U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

May 12, 2022

Nancy Buermeyer
Breast Cancer Prevention Partners
1388 Sutter Street, Suite 400
San Francisco, CA 94109

c/o Tom Neltner
Environmental Defense Fund
1875 Connecticut Ave., NW, Suite 600
Washington, DC 20009

Re: Docket Number FDA-2016-P-1171

Dear Ms. Buermeyer:

This letter responds to your citizen petition[1] requesting that the Food and Drug Administration (FDA or we) prohibit the use of eight *ortho*-phthalates in food and revoke the prior sanctioned uses for five *ortho*-phthalates in food. Specifically, your citizen petition asks us to:

> A) Add a new section to Part 189 of Title 21 prohibiting the use of eight *ortho*-phthalates as food contact substances that the Consumer Products Safety Commission's (CPSC) Chronic Health Advisory Panel on Phthalates (CHAP) concluded are unsafe or the evidence indicates developmental health effects are likely. These phthalates are:
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> Diisobutyl phthalate;
> Di-n-butyl phthalate;
> Butyl benzyl phthalate;
> Dicyclohexyl phthalate;
> Di-n-hexyl phthalate [also known as dihexyl phthalate];
> Diisooctyl phthalate;
> Di(2-ethylhexyl) phthalate [also known as DEHP]; and
> Diisononyl phthalate.

[1] See Citizen Petition from Nancy Buermeyer, Breast Cancer Fund, et al., submitted to the Division of Dockets Management, Food and Drug Administration, dated April 19, 2016 ("petition").

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> B) Strike section 181.27 from Title 21 of FDA's existing regulations. This section allows the use of five *ortho*-phthalates as prior-sanctioned substances. The regulation only authorizes their use "as plasticizers when migrating from food packaging material." The petition proposes that the following *ortho*-phthalates no longer meet the reasonable certainty of no harm safety standard are:
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> Butylphthalyl butyl glycolate;
> Diethyl phthalate;
> Ethylphthalyl ethyl glycolate;
> Di-(2-ethylhexyl) phthalate (use on foods of high water content only); and
> Diisooctyl phthalate (use on foods of high water content only).

(Petition at pages 1-2).

In accordance with 21 CFR 10.30(e)(3), and for the reasons stated in section II of this response, we are denying your petition.

I. Procedural Background and Related Regulatory Actions

On April 19, 2016, you provided a submission requesting that: 1) FDA revoke and/or amend certain specified food additive and prior-sanctioned regulations in Title 21 of the Code of Federal Regulations to no longer provide for the food contact use of 30 *ortho*-phthalates; and 2) FDA prohibit the use of eight specific *ortho*-phthalates by adding a new section in 21 CFR part 189. You designated this submission as a food additive petition. With respect to the portion of your submission requesting that FDA revoke food additive uses of *ortho*-phthalates, FDA published in the Federal Register a notice of the filing of your food additive petition (FAP) on *ortho*-phthalates (81 FR 31877), on May 20, 2016.[2] In a separate document that we have finalized for publication in the Federal Register, we are denying that petition.[3]

With respect to the requests in your petition that FDA revoke prior sanctions and issue regulations under 21 CFR part 189, we declined to file those requests as a food additive petition, because those requests are not within the scope of requests that the food additive petition process is designed to address (see section 409(b) of the Federal Food, Drug, and Cosmetic Act ("FD&C Act") (21 U.S.C. 348(b)) (referring to "a petition proposing the issuance of a regulation prescribing the conditions under which such [food] additive may be safely used"); section 201(s) of the FD&C Act (21 U.S.C. 321(s)) (exempting prior sanctioned materials from the definition of a food additive); see also FDA Letter from Francis S. Lin to Tom Neltner (April 12, 2016)).

Subsequently, you filed the instant citizen petition requesting that FDA take the above-mentioned actions. The statement of grounds in your petition provides, "See Food Additive

[2] FDA assigned this petition the tracking number FAP 6B4815. Following our May 20, 2016, announcement that we had filed the food additive petition, the petitioners provided supplementary information on October 8, 2016, that, among other things, requested that FDA remove two substances (diphenylguanidine phthalate (CAS Reg No. 17573-13-6) and di (2-ethylhexyl) hexahydrophthalate (CAS Reg No. 84-71-9)) from the petitioners' original list of 30 substances, stating that they are not *ortho*-phthalates. Consequently, the subject of the petition is limited to food additive regulations for 28 *ortho*-phthalates.

[3] We incorporate by reference our final rule denying the FAP.

Petition (FAP) No. 6B4815 and FDA's filing letter for that petition issued on April 12, 2016," and provides no additional data or analysis (see petition at page 2).[4]

While your citizen petition was pending, the Flexible Vinyl Alliance filed a food additive petition on the use of *ortho*-phthalates (see 83 FR 56750, November 18, 2018, (announcing the filing of FAP 8B4820)), requesting that FDA amend our food additive regulations to no longer provide for the use of certain *ortho*-phthalates because the uses have been abandoned ("the abandonment petition"). We have finalized for publication in the *Federal Register* a notice granting the abandonment petition FAP 8B4820 to no longer provide for the use of 25 plasticizers in various food contact applications. Appendix A includes a table of the *ortho*-phthalates affected by the final rule on this subject.[5]

Of the substances cited in your citizen petition, the following three *ortho*-phthalates will remain in our food additive regulations after our actions on petition FAP 8B4820: Dicyclohexyl phthalate (DCHP, Chemical Abstract Service (CAS) No. 84-61-7); Diisononyl phthalate (DINP, CAS No. 28553-12-0); and Di(2-ethylhexyl) phthalate (DEHP, CAS No. 117-81-7) (see Appendix A). These substances therefore will currently remain approved for the food additive uses specified in 21 CFR 175.105, 175.300, 176.170, 176.210, 177.1010, 177.1200, 178.3740, and 178.3910. Our actions on petition FAP 8B4820 will not have any bearing on prior-sanctioned authorizations. Furthermore, our actions on petition FAP 8B4820 will not result in any regulations prohibiting the use of food ingredients under 21 CFR part 189.

Regarding *ortho*-phthalates that are the subject of a marketing authorization (i.e., they remain approved as food additives or authorized as prior sanctioned substances), we have finalized a notice for publication in the *Federal Register* on this topic. That notice requests scientific data and information on current uses, use levels, dietary exposure, and safety data for DCHP, DINP, DEHP, DIDP, BPBG, DEP, EPEG, and DIOP. These substances comprise *ortho*-phthalates for which marketing authorizations will remain either as food additives or prior sanctioned substances or both.[6] The purpose of this request is to encourage stakeholders to provide FDA with all sources of relevant information to support our review of the current use levels and safe use of these *ortho*-phthalates in food contact applications. We may use this information to update the dietary exposure estimates and safety assessments for the permitted food contact uses of *ortho*-phthalates.

II. Specific Responses to the Actions Requested in Your Petition

In your petition, you request that we A) prohibit the use of eight *ortho*-phthalates under part 189 of our regulations for use in food; and B) revoke the prior sanctions for five *ortho*-phthalates that exist under part 181 of our regulations for use as plasticizers in food packaging. For the reasons

[4] "FDA's filing letter" is FDA's correspondence to Tom Neltner, dated April 12, 2016.
[5] We also note that we are denying your food additive petition requesting that we amend or revoke specified regulations to no longer provide for the food contact use of the 28 *ortho*-phthalates that are the subject of that petition.
[6] The notice requests this data and information for the four phthalates (DEHP, DCHP, DINP and DIDP) subject to FAP 6B4815 that remain in the food additive regulations as a result of the abandonment petition FAP 8B4820 final rule.

discussed below, we conclude that your petition does not contain information demonstrating that these requests should be granted.

A. Request to Prohibit Substances under 21 CFR Part 189

You have asked FDA to update its regulations in 21 CFR part 189 with the purpose of "prohibiting the use of" the following eight *ortho*-phthalates as food contact substances under part 189 of our regulations: Diisobutyl phthalate (DIBP); Di-n-butyl phthalate (DBP); Butyl benzyl phthalate (BBP); Dicyclohexyl phthalate (DCHP); Di-n-hexyl phthalate (DHexP) Diisooctyl phthalate (DIOP); Di(2-ethylhexyl) phthalate (DEHP); and Diisononyl phthalate (DINP) (collectively, "the Proposed part 189 Substances").[7] In addition to the food additive uses of the Proposed part 189 Substances, both DIOP and DEHP also have prior sanctioned uses.

Under 21 CFR 189.1(a), food ingredients that are listed as prohibited substances result from a "determination that they present a potential risk to the public health or have not been shown by adequate scientific data to be safe for use in human food." Substances that are the subject of part 189 prohibitions are generally not permitted at any added or detectable level, as specified by regulation (see generally 21 CFR part 189, subparts B-D). The regulation further states that "[u]se of any of these substances in violation of this section causes the food involved to be adulterated in violation of the act" (21 CFR 189.1(a)). In previous cases where FDA has issued part 189 regulations, FDA has issued such regulations upon finding the substance causes adulteration, for example, because: 1) use of the substance would cause food to be adulterated under section 402(a)(2)(C) of the FD&C Act (21 U.S.C. 342(a)(2)(C)),[8] i.e., it is an unsafe food additive; or 2) the substance that comes in contact with the food packaging may cause the food to be injurious to health and thus adulterated under section 402(a)(1) of the FD&C Act.[9]

Based on our regulations, we reviewed your citizen petition to determine if it demonstrates that each of the eight *ortho*-phthalates at issue cause adulteration, for example, either because: 1) the substance causes food to be adulterated under section 402(a)(2)(C) of the FD&C Act; or 2) the substance causes food to be adulterated under section 402(a)(1) of the FD&C Act.

FDA, on its own initiative or on behalf of any interested person who has submitted a citizen petition under 21 CFR 10.25 and 10.30, may publish a proposal to establish a regulation prohibiting the use of a substance in human food under 21 CFR part 189 on the basis of new scientific evaluation or information (see 21 CFR 189.1(c)). "When seeking to ban a substance from use in food, a petition must include 'an adequate scientific basis.'" *In re Natural Resources Defense Council*, 645 F.3d 400, 403 (D.C. Cir. 2011) (quoting § 189.1(c)). Under 21 CFR 10.30, citizen petitions are to be resolved based on information in the administrative record (see 21 CFR 10.30(j)). Under 21 CFR 10.30(i), the record consists of: 1) the petition, including all information on which it relies, filed by the Division of Dockets Management (now called the Dockets Management Staff); 2) all comments received on the petition, including all information

[7] As noted above, the abandonment final rule removes many of these substances from our food additive regulations.
[8] See, for example, the Federal Register notices supporting our part 189 prohibition of tin coated lead foil capsules for wine bottles, *available at* 57 FR 55485 and 61 FR 4816.
[9] See, for example, the Federal Register notices supporting our part 189 prohibition on lead-soldered food cans, *available at* 58 FR 33860, 60 FR 33106.

submitted as a part of the comments; 3) if the petition resulted in a proposal to issue, amend, or revoke a regulation, all of the documents specified in 21 CFR 10.40(g); 4) the record, consisting of any transcripts, minutes of meetings, reports, Federal Register notices, and other documents resulting from certain optional procedures; 5) the Commissioner's decision on the petition, including all information identified or filed by the Commissioner with the Dockets Management Staff as part of the record supporting the decision; and 6) all documents filed with the Dockets Management Staff under § 10.65(h).

For the reasons outlined below, we have concluded that the administrative record, which includes the information contained in and relied upon by your petition, does not set forth a sufficient showing that the scientific evidence supports amending our regulations to prohibit the use of these substances under part 189. Specifically, the administrative record does not support a determination that the substances caused food to be adulterated, for example either because: 1) the substance causes food to be adulterated under section 402(a)(2)(C) of the FD&C Act; and/or 2) the substance causes food to be adulterated under section 402(a)(1) of the FD&C Act.

1. Regulatory Framework

The FD&C Act authorizes us to regulate "food additives" (see section 409(a) of the FD&C Act). The FD&C Act defines "food additive," in relevant part, as any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component of food or otherwise affecting the characteristics of any food (see section 201(s) of the FD&C Act). Food additives can include both substances added directly to food and indirectly and may include "food contact substances." "Food contact substances" are substances intended for use in materials that come into contact with food, for instance in food packaging or manufacturing, but which are not intended to have any technical effect in the food (21 CFR 170.3(e)(3)).

Food additives are deemed unsafe and prohibited except to the extent that we permit their use (see, *e.g.*, sections 301(a), (k), and 409(a) of the FD&C Act (21 U.S.C. 331(a), (k), and 348(a))). Under section 409(c)(3) of the FD&C Act, we will not establish a regulation for the use of a food additive if a fair evaluation of the data fails to establish that the proposed use of the food additive, under the conditions of use, to be specified in the regulation, will be safe. Our regulations at 21 CFR 170.3(h)(i) define safety as a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.

The FD&C Act creates an exception to the "food additive" definition for substances that are generally recognized as safe ("GRAS"). If a substance is GRAS, it is not a "food additive" and therefore is not subject to the mandatory premarket review requirement in section 409 of the FD&C Act. A substance cannot be classified as GRAS under the conditions of its intended use if the available data and information do not satisfy the safety standard for a food additive under the FD&C Act (see 21 CFR 170.30). General recognition of safety requires common knowledge, throughout the expert scientific community knowledgeable about the safety of substances directly or indirectly added to food, that there is a reasonable certainty that the substance is not harmful under the conditions of its intended use (see id.). "Common knowledge" can be based

on either scientific procedures or on experience based on common use of a substance in food prior to January 1, 1958 (see id.).

To establish with reasonable certainty that a food additive is not harmful under its intended conditions of use such that it meets the safety standard under section 409 of the FD&C Act, FDA considers the projected human dietary exposure to the food additive, the additive's toxicological data, and other available relevant information (such as published literature). One method that FDA may use is to compare the Estimated Daily Intake (EDI) of the food additive to an Acceptable Daily Intake (ADI) level established by applying appropriate safety factors to applicable toxicological data. To determine whether a food additive is safe, section 409(c)(5) of the FD&C Act requires FDA to consider among other relevant factors the following: A) Probable consumption of the additive; B) the cumulative effect of such additive in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substances in such diet; and C) safety factors recognized by experts as appropriate for the use of animal experimentation data (section 409(c)(5) of the FD&C Act).

Section 402(a)(1) of the FD&C Act provides, in relevant part, that a food shall be deemed adulterated if it bears or contains any poisonous or deleterious substance which may render it injurious to health.[10] Courts have interpreted this language to mean that a food is adulterated when it contains enough of an added poisonous or deleterious substance to pose a reasonable possibility of injury to health.[11] Without such a possibility, the mere presence of an added poisonous or deleterious substance does not render food adulterated under section 402(a)(1) of the FD&C Act. Moreover, courts have concluded that a reasonable possibility of injury to health does not exist solely because it is physically possible for a person to consume enough of a food to harm themself if ingested in extreme amounts.[12]

2. Relevant Scientific Evidence

You have not demonstrated that it is appropriate to prohibit the use of the eight *ortho*-phthalates that are the subject of your request under part 189. In evaluating safety, it is important to identify both whether the substance can cause an adverse effect and, if so, at what levels.[13] A prohibition may be especially justified if it is shown that a substance cannot be safely consumed at any level.[14] But for the Proposed part 189 Substances, you have not demonstrated that they

[10] If a substance is not an added substance, section 402(a)(1) of the FD&C Act provides that the food shall not be considered adulterated under this provision if the quantity of such substance in such food does not ordinarily render it injurious to health. However, this provision for substances that are not added is not relevant to the discussion of *ortho*-phthalates, which are added substances for purposes of the uses subject to this petition.

[11] See, e.g., *United States v. Anderson Seafoods, Inc.,* 447 F. Supp. 1151, 1156 (N.D. FL 1978), aff'd, 622 F.2d 157 (5th Cir. 1980); *United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 411 (1914).

[12] See *Anderson Seafoods,* 447 F. Supp. at 1155.

[13] FDA guidance for industry, *Guidance for Industry and other Stakeholders. Toxicological Principles for the Safety Assessment of Food Ingredients: Redbook 2000* (July 2000, revised July 2007). We update guidances periodically. To ensure that you have the most recent version of a guidance, check the FDA Guidances Web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[14] But if a substance does not have a safe level, and also cannot be avoided, there may be more appropriate regulatory tools for limiting exposure to the substance other than a part 189 prohibition. Action levels issued under 21 CFR part 109, for example, may take into account both public health needs and the fact that the substance cannot

are unsafe at *any* level. To the contrary, two of the publications you rely on in your food additive petition 6B4815 (the CHAP report and the 1973 Shibko publication) refer to scientific studies showing that all eight of the Proposed part 189 Substances can be administered at levels that do not cause toxic effects.[15] Indeed, your food additive petition cites no-observed-adverse-effect-level (NOAELs) from the CHAP report. Thus, the scientific evidence you have provided indicates that there are in fact exposure levels that do not cause adverse effects.

In addition, you have not justified that each of the eight Proposed part 189 Substances are unsafe at any particular level.[16] The food additive framework under section 409 of the FD&C Act requires that FDA assess safety under the intended conditions of use (section 409(b)(2)(B) of the FD&C Act) and also provides that a food additive may not be permitted at levels above those required to achieve its technical effect (section 409(c)(4) of the FD&C Act). FDA may permit the use of a food additive for a specified use and use level at which reliable and sufficient data demonstrate that the additive has been shown to be safe under the intended conditions of use. FDA uses risk assessment to appropriately determine whether there is a reasonable certainty that no harm will result from the proposed use of an additive at its specified level. FDA's regulations provide us the option to establish prohibitions under part 189 when the science justifies such an approach, but notably do not provide that such prohibitions are the only path for managing risk.[17] Your petition does not explain why a prohibition is justified based on the available scientific data.

We also note that as justification for your part 189 request, you state that the "Consumer Product Safety Commission's (CPSC) Chronic Health Advisory Panel on Phthalates (CHAP) concluded" that eight specific *ortho*-phthalates "are unsafe or evidence indicates developmental health effects are likely" (Petition at page 1). However, the CHAP report's scientific evaluation was primarily conducted for the purpose of evaluating the safety of phthalates for use in children's toys and child care articles—not in food contact substances.[18] In evaluating the safety of

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be avoided. FDA makes case-by-case assessments on how best to manage risks from contaminants that cannot be avoided. Thus, if a substance is not safe at any level and also cannot be avoided, a part 189 prohibition is not necessarily the best approach.

[15] See 2014 Chronic Hazard Advisory Panel (CHAP) on Phthalates and Phthalate Alternatives Final Report, Table 2.1, page 81; see also Shibko, S. I.; Blumenthal, H., 1973, "Toxicology of phthalic acid esters used in food packaging material," Environmental health perspectives, 3:131-137.

[16] Although your food additive petition 6B4815 proposes an ADI for DEHP and proposed to apply it to all 28 phthalates, our response to that petition explains why the proposed ADI for DEHP is not justified and also why it is not justified to apply that ADI to the entire proposed class of 28 *ortho*-phthalates.

[17] See supra note 15.

[18] Notably, CPSC's handling of phthalates is more complex and goes beyond the CHAP. For example, section 108 of the Consumer Product Safety Improvement Act (15 U.S.C. 2057c) established a permanent prohibition on manufacture, sale, distribution, or importation of any children's toy or child care article containing more than 0.1 percent of di-(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), or benzyl butyl phthalate (BBP). The same section also created an "interim" prohibition with respect to the manufacture, sale, distribution, or importation of "any children's toy that can be placed in a child's mouth or child care article that contains concentrations of more than 0.1 percent of diisononyl phthalate (DINP), diisodecyl phthalate (DIDP), or di-n-octyl phthalate (DnOP)." The statute charged the CHAP with conducting an examination of "the full range of phthalates that are used in products for children" and to:

substances for food contact uses, FDA is required by statute to consider the safety of a substance for the particular food contact use,[19] and we are directed by statute to consider *dietary* exposure

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(i) examine all of the potential health effects (including endocrine disrupting effects) of the full range of phthalates;

(ii) consider the potential health effects of each of these phthalates both in isolation and in combination with other phthalates;

(iii) examine the likely levels of children's, pregnant women's, and others' exposure to phthalates, based on a reasonable estimation of normal and foreseeable use and abuse of such products;

(iv) consider the cumulative effect of total exposure to phthalates, both from children's products and from other sources, such as personal care products;

(v) review all relevant data, including the most recent, best-available, peer-reviewed, scientific studies of these phthalates and phthalate alternatives that employ objective data collection practices or employ other objective methods;

(vi) consider the health effects of phthalates not only from ingestion but also as a result of dermal, hand-to-mouth, or other exposure;

(vii) consider the level at which there is a reasonable certainty of no harm to children, pregnant women, or other susceptible individuals and their offspring, considering the best available science, and using sufficient safety factors to account for uncertainties regarding exposure and susceptibility of children, pregnant women, and other potentially susceptible individuals; and

(viii) consider possible similar health effects of phthalate alternatives used in children's toys and child care articles.

15 U.S.C. 2057c(b)(2)(B)(i) through (viii).
The CHAP recommended no further action on DBP, BBP, and DEHP due to the statutory prohibition in children's toys and child care articles at levels greater than 0.1% (see "Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives," dated July 2014, (CHAP Report) at page 7). It also recommended that the interim ban on DINP in children's toys and child care articles at levels greater than 0.1% be made permanent (id.), but that the interim bans on DNOP and DIDP be lifted (id. at page 8). It also recommended no action on dimethyl phthalate or diethyl phthalate (id.), although the CHAP recommended that U.S. agencies responsible for dealing with DEP exposures from food, pharmaceuticals, and personal care products "conduct the necessary risk assessments with a view to supporting risk management steps" (id.).
The CHAP report also discussed other phthalates, such as dimethyl phthalate (DMP), diethyl phthalate (DEP), di(2-propylheptyl) phthalate (DPHP), diisobutyl phthalate (DIBP), di-n-pentyl phthalate (DPENP), di-*n*-hexyl phthalate (DHEXP), dicyclohexyl phthalate (DCHP), and diisooctyl phthalate (DIOP) and recommended permanent bans for DIBP, DPENP, DHEXP, and DCHP in children's toys and child care articles at levels greater than 0.1% and an interim ban on DIOP in children's toys and child care articles at levels greater than 0.1% until sufficient toxicity and exposure data are available to assess potential risks (id.).
In short, the CPSC's handling of phthalates reflects a mixture of permanent and temporary statutory restrictions (as stated in section 108 of the Consumer Product Safety Improvement Act) and recommendations for permanent or temporary restrictions on certain phthalates. The CPSC, pursuant to section 8 of the Consumer Product Safety Improvement Act, was to use the CHAP's findings and recommendations to "declare any children's products containing any phthalates to be a banned hazardous substance….as the Commission determines necessary to protect the health of children" (15 U.S.C. 2057c(3)(B)). (The CPSC issued its final rule on phthalates on October 27, 2017 (82 FR 49938).)
[19] See 409(b) and 409(h)(1) of the FD&C Act (providing that sponsors may submit petitions or notifications with respect to the "intended use" of the substance).

in determining safety.[20] For example, FDA recommends specific testing protocols for assessing migration and resulting dietary exposure that reflects the intended use of the substance.[21] Migration of a substance may vary due to the physiochemical properties of the substance, the time and temperature conditions of its intended use (e.g., oven baking at 400 degrees Fahrenheit for one hour), and the types of food (e.g., aqueous foods, fatty foods, etc.) in contact with the food-contact article.[22] Accordingly, FDA's safety assessments consider the specific intended conditions of use at issue. Assessments conducted for the purpose of evaluating the safety of a use that does not result in dietary exposure (for example, the use of a substance in children's toys and articles) would use a different set of parameters as is expected for a different intended use and possibly different route of exposure. Therefore, assessments conducted for the purpose of evaluating children's toys and child care article uses do not necessarily apply to the safety of food contact uses due to the different conditions of use, and you have not provided an explanation in your petition for why the CHAP report's assessments of phthalates in children's toys and child care articles should apply directly to the safety of phthalates for food contact uses. As appropriate, FDA may consider the underlying evidence reviewed in such assessments. FDA's statutory responsibility is to evaluate safety in accordance with the FD&C Act and in consideration of the specific intended uses for which we have jurisdiction.

In evaluating requests to issue a regulation prohibiting a substance under 21 CFR part 189, we may also consider whether an added ingredient is poisonous or deleterious and may render a food injurious to health, such that the food would be adulterated under section 402(a)(1) of the FD&C Act. However, you have not provided any explanation as to why the 402(a)(1) standard is implicated. You have not explained why a food would be adulterated within the meaning of section 402(a)(1) of the FD&C Act whenever it contains any amount of the Proposed part 189 Substances. As stated above, courts have interpreted the standard of section 402(a)(1) of the FD&C Act to mean that a food is adulterated when it contains enough of an added poisonous or deleterious substance to pose a reasonable possibility of injury to health.[23] Without such a possibility, the mere presence of an added poisonous or deleterious substance does not render food adulterated under section 402(a)(1) of the FD&C Act. You have not provided any explanation or evidence that addresses this standard.

As an additional matter, you have not presented evidence that the specific Proposed part 189

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[20] See section 409(c)(5) of the FD&C Act (21 U.S.C. 348(c)(5) (providing that in determining safety, the Secretary shall consider among other relevant factors "the probable consumption of the additive and of any substance formed in or on food because of the use of the additive")). See also FDA guidance for industry, *Estimating Dietary Intake of Substances in Food* (August 2006).

[21] See FDA guidance for industry, *Preparation of Premarket Submissions for Food Contact Substances (Chemistry Recommendations)* (December 2007).

[22] FDA then applies this migration information to an 100% market capture assumption (*i.e.,* FDA assumes that all products of the particular type authorized will utilize the FCS at the highest authorized use level, even though other competing FCSs that serve the same function may be used instead or the FCS may be used at lower use levels in some products). Using a migration protocol that reflects the "worst-case" conditions of the intended use (e.g., highest temperature and use level) and assuming 100% market capture ensures that dietary exposure estimates do not underestimate potential dietary exposure to the substance under its intended condition of use (see FDA guidance for industry, *Preparation of Premarket Submissions for Food Contact Substances (Chemistry Recommendations)* (December 2007)).

[23] See, e.g., *United States v. Anderson Seafoods, Inc.*, 447 F. Supp. 1151, 1156 (N.D. FL 1978), aff'd, 622 F.2d 157 (5th Cir. 1980); *United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 411 (1914).

Substances are not GRAS and do not meet the food additive safety standard in any amount, thereby causing food to be adulterated under section 402(a)(2)(C) of the FD&C Act. Instead, the scientific evidence you have provided is a reference to your food additive petition (FAP 6B4815). This petition proposes a grouping of 28 *ortho*-phthalates for the purpose of assessing their safety, but the submission does not analyze each of the Proposed part 189 Substances individually. In our notice denying your food additive petition that we have finalized for publication in the *Federal Register*, we explain why you have not demonstrated lack of safety for the 28 *ortho*-phthalates that are the subject of the food additive petition. Your citizen petition does not fill in any of those gaps to provide evidence regarding the specific Proposed part 189 Substances.

We are denying your request for part 189 prohibitions because the administrative record does not contain information showing that the Proposed part 189 Substances are never safe for use as food contact substances. The administrative record does not contain sufficient information showing that the Proposed part 189 Substances cause food to be adulterated in any amount, including under sections 402(a)(1) and 402(a)(2)(C) of the FD&C Act. Although we are denying your request, we note that we are nevertheless committed to ensuring that any *ortho*-phthalates allowed for food contact uses are safe. If we become aware of scientific evidence showing that any of the eight subject *ortho*-phthalates cause food to be adulterated,[24] we will take appropriate action. Here, with your citizen petition, you have not adduced evidence to support your requested action.

B. Request to Revoke Prior Sanctions

You have asked us to revoke the prior sanctions for five *ortho*-phthalates that are codified under part 181 of our regulations for use in food or food packaging: Butylphthalyl butyl glycolate (BPBG); Diethyl phthalate (DEP); Ethylphthalyl ethyl glycolate (EPEG); Di-(2-ethylhexyl) phthalate (DEHP) (use on foods of high water content only); and Diisooctyl phthalate (DIOP) (use on foods of high water content only) (the "Proposed Prior Sanction Revocation Substances").

A "prior sanction" is "an explicit approval granted with respect to use of a substance in food prior to September 6, 1958," by FDA or the United States Department of Agriculture (USDA), pursuant to the FD&C Act, the Poultry Products Inspection Act, or the Meat Inspection Act (21 CFR 170.3(l)). The term "prior sanction" derives from section 201(s)(4) of the FD&C Act, which excepts from the definition of a food additive any substance "used in accordance with a sanction or approval granted prior to" September 6, 1958, the date of enactment of the Food Additives Amendment to the FD&C Act. Before that date, FDA had approved specific uses of various food-contact materials or food ingredients by issuing letters and other statements that stated that in FDA's view these substances were "not considered unsafe," that they did "not present a hazard," or that FDA "did not object to their use." The existence of a prior sanction exempts sanctioned uses from the food additive provisions of the FD&C Act but not from the other adulteration or the misbranding provisions of the FD&C Act (21 CFR 181.5(b)). The prior sanction exists "only for a specific use(s) of a substance in food, i.e., the level(s), condition(s),

[24] We note that we are issuing a notice on this subject in the *Federal Register* requesting scientific data and information on current uses, use levels, dietary exposure, and safety data of certain *ortho*-phthalates.

product(s), etc., for which there was explicit approval" by FDA or USDA before September 6, 1958 (21 CFR 181.5(a)). Some prior sanctioned substances are codified in 21 CFR part 181.

Notably, 21 CFR 181.1(b) states: "Based upon scientific data or information that shows that use of a prior-sanctioned food ingredient may be injurious to health, and thus in violation of section 402 of the [FD&C] Act, the Commissioner will establish or amend an applicable prior sanction regulation to impose whatever limitations or conditions are necessary for the safe use of the ingredient, or to prohibit use of the ingredient." Furthermore, 21 CFR 181.5(c) allows for the revocation of a regulation of a prior sanctioned substance "to prohibit use of the ingredient, in order to prevent the adulteration of food in violation of section 402 of the [FD&C] Act." We therefore evaluate your citizen petition's request regarding prior sanctions to determine whether it shows that the use of the prior sanctioned use may be injurious to health under section 402(a)(1) of the FD&C Act.

The only evidence you submitted in support of this request is your food additive petition, which proposes to treat a large, diverse number of *ortho*-phthalates as a class for purposes of a safety assessment, apply a proposed ADI value for one phthalate to all the phthalates in the purported class, and compare the exposure of all the phthalates against that single proposed ADI. This approach is flawed for the reasons outlined in our notice denying your food additive petition that is finalized for publication in the *Federal Register*.

In submitting your citizen petition, you did not provide any additional evidence beyond what you submitted in your food additive petition. Neither your food additive petition nor your citizen petition explains any basis for concluding that the Proposed Prior Sanction Revocation Substances cause food to be regarded as adulterated within the meaning of section 402(a)(1) of the FD&C Act. Furthermore, neither your food additive petition nor your citizen petition addresses the safety of the specific uses for which the Proposed Prior Sanction Revocation Substances have received prior sanction.

As described above, FDA does not evaluate safety in a vacuum. Rather, to assess the safety of a food contact substance, FDA evaluates the particular intended use of a substance. You have not demonstrated that the Proposed Prior Sanction Revocation Substances may render food injurious to health at any level of exposure, or even at specified levels of exposure caused by the prior sanctioned uses. By failing to demonstrate health risks at levels of exposure linked to the prior sanctioned uses, you have failed to provide a record showing that the prior sanction uses cause food to be regarded as adulterated within the meaning of section 402(a)(1) of the FD&C Act. Your citizen petition request therefore lacks scientific support.

In addition, by not addressing why the Proposed Prior Sanction Revocation Substances are adulterated within the meaning of section 402(a)(1) of the FD&C Act, your citizen petition request lacks legal support. Consequently, you have not provided adequate legal grounds for your requested action (see 21 CFR 10.30(b)(3) (requiring citizen petitions to set forth the legal grounds on which the petition relies)).

III. Conclusion

Based on our consideration of the scientific evidence and other information submitted with your petition, we conclude that the evidence is insufficient to support the actions that you request. Therefore, in accordance with 21 CFR 10.30(e)(3), we are denying your petition.

Sincerely,

Leslie Kux -S
Digitally signed by Leslie Kux -S
Date: 2022.05.12 12:45:19 -04'00'

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APPENDIX A

Table 1: *Ortho*-phthalates Affected by Final Rule on FAP 8B4820	
Food additive	**CAS No.**
Dimethyl phthalate (dimethyl *ortho*-phthalate)	131-11-3
Diphenyl phthalate	84-62-8
Methyl phthalyl ethyl glycolate (1,2-Benzenedicarboxylicacid, 1-(2-ethoxy-2-oxoethyl) 2-methyl ester)	85-71-2
Diethyl phthalate	84-66-2
Diphenylguanidine phthalate[1]	17573-13-6
Ethyl phthalyl ethyl glycolate (Ethyl carbethoxymethyl phthalate)	84-72-0
Diisobutyl phthalate	84-69-5
Butyl benzyl phthalate[2]	85-68-7
Di-n-butyl phthalate[3]	84-74-2
Butyl phthalyl butyl glycolate[4] (Butyl carbobutoxymethyl phthalate)	85-70-1
Dihexyl phthalate (Di-n-hexyl phthalate)	84-75-3
Di(butoxyethyl) phthalate (Bis(2-n- butoxyethyl) phthalate)	117-83-9
Dimethylcyclohexyl phthalate	1322-94-7
Diisooctyl phthalate	27554-26-3
Dioctyl phthalate (Di-n-octyl phthalate)	117-84-0
Butyloctyl phthalate (n-butyl n-octyl phthalate)	84-78-6
Di(2-ethylhexyl) hexahydrophthalate[1]	84-71-9
Amyl decyl phthalate (n-amyl n-decyl phthalate)	7493-81-4
Butyl decyl phthalate[5] (n-butyl n-decyl phthalate)	89-19-0
Decyl octyl phthalate (Octyldecyl phthalate / n-octyl n-decyl phthalate)	119-07-3
Didecyl phthalate (Di-n-decyl phthalate)	84-77-5
Dodecyl phthalate	21577-80-0
Dihydroabietyl phthalate	26760-71-4
Castor oil phthalate, hydrogenated	None Available
Castor oil phthalate with adipic acid and fumaric acid-diethylene glycol[6]	68650-73-7

[1]We note that while these substances are not chemically classified as *ortho*-phthalates, they are included in FAP 8B4820.