associated with exposure to the additive or of the extent to which the experimental

conditions of the animal study or the carcinogenic mode of action provide insight into the health effects of human consumption and use of the additive in question" (83 FR 50490 at 50492, October 9, 2018).

Section 721(d) of the FD&C Act provides for the issuance, amendment, or repeal of regulations authorizing the use of a color additive, and, among other things, it specifies that the safety provisions of section 721(b)(5) of the FD&C Act apply to such actions. For FDA to grant a petition that seeks repeal of a color additive regulation based upon new data concerning the safety of the color additive, such data must be adequate for FDA to conclude that there is no longer a reasonable certainty of no harm for the intended use of the color additive or that it must be deemed unsafe under the Delaney Clause.

B. History of the Color Additive Regulations Where Amendments Are Requested

In the *Federal Register* of June 20, 1963 (28 FR 6351), FDA established 21 CFR 8.305 for the listing of annatto extract in food use exempt from certification, now codified in § 73.30. Ethylene dichloride, methylene chloride, and trichloroethylene are allowed as food-grade extractants in the preparation of annatto extract (§ 73.30(a)(1)(ii)). In the *Federal Register* of October 8, 1964 (29 FR 13893), FDA established 21 CFR 8.390 for the listing of diluents in color additive mixtures for food use exempt from certification, including methylene chloride (with a restriction of no residues) for the special use in inks for marking fruit and vegetables, now codified in § 73.1.

In the *Federal Register* of January 27, 1966 (31 FR 1063), FDA established, among other things, 21 CFR 8.308 and 8.310 for the listing of paprika oleoresin and turmeric oleoresin, now codified in §§ 73.345 and 73.615, respectively. Ethylene dichloride, methylene chloride, and trichloroethylene are allowed as solvents in the preparation of both paprika oleoresin and turmeric oleoresin (§§ 73.345(a)(1) and 73.615(a)(1)).

III. Summary and Context of Determination

We have evaluated the data and other information submitted in the petition, as well as other relevant data. FDA finds that ethylene dichloride, methylene chloride, and trichloroethylene induce cancer in animals. We must revoke the authorizations providing for any color additive use of these substances on the basis of the Delaney Clause. As described further in section IV of this document, we conclude that methylene chloride is a color additive in § 73.1. Therefore, we are amending the regulations to remove the use of this color additive under section 721(b)(5)(B) of the FD&C Act as a matter of law.

We are denying the petition's remaining requests. As described further in section IV of this document, we conclude that ethylene dichloride, methylene chloride, and trichloroethylene are not color additives in §§ 73.30, 73.345, and 73.615. Therefore, the Delaney Clause does not apply to these uses.

IV. Evaluation of Petition

The petitioners assert that the Delaney Clause applies to ethylene dichloride, methylene chloride, and trichloroethylene in §§ 73.1, 73.30, 73.345, and 73.615. The petitioners state that ethylene dichloride, methylene chloride, and trichloroethylene have been shown to induce cancer in animals. The petitioners cite to studies sponsored by the Department of Health and Human Services' National Toxicology Program (NTP) (Refs. 1-3).

For ethylene dichloride, in the National Cancer Institute Technical Report No. 55 (1978) on 1, 2 – dichloroethane, the authors reported that the test material caused significantly increased incidence of squamous cell carcinomas of the forestomach and hemangiosarcomas of the circulatory system in male rats and adenocarcinomas of the mammary gland in female rats (Ref. 1). FDA previously evaluated these data and found that ethylene dichloride induced cancer in animals (Refs. 4 and 5).

For methylene chloride, in the NTP Report No. 306 (January 1986) on inhalation studies in F344/N rats and $B6C3F_1$ mice, the authors reported that the test material (Dichloromethane (Methylene Chloride) (CAS Reg. No. 75–09–2)) caused an increased incidence of liver cell

neoplasms and lung neoplasms in both male and female $B6C3F_1$ mice (Ref. 2). FDA previously evaluated these data and found that methylene chloride induced cancer in animals (Ref. 6).

For trichloroethylene, the National Cancer Institute Technical Report No. 2 presents a synopsis of the results of a carcinogenesis bioassay of trichloroethylene using mice and rats and concludes that trichloroethylene induces liver cancer in mice (Ref. 3). FDA previously evaluated these data and found that trichloroethylene induced cancer in animals (Ref. 7).

Based on these studies, we conclude that ethylene dichloride and trichloroethylene have been "found by the Secretary to induce cancer when ingested by…animal[s]" (Refs. 1 and 3).

We also conclude that methylene chloride is an animal carcinogen based on an NTP-sponsored two-year inhalation study in mice (NTP inhalation mouse study) and that this study is appropriate for evaluating the safety of this additive for its intended use. Previously, FDA concluded that data from the NTP inhalation mouse study were appropriate for the safety evaluation of methylene chloride as a food additive (50 FR 51551 and Refs. 8 and 9).

In the NTP inhalation mouse study with methylene chloride, carcinogenic incidences were reported in lungs and also in liver, an organ removed from the site of administration (Ref. 8). These effects occurred independent of each other (id.). Further, FDA compared data from the NTP inhalation mouse study with those from a National Coffee Association-sponsored two-year drinking water study conducted with the same strain of mice but at lower dose levels (Ref. 8). While the drinking water studies did not demonstrate any carcinogenic effects in the liver or lungs, increased incidences of non-neoplastic proliferative lesions were observed in the liver (Ref. 6), and FDA concluded that mice receiving methylene chloride in the drinking water study may not have been tested at levels comparable to the NTP inhalation study (Ref. 6). Making an assumption that methylene chloride induced cancer just below the detection limit of the doses tested in the drinking water studies, FDA concluded that the upper-bound cancer risk of methylene chloride from the drinking water studies was approximately the same as its upper-bound cancer risk from the NTP inhalation study (Ref. 9).

On a case-by-case basis, data from non-oral animal toxicity studies, such as studies based on inhalation exposure route, can be used in place of oral animal toxicity studies to evaluate the safety of substances after oral exposure (Refs. 10 and 11). This assessment involves examining and comparing chemical and toxicological profiles of the substance between oral and inhalation exposure routes (id.). In general, substances that have a high vapor pressure and are therefore considered volatile can enter the blood after inhalation exposure and potentially induce toxic effects in internal organs away from the site of administration (id.). For such substances, data from non-oral exposure studies (e.g., inhalation studies) are considered relevant to evaluate their safety after oral exposure (Ref. 10). Methylene chloride is a volatile substance with a high vapor pressure (see 29 CFR 1910.1052 Appendix A). Further, in the NTP inhalation mouse study, methylene chloride induced carcinogenic effects in the liver—an organ removed from the site of administration.

Therefore, data from the NTP inhalation mouse study of methylene chloride is applicable to its evaluation of safety after oral exposure, and this study is appropriate for the evaluation of the safety of this additive for color additive use. Thus, the reported results from the NTP inhalation mouse study are appropriate when considering the applicability of the Delaney Clause for methylene chloride, and based on this study, we conclude that methylene chloride has been found "to induce cancer in…animal." We also conclude that the NTP inhalation mouse study (Ref. 2) for methylene chloride is "appropriate for the evaluation of the safety of additives for such use."

Because these solvents (ethylene dichloride, methylene chloride, and trichloroethylene) have been "found to induce cancer in…animal[s]," the Delaney Clause applies to their use as a color additive. The Delaney Clause prevents FDA from finding the color additive uses of these solvents to be safe if the solvents have been found to induce cancer in animals, regardless of the probability, or risk, of cancer associated with exposure from the color additive uses.

Finally, we evaluated the uses of ethylene dichloride, methylene chloride, and trichloroethylene in these color additive regulations to determine whether, based on the specific authorized uses, these substances are color additives (which are subject to the Delaney Clause) or are constituents or impurities in a color additive (which are not subject to the Delaney Clause).

The discussion that follows describes FDA's evaluation of whether ethylene dichloride, methylene chloride, and trichloroethylene, as they appear in §§ 73.1, 73.30, 73.345, and 73.615, are considered color additives or constituents or impurities in the color additive. For uses of substances that we determine to be color additives, the Delaney Clause applies, and the authorization for such uses must be revoked. For uses of substances that we determine to be constituents or impurities in a color additive, the Delaney Clause does not apply. As the petition's request is based on the Delaney Clause, we are denying its request to revoke the applicable authorizations on the basis of the Delaney Clause for uses that we determine result in these solvents being constituents or impurities in a color additive rather than the color additive itself.

A. 21 CFR 73.1 "Diluents in color additive mixtures for food use exempt from certification"

Under § 73.1(b)(1)(ii), methylene chloride is allowed as a diluent in color additive mixtures for use in inks for marking fruit and vegetables with the restriction of no residue. A color additive mixture is a color additive that is made, in relevant part, by mixing "one or more straight colors and one or more diluents" (§ 70.3(k)). While such diluents do not impart color and are not by themselves a color additive (§ 70.3(m)), they are regulated as color additives when they are intentionally mixed with a color to make a color additive mixture. Because of a diluent's functional purpose in the color additive mixture, we consider the authorized use of methylene chloride in § 73.1(b)(1)(ii), as a diluent in color additive mixtures for use in inks for marking fruit and vegetables, to be a color additive that is subject to the Delaney Clause. Therefore, we are amending the regulation to no longer provide for the use of methylene chloride as a diluent in

color additive mixtures for use in inks for marking fruit and vegetables in § 73.1(b)(1)(ii) under section 721(b)(5)(B) of the FD&C Act as a matter of law.

B. 21 CFR 73.30 "Annatto extract"

Under § 73.30(a)(1)(ii), ethylene dichloride, methylene chloride, and trichloroethylene are each allowed as a food-grade extractant to manufacture the color additive "annatto extract." Annatto extract must contain no more solvent residue than is allowed of the corresponding solvents in spice oleoresins under applicable food additive regulations in parts 170 through 189 (21 CFR parts 170 through 189) (see § 73.30(b)). Total chlorinated solvents residues are limited to 30 parts per million (ppm) (milligram per kilogram (mg/kg)) (see §§ 173.230 (21 CFR 173.230), 173.255 (21 CFR 173.255), and 173.290 (21 CFR 173.290)). Through the extraction process, ethylene dichloride, methylene chloride, and trichloroethylene may end up as a residue of, and therefore an impurity in, the color additive "annatto extract." While these extractants may end up as impurities in the color additive "annatto extract," they are not color additives themselves in § 73.30. Therefore, we are denying the petition's request to remove ethylene dichloride, methylene chloride, and trichloroethylene from the list of approved food-grade extractants in § 73.30 under section 721(b)(5)(B) of the FD&C Act. As discussed in section II.A of this document, the Delaney Clause is applicable to color additives but not to impurities in a color additive.

C. 21 CFR 73.345 "Paprika oleoresin"

Under § 73.345(a), ethylene dichloride, methylene chloride, and trichloroethylene are each allowed as a solvent for the extraction of paprika to obtain the color additive "paprika oleoresin." Paprika oleoresin must contain no more solvent residue than is allowed of the corresponding solvents in spice oleoresins under applicable food additive regulations in parts 170 through 189 (see § 73.345(b)). Total chlorinated solvents are limited to 30 ppm (mg/kg) (see §§ 173.230, 173.255, and 173.290). Through the extraction process, ethylene dichloride, methylene chloride, and trichloroethylene may end up as a residue of, and therefore an impurity in, the color

additive "paprika oleoresin." While these solvents may end up as impurities in the color additive "paprika oleoresin," they are not color additives themselves in § 73.345. Therefore, we are denying the petition's request to remove ethylene dichloride, methylene chloride, and trichloroethylene from the list of approved solvents in § 73.345 under section 721(b)(5)(B) of the FD&C Act. As discussed in section II.A of this document, the Delaney Clause is applicable to color additives but not to impurities in a color additive.

D. 21 CFR 73.615 "Turmeric oleoresin"

Under § 73.615(a), ethylene dichloride, methylene chloride, and trichloroethylene are each allowed as a solvent for extraction of turmeric to obtain the color additive "turmeric oleoresin." Turmeric oleoresin must contain no more solvent residue than is allowed of the corresponding solvents in spice oleoresins under applicable food additive regulations in parts 170 through 189 (see § 73.615(b)). Total chlorinated solvents are limited to 30 ppm (mg/kg) (see §§ 173.230, 173.255, and 173.290). Through the extraction process, ethylene dichloride, methylene chloride, and trichloroethylene may end up as a residue of, and therefore an impurity in, the color additive "turmeric oleoresin." While these solvents may end up as an impurity in the color additive "turmeric oleoresin," they are not color additives themselves in § 73.615. Therefore, we are denying the petition's request to remove ethylene dichloride, methylene chloride, and trichloroethylene from the list of approved extractants in § 73.615 under section 721(b)(5)(B) of the FD&C Act. As discussed in section II.A of this document, the Delaney Clause is applicable to color additives but not to impurities in a color additive.

V. Comments Related to the Petition

FDA received several comments in response to the notification of petition and the reopening of the comment period. Most comments expressed general support for the petition's requested revocation of the provisions allowing for the use of these solvents in foods. Some comments addressed matters outside the scope of this petition, and some comments were duplicate submissions.

We summarize and respond to relevant portions of comments in this final order. We have numbered each comment to help distinguish between different comments. We have grouped similar comments together under the same number, and, in some cases, we have separated different issues discussed in the same comment and designated them as distinct comments for purposes of our responses. The number assigned to each comment is for organizational purposes only and does not signify the comment's value, importance, or the order in which it was submitted.

(Comment 1) One comment stated that chlorinated solvents are no longer used for the manufacture of color additives. The comment further encouraged FDA to take this opportunity to consider removing ethylene dichloride, methylene chloride, and trichloroethylene as extraction solvents, as well as methylene chloride as a diluent in inks for marking fruits and vegetables based on the abandonment of these authorized uses.

(Response 1) We did not consider abandonment for the approved uses of these solvents as part of our evaluation of this petition because the petition is based on the Delaney Clause. We note, however, that elsewhere in this issue of the *Federal Register*, we have published a final order in response to CAP 5C0340, submitted by the International Association of Color Manufacturers, partially granting that petition and amending the color additive regulations to no longer provide for the extraction solvent uses of ethylene dichloride, methylene chloride, and trichloroethylene which are covered by this petition because these uses have been abandoned.

(Comment 2) Some comments raised EPA's proposed actions to eliminate or restrict the use of trichloroethylene and methylene chloride under the Toxic Substances Control Act or otherwise noted uses(s) of a chlorinated solvent that would be under EPA's jurisdiction.

(Response 2) While FDA and EPA may both regulate a particular substance, each agency regulates the uses of substances under its own applicable legal authority.

(Comment 3) Several comments expressed support for the removal of the authorizations for the use of these solvents from our color additive regulations. Some comments stated that these authorizations should be removed because there are alternatives.

(Response 3) We are taking this action to revoke the authorization for the use of methylene chloride as a diluent in color additive mixtures in inks for marking fruit and vegetables, because the color additive use of this solvent is deemed unsafe under the Delaney Clause. The existence of alternatives is not a factor in determining whether a color additive is safe under either the Delaney Clause or the general safety clause (see section 721(b)(5)(B) of the FD&C Act).

(Comment 4) Some comments mentioned other substances that FDA should also review for removal from our color additive regulations.

(Response 4) This color additive petition requests the removal of the three specified solvents from §§ 73.1, 73.30, 73.345, and 73.615. Therefore, these comments are outside the scope of this order.

(Comment 5) Some comments discussed the regulatory status of ethylene dichloride, methylene chloride, and trichloroethylene in other countries and questioned how FDA could continue to allow these substances in the U.S. food supply.

(Response 5) FDA's regulatory decisions are based on its own assessments of the available scientific information supporting the safety of color additives and on the statutory and regulatory framework in the United States.

(Comment 6) One comment expressed support for the petition and discussed evidence related to the use of these solvents and potential negative health impacts to humans. The comment cited certain studies to support their claims.

(Response 6) The petition's request is based on the Delaney Clause, and therefore our review of these solvents is based on the Delaney Clause. If the Delaney Clause applies, regardless of the safety of this use under the general safety clause, such an additive may not "be

deemed to be safe" as a matter of law. Therefore, under the Delany Clause, FDA must revoke the authorization for the color additive use of methylene chloride. By contrast, ethylene dichloride, methylene chloride, and trichloroethylene are not color additives in §§ 73.30, 73.345, and 73.615, but rather they are impurities in those color additives. Therefore, we are denying the petition's request to revoke these authorizations, and any further review is outside the scope of this order responding to the petition.

VI. Conclusion

Ethylene dichloride, methylene chloride, and trichloroethylene have been shown to cause cancer in laboratory animals. Under the Delaney Clause, this finding of carcinogenicity renders a color additive "unsafe" as a matter of law. Therefore, FDA is revoking the authorization for methylene chloride as a diluent in color additive mixtures in inks for marking fruit and vegetables. We are amending § 73.1 as set forth in this document.

Our revocation of this authorization is based on a finding under the Delaney Clause that methylene chloride can induce cancer in animals. It is not based on a finding that the intended use is no longer safe under the general safety clause. Upon the effective date of this order (see DATES), the use of methylene chloride as a diluent in color additive mixtures in inks for marking fruit and vegetables is no longer authorized. FDA is revoking this authorization in a manner consistent with its international obligations. This decision is consistent with the United States' long-standing Appropriate Level of Protection regarding carcinogenic additives in food, which seeks to eliminate exposure to additives that have been found to induce cancer in man or animals.

The Delaney Clause is applicable to the color additive itself but not to constituents or impurities in the additive. Residues of ethylene dichloride, methylene chloride, and trichloroethylene, when used as an extractant for annatto extract, paprika oleoresin, and turmeric oleoresin, may end up as an impurity in the color additive and would be considered an impurity in the color additive, not a color additive itself. The Delaney Clause applies to color additives,

and not to impurities in a color additive. Because the Delaney Clause does not provide a basis for removing these authorizations, FDA is denying the petition's request to remove the authorized uses of ethylene dichloride, methylene chloride, and trichloroethylene in §§ 73.30, 73.345, and 73.615. We note, however, that elsewhere in this issue of the *Federal Register*, we have published a final order amending the color additive regulations to no longer provide for these uses of ethylene dichloride, methylene chloride, and trichloroethylene because these uses have been abandoned. Therefore, FDA is taking all of the actions requested by the petitioners.

VII. Public Disclosure

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 in part and to deny the petition in part 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. As stated in the notification of filing for CAP 4C0327, the petition is available in the docket.

VIII. Analysis of Environmental Impacts

As stated in the January 11, 2024, *Federal Register* notification of petition for CAP 4C0327 (89 FR 1856), the petitioner claimed that this action is categorically excluded under § 25.32(m) (21 CFR 25.32(m)) because it constitutes an action to prohibit or otherwise restrict or reduce the use of a substance in food, food packaging, or cosmetics. We further stated that, if FDA determines a categorical exclusion applies, neither an environmental assessment nor an environmental impact statement is required. We did not receive any new information or comments regarding this claim of categorical exclusion. We considered the petitioner's claim of categorical exclusion and determined that this action is categorically excluded under § 25.32(m) (Ref. 12). Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

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

X. Objections

This order is effective as shown in the "DATES" section, except as to any provisions that may be stayed by the filing of proper objections. If you will be adversely affected by one or more provisions of this regulation, you may file with the Dockets Management Staff (see ADDRESSES) either electronic or written objections. You must separately number each objection, and within each numbered objection you must specify with particularity the provision(s) to which you object and the grounds for your objection. Within each numbered objection, you must specifically state whether you are requesting a hearing on the particular provision that you specify in that numbered objection. If you do not request a hearing for any particular objection, you waive the right to a hearing on that objection. If you request a hearing, your objection must include a detailed description and analysis of the specific factual information you intend to present in support of the objection in the event that a hearing is held. If you do not include such a description and analysis for any particular objection, you waive the right to a hearing on the objection.

Any objections received in response to the regulation may be seen in the Dockets Management Staff office between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at https://www.regulations.gov. We will publish notice of the objections that we have received or lack thereof in the *Federal Register*.

XI. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at https://www.regulations.gov. References without asterisks are not on public display at https://www.regulations.gov because they have copyright restriction. Some may be available at

the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

*1. National Cancer Institute. 1978. Bioassay of 1,2-Dichloroethane for Possible Carcinogenicity. Bethesda, MD: National Cancer Institute. DHEW Publication No. (NIH) 78-1361. Accessed February 4, 2026. Available at: https://ntp.niehs.nih.gov/publications/reports.

*2. National Toxicology Program. 1986. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Dichloromethane (Methylene Chloride) (CAS Reg. No. 75–09–2) in F344/N Rats and B6C3F$_1$ Mice (Inhalation Studies). Research Triangle Park, NC: National Toxicology Program. Technical Report 306. Accessed February 4, 2026. Available at: https://ntp.niehs.nih.gov/publications/reports.

*3. National Cancer Institute. 1976. Carcinogenesis Bioassay of Trichloroethylene. Bethesda, MD: National Cancer Institute. DHEW Publication No. (NIH) 76-802. Accessed February 4, 2026. Available at: https://ntp.niehs.nih.gov/publications/reports.

*4. Memorandum of Conference concerning "1,2-Dichloroethane," Cancer Assessment Committee, Bureau of Foods, March 20, 1979.

*5. Memorandum of Conference concerning "1,2-Dichloroethane," Cancer Assessment Committee, Bureau of Foods, June 12, 1979.

*6. Memorandum of Conference concerning "Methylene Chloride," Cancer Assessment Committee, Bureau of Foods, January 20, 1983, August 8, 1984, and June 13, 1985.

*7. Memorandum of Conference concerning "1,1,2-Trichloroethylene," Cancer Assessment Committee, Bureau of Foods, July 24, 1979.

*8. Quantitative Risk Assessment Committee, "Preliminary Assessment of Upper-Bound Cancer Risk from Exposure to Methylene Chloride Used in Cosmetic Aerosol Sprays," April 23, 1985.

*9. Quantitative Risk Assessment Committee, "Upper Bound Estimate of Cancer Risk of Methylene Chloride (MC) in MC-based Decaffeinated Coffee Products," November 15, 1985.

10. Kabadi, S.V., J. Fisher, B. Hung, and J. Aungst. "Considerations for applying route-to-route extrapolation to assess the safety of oral exposure to substances." *Biomolecules*, 13(1), 5, 2023. Accessed February 4, 2026. Available at https://doi.org/10.3390/biom13010005.

11. Gerrity, T.R.; and C. J. Henry. *Principles of Route-Route Extrapolation for Risk Assessment: Proceedings of the Workshops on Principles of Route-to-Route Extrapolation for Risk Assessment held March 19–21, 1990, in Hilton Head, South Carolina and July 10–11, 1990, in Durham, North Carolina*; Elsevier: New York, NY, USA, 1990.

*12. Memorandum from L. Proffitt, Office of Policy Initiatives and Projects, Office of Policy and International Engagement, Human Foods Program (HFP), FDA to P. Gaynor, Division of Food Ingredients, Office of Pre-Market Additive Safety, Office of Food Chemical Safety, Dietary Supplements and Innovation, HFP, FDA, April 9, 2026.

List of subjects in 21 CFR Part 73

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

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 73 is amended as follows:

PART 73--LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

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

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

§ 73.1 [Amended]

2. Amend § 73.1 in the table in paragraph (b)(1)(ii) by removing the entry for "Methylene chloride".

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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