CENTER FOR Science IN THE Public Interest
The nonprofit publisher of Nutrition Action

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Dockets Management Staff (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Two Petitions from Environmental Defense Fund, et al. to Remove the Solvents Benzene, Ethylene Dichloride, Methylene Chloride, and Trichloroethylene from Food Additive and Color Additive Regulations (**Docket No. FDA-2023-F-5684**) and **Docket No. FDA-2023-C-5679**)

The Center for Science in the Public Interest is writing to express strong support for two petitions filed by Environmental Defense Fund, et al. One requests that FDA amend the food additive regulations to remove approvals for four solvents: benzene, ethylene dichloride, methylene chloride, and trichloroethylene (TCE). The other requests that FDA amend the color additive regulations to remove approvals for the three of these four solvents appearing in the color additive regulations: ethylene dichloride, methylene chloride, and TCE.

CSPI is your food and health watchdog. Since 1971, we have been a rigorous driver of food system change to support healthy eating, safe food, and the public's health. We transform the food environment through leading-edge policy innovations grounded in meticulous research and advocacy at the national, state, and local level. A core part of CSPI's mission is providing consumers with current information about their health and well-being. CSPI publishes Nutrition Action, which provides science-based advice on health and nutrition to hundreds of thousands of readers. CSPI regularly advocates for greater transparency, disclosure, and the safety of food ingredients.

The law is clear. Under the Delaney Clause of the Federal Food, Drug, and Cosmetic Act, no food or color additive shall be considered 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."[1] In 2018, FDA recognized its obligations under the Delaney Clause in its decision to grant a petition to withdraw its approval of seven carcinogenic flavors from the food additive regulations because they were shown to cause cancer in animal studies.[2]

The carcinogenic potential of all four solvents subject to these petitions is recognized by US

[1] 21 USC §§ 348(c)(3)(A), 379e(b)(5)(B) (quoted text is from the food additive Delaney clause at 348(c)(3)(A); the color additive Delaney clause uses nearly identical language stating a color additive, "shall be deemed unsafe, and shall not be listed, 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…")
[2] 83 Fed. Reg. 50490 (October 9, 2018). Food Additive Regulations; Synthetic Flavoring Agents and Adjuvants.

and international authorities. Benzene[3] and TCE[4] are each classified as "known to be a human carcinogen" and ethylene dichloride[5] and methylene chloride[6] are each classified as "reasonably anticipated to be a human carcinogen" in the Report on Carcinogens published by the United States National Toxicology Program. The United States Environmental Protection Agency classifies benzene[7] as a "known human carcinogen," TCE[8] as "carcinogenic to humans," ethylene dichloride[9] as a "probable human carcinogen," methylene chloride[10] as "likely to be carcinogenic to humans." The World Health Organization's International Agency for Research on Cancer classifies benzene[11] and TCE[12] as "carcinogenic to humans," methylene chloride[13] as "probably carcinogenic to humans," and ethylene chloride[14] as "possibly carcinogenic to humans."

FDA itself has acknowledged the carcinogenicity of benzene, TCE, and methylene chloride. FDA has stated that, "Benzene is a known human carcinogen that causes leukemia and other blood disorders" in an alert to drug manufacturers.[15] Based on government-sponsored cancer studies in animals, FDA proposed to prohibit TCE in food in 1977.[16] In 1989, FDA prohibited use of methylene chloride in cosmetic products due to cancer risk.[17]

FDA assessed the risk associated with the use of methylene chloride to decaffeinate coffee in 1985, and permitted this use despite acknowledging the cancer hazard because the agency determined the risk to be minimal, citing the de minimis doctrine.[18] However, in 1987 in

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[3] US National Toxicology Program. *Benzene*. Report on Carcinogens, Fifteenth Edition. 2021. Available: https://ntp.niehs.nih.gov/sites/default/files/ntp/roc/content/profiles/benzene.pdf.
[4] US National Toxicology Program. *Trichloroethylene*. Report on Carcinogens, Fifteenth Edition. 2021. Available: https://ntp.niehs.nih.gov/sites/default/files/ntp/roc/content/profiles/trichloroethylene.pdf.
[5] US National Toxicology Program. *1,2-Dichloroethane*. Report on Carcinogens, Fifteenth Edition. 2021. Available: https://ntp.niehs.nih.gov/sites/default/files/ntp/roc/content/profiles/dichloroethane.pdf.
[6] US National Toxicology Program. *Dichloromethane*. Report on Carcinogens, Fifteenth Edition. 2021. Available: https://ntp.niehs.nih.gov/sites/default/files/ntp/roc/content/profiles/dichloromethane.pdf.
[7] US Environmental Protection Agency. *Benzene; CASRN 71-43-2*. Integrated Risk Information System (IRIS). Updated: September 28, 2011. Available: https://iris.epa.gov/ChemicalLanding/&substance_nmbr=199. Accessed: March 5, 2024.
[8] US Environmental Protection Agency. *Trichloroethylene; CASRN 79-01-6*. Integrated Risk Information System (IRIS). Updated: January 9, 2000. Available: https://iris.epa.gov/ChemicalLanding/&substance_nmbr=276. Accessed: March 5, 2024.
[9] US Environmental Protection Agency. *1,2-Dichloroethane; CASRN 107-06-2*. Integrated Risk Information System (IRIS). Updated: March 31, 1987. Available: https://iris.epa.gov/ChemicalLanding/&substance_nmbr=149. Accessed: March 5, 2024.
[10] US Environmental Protection Agency. *Dichloromethane; CASRN 75-09-2*. Integrated Risk Information System (IRIS). Updated: November 18, 2011. Available: https://iris.epa.gov/ChemicalLanding/&substance_nmbr=70. Accessed: March 5, 2024.
[11] International Agency For Research on Cancer. Benzene. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. 2018:120. Available: https://publications.iarc.fr/576.
[12] International Agency For Research on Cancer. Trichloroethylene, Tetrachloroethylene, and Some Other Chlorinated Agents. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. 2014:106. Available: https://publications.iarc.fr/130.
[13] International Agency For Research on Cancer. Some Chemicals Used as Solvents and in Polymer Manufacture. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. 2016:110. Available: https://publications.iarc.fr/547.
[14] International Agency For Research on Cancer. Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide (Part 1, Part 2, Part 3). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. 1999:71. Available: https://publications.iarc.fr/89.
[15] US Food and Drug Administration. *FDA alerts drug manufacturers to the risk of benzene contamination in certain drugs*. December 27, 2023. Available: https://www.fda.gov/drugs/pharmaceutical-quality-resources/fda-alerts-drug-manufacturers-risk-benzene-contamination-certain-drugs. Accessed: March 5, 2024.
[16] 42 Fed. Reg. 49465 (September 27, 1977). Trichloroethylene Removal From Food Additive Use.
[17] 54 Fed. Reg. 27328 (June 29, 1989). Cosmetics; Ban on the Use of Methylene Chloride as an Ingredient of Cosmetic Products.
[18] 50 Fed. Reg. 51551 (December 18, 1985). Cosmetics; Proposed Ban on the Use of Methylene Chloride as an Ingredient of Aerosol Cosmetic Products.

Public Citizen v. Young, the Court of Appeals for the D.C. Circuit held that Congress barred the FDA from employing a de minimis exception to the Delaney Clause,[19] and FDA acknowledged this in 2018 in the context of other chemicals violating the Delaney Clause, stating:

> The Delaney Clause limits FDA's discretion to determine the safety of food additives, in that it 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. In Public Citizen v. Young, the DC Circuit Court of Appeals 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, which was subject to a similarly worded Delaney Clause for color additives, should be approved because it did not pose more than a de minimis cancer risk.[20]

Thus, following this 1987 ruling, FDA should have revisited its 1985 methylene chloride decision and prohibited the use of methylene chloride to decaffeinate coffee. As such, the ban requested by Environmental Defense Fund et al. is long overdue and required by law.

The cancer risks resulting from the use of these solvents in food may be small, but they are completely unnecessary, as there are safe alternatives that can be used. We urge FDA to act swiftly to grant these petitions and remove approvals for all uses of these solvents in food. Thank you for considering these comments.

Sincerely,

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[19] *Public Citizen v. Young*, 831 F.2d 1108, 1122 (D.C. Cir. 1987); Les v. Reilly, 968 F.2d 985, 989 (9th Cir. 1992) (providing that "[t]hroughout its 30-year history, the Delaney clause has been interpreted as an absolute bar to all carcinogenic food additives" and that ". . . Congress has repeatedly ratified a strict interpretation of the Delaney clause" (internal citations omitted)).
[20] 83 Fed. Reg. 50490.