[ORAL ARGUMENT NOT SCHEDULED]

No. 24-1382

IN THE UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

ALASKA COMMUNITY ACTION ON TOXICS, *et al.*,

Petitioners,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,

Respondents.

On Petition for Review of an Order of the
United States Food and Drug Administration

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CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to D.C. Circuit Rule 28(a)(1), the undersigned counsel certifies as follows:

A. Parties and Amici

Petitioners in this Court are Alaska Community Action on Toxics, Breast Cancer Prevention Partners, Center for Environmental Health, Center for Food Safety, Center for Science in the Public Interest, Defend Our Health, Environmental Defense Fund, and Learning Disabilities Association of Illinois.

Respondents in this Court are the U.S. Food and Drug Administration (FDA) and Dr. Martin Makary, in his official capacity as Commissioner of the U.S. Food and Drug Administration.[1]

Dr. Deborah H. Bennett, Dr. Linda S. Birnbaum, Dr. Stephanie M. Engel, Dr. Russ Hauser, Dr. Susan Schantz, and Dr. Ami Zota, filed a brief in this Court as amici curiae in support of petitioners.

B. Rulings Under Review

On October 30, 2024, FDA denied petitioners' administrative objections and hearing requests regarding FDA's prior denial of petitioners'

[1] Commissioner Makary was automatically substituted as a party under Federal Rule of Appellate Procedure 43(c).

food-additive petition. *See* 89 Fed. Reg. 86,290 (Oct. 30, 2024); JA__[FDA-000001-16]. Petitioners seek review of that decision.

C. Related Cases

The undersigned counsel is not aware of any currently pending related cases within the meaning of D.C. Circuit Rule 28(a)(1)(C). Although this specific case has not previously been before this Court, there was previously a petition for writ of mandamus filed regarding FDA's decision on the underlying food-additive petition, which was voluntarily dismissed on July 5, 2022. *See In re Environmental Def. Fund*, No. 21-1255 (D.C. Cir.).

/s/ McKaye L. Neumeister
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GLOSSARY

ATSDR	Agency for Toxic Substances and Disease Registry
CPSC	Consumer Product Safety Commission
DIDP	Diisodecyl phthalate
EPA	Environmental Protection Agency
FAP	Food-additive petition
FDA	U.S. Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetic Act
FWW	*Food & Water Watch, Inc. v. Vilsack*, 808 F.3d 905 (D.C. Cir. 2015)
JA	Joint Appendix
NRDC	Natural Resources Defense Council
OECD	Organization for Economic Cooperation and Development

STATEMENT OF JURISDICTION

The U.S. Food and Drug Administration (FDA) issued an order denying petitioners' administrative objections and hearing requests on October 30, 2024. JA__[FDA-000001-16]. Petitioners timely filed a petition for review on December 19, 2024. This Court has jurisdiction under 21 U.S.C. § 348(g)(1), if petitioners have demonstrated standing. *See infra* Part I.

STATEMENT OF THE ISSUES

Under the Federal Food, Drug, and Cosmetic Act, FDA may promulgate regulations authorizing food additives—which include certain substances used in food packaging—when they are shown to be safe for use. Phthalates are substances used to soften plastic products, and FDA previously authorized certain phthalates as food additives for use in food packaging. Petitioners requested that FDA repeal those authorizations, and FDA denied that request and subsequently denied petitioners' objections and requests for a hearing regarding that decision.

The issues presented are:

1. Whether petitioners have established associational standing to challenge FDA's denial of their food-additive petition (FAP) and their subsequent objections and hearing requests;

2. Whether FDA reasonably determined that the record contained insufficient scientific information to require setting aside the finding that the subject phthalates' authorized food-additive uses are safe; and

3. Whether FDA reasonably determined that petitioners had raised no material issue of fact that would warrant an administrative hearing before overruling petitioners' objections to the denial of their food-additive petition.

PERTINENT STATUTES AND REGULATIONS

Pertinent statutes and regulations are reproduced in the addendum to this brief.

STATEMENT OF THE CASE

A. Statutory and Regulatory Framework

1. The Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 301 *et seq.*, prohibits the marketing of "adulterated" foods. *Id.* § 331(a)-(c). Food is adulterated if, among other things, it contains "any food additive that is unsafe within the meaning of [21 U.S.C. § 348]." *Id.* § 342(a)(2)(C)(i). A food additive is "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. *Id.* § 321(s). Food additives can include "food contact substances," which are "intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food" but which are "not intended to have any technical effect in such food."

Id. § 348(h)(6). As relevant here, a food additive is "deemed … unsafe" until FDA promulgates a regulation prescribing the conditions under which the additive may be safely used. *Id.* § 348(a)(2), (a)(3)(A), (c)(1)(A).[2] To promulgate such a regulation, FDA must determine "that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the conditions of its intended use." 21 C.F.R. § 170.3(i) (defining "[s]afe"). FDA is thus responsible for the premarket approval of food additives. *See* 21 U.S.C. § 393(b)(2)(A), (d)(2).

2. There are two ways by which the process for promulgating a regulation authorizing a food-additive use can be initiated. FDA itself may initiate this process, or private parties may submit a petition to FDA "proposing the issuance of a regulation prescribing the conditions under which such additive may be safely used." 21 U.S.C. § 348(b)(1), (d). Such food-additive petitions (authorization petitions) must contain specified information. *See id.* § 348(b)(2); 21 C.F.R. § 171.1(c). And the petitioner bears the evidentiary burden of establishing that the proposed use of the food additive "will be safe." *See* 21 U.S.C. § 348(c)(3). In response, FDA must by

[2] An alternative pathway for a specific manufacturer of a food-contact substance to obtain premarket authorization has existed since 1997, known as the food-contact notification process. *See* 21 U.S.C. § 348(a)(3)(B), (h). The marketing of the subject phthalates was authorized pursuant to regulations promulgated under § 348, not the notification process.

order either grant the authorization petition and establish a regulation prescribing the conditions under which the additive may be safely used, or deny the petition and notify the petitioner of the reasons for the denial. *See id.* § 348(c)(1)(A)-(B).

FDA also may amend or repeal existing food-additive regulations, either on its own initiative or in response to private-party petitions (repeal petitions). *See* 21 U.S.C. § 348(i); 21 C.F.R. § 171.130(a). Congress directed the agency to issue regulations "prescrib[ing] the procedure by which [food-additive] regulations … may be amended or repealed." 21 U.S.C. § 348(i). The statute specifies that this "procedure shall conform to the procedure provided in [§ 348] for the promulgation of such regulations." *Id.*

Repeal petitions must "include an assertion of facts, supported by data, showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption may justify its amendment or repeal." 21 C.F.R. § 171.130(b). And such petitions must contain "full information on each proposed change that is to be made in the original regulation." *Id.* § 171.1(c). This includes, as relevant, "[f]ull reports of investigations made with respect to the safety of the food additive." *Id.* As with authorization petitions, repeal

petitions bear the evidentiary burden of justifying the action sought. *See* 21 U.S.C. § 348(c), (i); 21 C.F.R. § 171.1(c). Accordingly, where a petition seeks to repeal a regulation because the approved food-additive use is no longer safe, it "must contain sufficient data to establish the existence of safety questions significant enough to support a finding that there is no longer a reasonable certainty of no harm from the currently approved uses." JA__[FDA-002005]; *see* 21 C.F.R. § 170.3(i).

3. After FDA publishes an order granting or denying a petition, "any person adversely affected" can file objections to the order and request a public hearing to address the objections. *See* 21 U.S.C. § 348(e)-(f); 21 C.F.R. § 171.110. Each objection on which a hearing is requested must "includ[e] a detailed description and analysis of the factual information to be presented." 21 C.F.R. § 12.22(a)(5). FDA will grant a hearing request only if there are "genuine and substantial issue[s] of fact for resolution at a hearing" that can be "resolved by … specifically identified reliable evidence"; the "data and information submitted, if established" would be "[s]ufficient to justify the factual determination urged"; and the sought factual determination would be "determinative with respect to the action requested." *Id.* § 12.24(b)(1)-(4).

The denial of objections and hearing requests is final agency action subject to judicial review. 21 C.F.R. §§ 12.28(d), 12.30(c); *see* 21 U.S.C. § 348(g)(1).

B. FDA's Prior Authorization of Phthalates For Food-Contact Uses

This case involves certain substances known as "ortho-phthalates" or simply "phthalates." Phthalates are commonly used to soften plastic products, including food packaging.[3] In that capacity, phthalates can indirectly become a part of food, and are thus considered a food-contact substance. Decades ago, FDA authorized the use of several different phthalates in specific food-contact applications, determining that the evidence before the agency established that those substances met the safety standard in 21 U.S.C. § 348 when they come into contact with food under the prescribed conditions. FDA thus issued regulations specifying the approved food-contact uses of those phthalates. *See* JA__[FDA-002005-06] (listing regulations at issue).

C. Procedural Background

In May 2016, a group of organizations submitted a petition to FDA seeking the repeal of regulations authorizing the food-contact uses of 28

[3] *See* FDA, *Phthalates in Food Packaging and Food Contact Applications* (Oct. 29, 2024), https://perma.cc/J9CD-W6H4.

phthalates. JA__[FDA-012416-84] (FAP 6B4815, referred to herein as the petition); *see* JA__[FDA-002005]. The petition was premised on three assertions: (1) the 28 phthalates are "chemically- and pharmacologically-related substances" and should be considered as a class for determining safety; (2) the acceptable daily intake for one phthalate "should be assigned to all [28]phthalates" in the class; and (3) the estimated daily intake of the phthalates "significantly exceeds the [acceptable daily intake]" of the selected phthalate. JA __[FDA-012417, 26]. Based on these three assertions, the petition urged FDA to conclude that "there is no longer a reasonable certainty of no harm for the food contact use" of the 28 phthalates. JA__[FDA-012418]. FDA published a notice of this petition in the Federal Register, soliciting comments. JA__[FDA-002643-45].

1. In May 2022, FDA denied the petition. JA__[FDA-002004-17] (87 Fed. Reg. 31,066 (May 20, 2022)) (denial order). FDA concluded that the record did not contain adequate support for any of the petition's three assertions. JA__[FDA-002013].

First, the agency observed that, based on the record evidence, "[t]he 28 phthalates do not have a common functional group, do not have similar or related pharmacological effects, do not share a 'common metabolic pathway' or even a common mechanism of action, and do not have effects on the same

or similar target or system." JA__[FDA-002010]; *see* JA__[FDA-002006-10]. Accordingly, there was not an adequate basis for treating the 28 phthalates as a class for purposes of a single safety assessment. *See* JA__[FDA-002010].

Second, FDA rejected the proposed acceptable daily intake value for cumulative exposure to all 28 phthalates at issue, which relied on values reported in publications without "evaluat[ing] the underlying evidence," "provid[ing] additional information that would allow FDA to fill the gaps," or addressing other studies supporting higher levels. JA__[FDA-002010-12].

Third, FDA concluded that the petition's proposed exposure estimates did "not account for: (1) The imprecision of relying on exposur[e] estimates derived from biomonitoring studies to assess dietary exposure; (2) the diverse parameters used in the cited dietary exposure analyses to determine which analysis, if any, most accurately reflects true U.S. dietary exposure; and (3) the contradiction in reported dietary exposure values between those analyses." JA__[FDA-002013].

FDA noted, however, that it would "continue to examine [new] data as appropriate to assess whether there remains a reasonable certainty of no harm." JA__[FDA-002013]. Accordingly, the same day it denied the

petition, FDA issued a request for information in the Federal Register seeking "all updated information regarding the food contact uses, use levels, and dietary exposure and safety data for the [p]hthalates" at issue. JA__[FDA-021102]. FDA explained that it "may use this information to update the dietary exposure estimates and safety assessments for the permitted food contact uses of [p]hthalates." JA__[FDA-021102]. Indeed, phthalates remain on FDA's list of chemicals in the food supply that are under review. *See* FDA, *List of Select Chemicals in the Food Supply Under FDA Review* (June 18, 2025), https://perma.cc/254K-NXM9 ("The FDA is working on an updated safety assessment of the remaining authorized uses of phthalates, including considering information the FDA has received through a request for information.").

2. While FDA was considering the petition at issue here, a different petition was filed that proposed repealing the authorizations for food-contact use of 25 phthalates on the grounds that those uses were permanently abandoned. JA__[FDA-000002]. In response, FDA repealed the regulations authorizing those phthalates. JA__[FDA-000002]; *see* JA__[FDA-021091-100]. As a result, of the 28 substances implicated in FAP

6B4815, food-additive authorizations for only five phthalates remain in effect. JA__[FDA-000007].[4]

3. Petitioners in this action filed eight objections to FDA's decision denying their petition and requested a public evidentiary hearing. JA__[FDA-010642-96]. In October 2024, FDA overruled the objections and denied the hearing requests. JA__[FDA-000001-16] (89 Fed. Reg. 86,290 (Oct. 30, 2024)) (objections order). FDA explained that it had properly followed statutory and regulatory requirements, and acted consistent with past practice, in finding that the petition failed to provide sufficient evidence to support the requested repeals. JA__[FDA-000003-6]. The agency thoroughly considered petitioners' various objections and explained why they did not support revisiting its denial order. *See* JA__[FDA-000003-16]. FDA further concluded that none of the objections raised the sort of material factual questions that would warrant an evidentiary hearing. JA_[FDA-000008-10, 12-15].

Petitioners timely filed a petition for review in this Court.

[4] Some other phthalates are "prior sanctioned" and thus also remain "authorized for use as food-contact substances" because they were approved through a different process pre-dating the statutory scheme at issue. JA__[FDA-000012].

SUMMARY OF ARGUMENT

I. Petitioners have not demonstrated standing to challenge FDA's denial of their food-additive petition. To establish associational standing based on an increased-risk-of-harm theory, petitioners must show both that an identified member of their organizations faces "a substantially increased risk of harm" due to FDA's decision not to repeal the food-additive authorizations at issue, and that there is "a substantial probability of harm with that increase taken into account." *Food & Water Watch, Inc. v. Vilsack* (*FWW*), 808 F.3d 905, 914 (D.C. Cir. 2015) (citation modified). Petitioners have made neither showing.

For the most part, petitioners' declarants express only vague concerns about the potential health impacts of exposure to phthalates. And even when declarants identify some feared health issues with more specificity, petitioners fail to demonstrate that those declarants suffer "a substantially increased risk of harm" due to the continued authorizations of the five specific phthalates at issue. Nor do petitioners establish a "substantial probability" that those declarants will experience the feared health issues absent repeal of the specific food-additive regulations. The Court should thus dismiss the petition for review for lack of jurisdiction.

II. Petitioners' claims also fail on the merits. FDA fairly evaluated the record evidence and determined that the scientific information was inadequate to justify a deviation from the agency's conclusion that there is a reasonable certainty that the authorized uses of the subject phthalates will not be harmful.

A. In reaching that determination, FDA properly required petitioners, as the parties seeking repeal of existing food-additive regulations, to satisfy the evidentiary burden of providing adequate scientific data to support the necessary safety finding justifying repeal. The statute, regulations, and prior agency practice provide no support for petitioners' view that they need only submit some quantum of evidence raising questions about a food additive's safety to shift the burden to FDA to conduct a full de novo reassessment of the additive's safety.

B. FDA reasonably rejected all three factual premises of the petition, each of which would have been necessary to justify the requested repeal.

1. After FDA reasonably rejected the petition's core premise that all 28 phthalates could be grouped together into a single safety analysis, at the objections stage petitioners receded from that position and suggested that some smaller set of phthalates should have been considered. The FDCA does

not permit objectors to belatedly propose entirely new agency actions at the objections stage and deprive FDA of the full opportunity to analyze the complex scientific questions involved.

2. FDA fairly evaluated the toxicological data in the record and concluded that the petition failed to adequately support its estimate of the acceptable level of exposure to the phthalates. Petitioners allege various missteps with FDA's consideration of discrete pieces of evidence, which are not only mistaken on their own terms but also ignore that this Court does not review FDA's analysis with such granularity. Instead, the Court must uphold "FDA's decision if it reveals that significant evidence on both sides of the question has been considered and that the agency has explained its conclusions in light of significant objections." *Simpson v. Young*, 854 F.2d 1429, 1434 (D.C. Cir. 1988). FDA amply satisfied those requirements here.

3. FDA also fairly evaluated the exposure data in the record and concluded that the petition failed to adequately support the use of its proposed value estimating the daily dietary intake of phthalates. Petitioners contend that they had no obligation to submit any evidence of exposure levels, but that rehashing of their burden-allocation argument runs contrary to the statutory and regulatory text. Petitioners also assert that FDA irrationally dismissed evidence regarding overall exposure to phthalates—

from both dietary and non-dietary sources—and evidence that diet is the primary source of phthalate exposure. As the record demonstrates, however, FDA squarely addressed the evidence and explained why it was insufficient to support the requisite factual finding regarding ongoing safety. Petitioners offer no basis for the Court to second-guess FDA's expert scientific judgment.

III. Finally, FDA did not abuse its discretion in denying petitioners' requests for an evidentiary hearing. For each request, FDA reasonably explained why petitioners' evidence was not sufficient to justify resolving the ultimate safety question in petitioners' favor, or why resolving such matters in their favor would not be outcome-determinative. Those "'highly technical and factual'" conclusions, based on thorough consideration of the record, warrant this Court's deference. *See National Corn Growers Ass'n v. EPA*, 613 F.3d 266, 271-72 (D.C. Cir. 2010).

STANDARD OF REVIEW

FDA's factual findings "shall be sustained if based upon a fair evaluation of the entire record." 21 U.S.C. § 348(g)(2). This Court must "uphold the FDA's decision if it reveals that significant evidence on both sides of the question has been considered and that the agency has explained its conclusions in light of significant objections." *Simpson*, 854 F.2d at 1434.

FDA's denial of a hearing request is reviewed for abuse of discretion. *Community Nutrition Inst. v. Young*, 773 F.2d 1356, 1363 (D.C. Cir. 1985).

ARGUMENT

I. Petitioners Have Failed To Establish Standing.

The petition for review fails on jurisdictional grounds because petitioners have not established standing to challenge FDA's response to their food-additive petition and objections. *See* Petitioners' Brief (Br.) 19-22.

Petitioners attempt to invoke associational standing. Br.19. Therefore, they must demonstrate, among other requirements, that: "'at least one of [their] members would have standing to sue in [their] own right.'" *Animal Legal Def. Fund, Inc. v. Vilsack*, 111 F.4th 1219, 1225 (D.C. Cir. 2024). And petitioners must exhibit "'indicia of membership'" and identify members with standing, rather than individuals merely affiliated with their organizations. *See Flyers Rts. Educ. Fund, Inc. v. U.S. Dep't of Transp.*, 957 F.3d 1359, 1361-62 (D.C. Cir. 2020).

Because petitioners' members are "not directly subjected to the regulation they challenge, standing is substantially more difficult to establish." *FWW*, 808 F.3d at 914 (quotation marks omitted); *see FDA v. Alliance for Hippocratic Med.*, 602 U.S. 367, 382 (2024). Petitioners seek to establish member standing under an increased-risk-of-harm theory.

Br.19-20 ("Petitioners' members and supporters are exposed to the Additives in food, putting them and their children at risk of serious health harms."). This Court has "repeatedly expressed skepticism" about this theory of standing "because any future injury—no matter how speculative—can be recast as a present risk of future harm, thus purportedly meeting the imminence requirement of Article III." *Jeffries v. Volume Servs. Am., Inc.*, 928 F.3d 1059, 1067 (D.C. Cir. 2019). Accordingly, the Court has limited such standing to litigants who demonstrate "both (i) a substantially increased risk of harm and (ii) a substantial probability of harm with that increase taken into account." *FWW*, 808 F.3d at 914 (emphases omitted) (quoting *Public Citizen, Inc. v. NHTSA*, 489 F.3d 1279, 1295 (D.C. Cir. 2007)). In doing so, this Court has emphasized that "the constitutional requirement of imminence necessarily compels a very strict understanding of what increases in risk and overall risk levels can count as substantial." *Electronic Priv. Info. Ctr. v. FAA*, 892 F.3d 1249, 1255 (D.C. Cir. 2018) (citation modified). For example, in *Food and Water Watch*, this Court held that consumers of poultry did not have standing to challenge the adequacy of agency procedures for inspecting poultry because it was too speculative that the consumers would suffer any adverse health consequences. *See* 808 F.3d at 914-19.

Accordingly, petitioners must demonstrate (1) that FDA's existing food-additive authorizations substantially increase the risk of members developing their feared health issues compared to a scenario in which FDA repealed those authorizations, and (2) a substantial probability that members will develop those health issues given that increased risk. *See FWW*, 808 F.3d at 915. Petitioners have satisfied neither prong.

A. Petitioners have not shown that their members face a substantially increased risk of harm.

In increased-risk standing cases, "the ultimate alleged harm—such as death, physical injury, or property damage—[is] the concrete and particularized injury" at issue. *FWW*, 808 F.3d at 915 (citation modified). And it is a "petitioner's burden to produce evidence of the imminent nature of a specific harm to a specific party when an actual harm is absent." *American Chemistry Council v. Department of Transp.*, 468 F.3d 810, 820-21 (D.C. Cir. 2006).

Petitioners' declarations are entirely lacking in this regard. For the most part, they allude to general health concerns about phthalates without even alleging, much less demonstrating, that their personal exposure to the five subject phthalates from food threatens any specific imminent harm. *See* DEC011; DEC043; DEC048-49, 051; DEC062; DEC097; DEC102; DEC121.

One declarant actually alleges experiencing a specific health issue (attention deficit hyperactivity disorder), but only speculates as to whether it resulted from phthalate exposure. DEC011 ("I'm concerned that this *may* be a result of exposure to phthalates *or other chemicals*." (emphases added)). Nor does this declarant demonstrate that *future* exposure to phthalates would subject this declarant to a substantial risk of *future* harm, as would be necessary to show standing for prospective relief. *See id.*; *Alliance*, 602 U.S. at 381.

Some declarants express slightly more specific health concerns about phthalates. *See, e.g.*, DEC018 (Cole Declaration) ("I am concerned about … the possibility of breast cancer recurrence due to exposure[.]"); DEC065 (Bissell Declaration) ("the risks of cancer"); DEC121 (Larson Declaration) ("[P]hthalates are endocrine-disrupting chemicals and could have other harmful health effects such as elevated risks of cancer[.]"); DEC102 (Ames Declaration) ("Phthalates are … possible carcinogens[.]"); DEC043 (Doughty Declaration) ("[E]xposure … is linked to harmful effects on brain development and reproductive development."); DEC098 (Durrant Declaration) ("I worry this exposure will contribute to the early onset of puberty, harm their reproductive health, or have other negative outcomes."). But these subjective statements do nothing to demonstrate that "the increased risk of such harm[s] makes injury to an individual citizen

sufficiently imminent for standing purposes." *FWW*, 808 F.3d at 915 (quotation marks omitted).

And most of them are quite general. The most specific declaration, expressing concerns about recurrence of breast cancer, not only fails to provide any objective evidence of imminent harm but also does not come from a member of any petitioner organization. *See* DEC015-21. Instead, it comes from a "supporter" of Breast Cancer Prevention Partners, DEC016, which is not a traditional membership organization, DEC023-25; *see also* DEC016, DEC025 (failing to allege that "supporters" have any control over organization's activities, that supporters provide a majority of the budget, or that the supporter-declarant donates any money to the organization).

In any event, all of declarants' allegations are insufficient to show a *substantial* difference in the risk of *specific* health harms. As this Court has explained, "[a]n ambiguous increase in risk is hardly a substantial increase in risk." *FWW*, 808 F.3d at 917; *see Sierra Club v. EPA*, 754 F.3d 995, 1001 (D.C. Cir. 2014) (Such "increased risk must be nontrivial, and sufficient to take a suit out of the category of the hypothetical." (citation modified)). Declarants provide no indication of the magnitude of the risks they claim to face from dietary exposure to the five subject phthalates. Petitioners claim (Br.20) that declarants "eat numerous foods in which the [five phthalates]

have been detected." But the cited declarations provide, at best, ambiguous descriptions of the foods consumed and lack specific information about declarants' exposure to the five subject phthalates due to consuming those foods. *See* DEC012; DEC018-19; DEC044-45; DEC048-50; DEC062-64; DEC096-97; DEC102-03; DEC121-22. Moreover, multiple declarants assert that the health risks from dietary exposure to phthalates also arise from exposure to "other toxic chemicals" in their food and environment. DEC062; *see* DEC041-43; DEC049; DEC096-98; DEC018 (expressing "concer[n] about my health and the possibility of breast cancer recurrence due to exposure to endocrine-disrupting chemicals *such as* phthalates" (emphasis added)); *see also* DEC013. This makes it unclear whether repealing the food-additive authorizations for the five subject phthalates would substantially reduce the risks declarants claim to face.

B. For similar reasons, petitioners have not shown that, unless FDA repeals the authorizations, there is a "substantial probability" their identified members will suffer specific health effects. As noted, their declarations neither substantiate nor quantify their claims of imminent prospective harm. And although petitioners' declarants may seek to avoid consuming products with phthalates and incur costs in doing so, *see, e.g.*, DEC019, it is well-established that "plaintiffs 'cannot manufacture standing merely by inflicting

harm on themselves based on their fears of hypothetical future harm that is not certainly impending' because such injuries 'are not fairly traceable' to the conduct creating that fear." *FWW*, 808 F.3d at 919 (quoting *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 416 (2013)); *see also id.* at 922 (Henderson, J., concurring in the judgment) (concluding that where there is "readily available" and "reasonably priced" alternative to product alleged to cause injury, litigant cannot establish standing (citation modified)).

II. FDA Reasonably Declined To Repeal The Relevant Food-Additive Regulations.

A. Petitioners Must Establish Sufficiently Significant Safety Questions.

FDA thoroughly considered the scientific record and concluded that the petition had not justified repealing the food-additive regulations at issue.

1. FDA previously determined that the subject phthalates could be safely used as food additives, and thus issued regulations prescribing their authorized conditions of use. *See* 21 U.S.C. § 348(a)(2). For decades, industry has relied on those authorizations, using the approved phthalates in various plastic materials necessary for food processing and packaging activities. Repealing the authorizations would render unlawful all such food-contact applications of those substances. *See id.* § 342(a)(2)(C).

To take such an action requires reaching a factual conclusion that FDA's original safety determination is no longer justified. In particular, a repeal petition must "contain sufficient data to establish the existence of safety questions significant enough to support a finding that there is no longer a reasonable certainty of no harm from the currently approved uses." JA__[FDA-002005]. The requirements for repeal petitions mirror those for authorization petitions, 21 U.S.C. § 348(i), and repeal petitions thus must provide "full reports of investigations made with respect to the safety for use of such additive" and "any explanatory or supporting data," *id.* § 348(b)(2).

Instead of trying to meet this burden, petitioners seek to evade it.[5] They contend that upon receiving their petition, FDA should have required proponents of the established regulation to prove all over again that the phthalates at issue are safe. *See* Br.25 (seeking "a presumption that additives are unsafe and prohibited unless the company advocating for their use proves that their use 'will be safe,' 21 U.S.C. § 348(c)(3)(A)"). If petitioners'

[5] Petitioners purport to agree that FDA's denial and objection orders articulate "the correct standard." Br.26 (citing JA__[FDA-002005]; JA__[FDA-000006]). But that standard does not merely require the submission of some quantum of evidence suggesting "significant questions regarding … safety" in the abstract. Br.24 n.6, 26. Rather, the questions must be "significant enough to support a finding that there is no longer a reasonable certainty of no harm from the approved [p]hthalates' uses." JA__[FDA-000006]. Petitioners do not attempt to make that showing. *But see* JA__[FDA-012418, FDA-012430].

theory were correct, FDA would grind to a halt. Any time a petitioner "tender[ed]" any quantum of "new information" to FDA supposedly raising significant safety questions about an authorized additive, JA__[FDA-010651], FDA would need to choose between repealing the authorization or expending substantial resources to evaluate all the data necessary to assess the additive's safety. *See generally* JA__[FDA-000027-312] (describing detailed toxicological analyses that inform FDA's safety reviews); JA__[FDA-013116-40] (similar for chemistry analyses). Given FDA's limited resources, petitioners' approach would threaten repeal whenever an interested party discovers a new publication touching on an additive's safety, regardless of the publication's scientific merit or other available evidence.[6] This could create incentives for manufacturers to attempt to "block" authorizations that benefit competitors by merely submitting a petition with new information pertaining to an additive's safety. *Cf.* 21 U.S.C. § 355(q)(1)(E) (addressing similar blocking tactics by drug manufacturers).

It would also disturb the well-settled reliance interests of industry participants who expect that they can build their business around regulations

[6] The mere reporting by a publication that an authorized additive has toxic effects does not resolve whether the authorized use is safe. *See* JA_[FDA-000008] (describing how toxic effects "must be placed in the context of exposure").

that are not displaced without sufficient scientific justification. Eliminating that security would frustrate the congressional objective to encourage "responsible processors" to develop and market food additives that "enable [consumers] to safely keep food longer, the processor[s] to make [food] more tasteful and appetizing, and the Nation to make use of advances in technology calculated to increase and improve our food supplies." *See* S. Rep. No. 85-2422, at 2 (1958).

2. Unsurprisingly, the statute and regulations do no such thing. Rather, to justify repealing a regulation authorizing an additive's use that was supported by appropriate scientific evidence, a repeal petition must "include an assertion of facts, supported by data, showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation … may justify its … repeal." 21 C.F.R. § 171.130(b). And such petitions must contain "full information on each proposed change that is to be made in the original regulation," including as relevant "[f]ull reports of investigations made with respect to the safety of the food additive." *Id.* § 171.1(c).

a. Petitioners' effort to sidestep this burden by essentially requiring FDA to continually justify its existing regulations de novo finds no support

in the FDCA, which confers authority on FDA to prescribe the relevant procedures. 21 U.S.C. § 348(i). The statute also provides that the procedure for repealing food-additive regulations "shall conform to the procedure provided in [§ 348] for the promulgation of such regulations." *Id.* Accordingly, for a petition seeking repeal, the petitioner bears the burden of justifying that proposed action (just as for authorization petitions, where the petitioner bears the burden of justifying the proposed use). And justifying repeal requires establishing that there is no longer a reasonable certainty that the authorized use will not harm—the inverse of the "will be safe" showing necessary to justify promulgating a regulation authorizing an additive's use. *See* JA__[FDA-000004-5]; 21 U.S.C. § 348(c)(3)(A); 21 C.F.R. § 170.3(i).

Nothing in the statute supports an approach whereby repeal petitions benefit from vastly more lenient burdens than authorization petitions. *See* 21 U.S.C. § 348(i). Petitioners seem to suggest (Br.27, 31-33) that, whenever FDA receives a repeal petition containing any new information on an additive's safety, 21 U.S.C. § 348(c)(3)(A) compels repeal unless a comprehensive reassessment affirmatively proves that the additive "will be safe." That misunderstands the statute. The FDCA provides that, in a proceeding on a petition "proposing the *issuance* of a regulation prescribing the conditions under which such additive may be safely used," 21 U.S.C.

§ 348(b)(1) (emphasis added), "[n]o such regulation shall *issue* if … the data before [FDA] fails to establish that the *proposed* use of the food additive … *will be* safe," *id.* § 348(c)(3)(A) (emphases added). That is, when an authorization petition is received, FDA can only authorize the proposed use of an additive after determining that it "will be safe."

The statutory text does not require a fresh "will be safe" finding any time FDA receives a petition containing new safety information that proposes to repeal an existing regulation; in that scenario, there has already been an FDA determination that the approved food-additive use "will be safe." Instead, it is petitioners' burden to demonstrate that an approved use is no longer safe, *i.e.*, that the evidence in its repeal petition proves there are such significant safety questions concerning that use that it can no longer be concluded that the use has a reasonable certainty of no harm. Requiring a petitioner to justify the action requested is consistent with the default distribution of burdens in administrative proceedings. *See, e.g.*, *Schaffer ex rel. Schaffer v. Weast*, 546 U.S. 49, 57-58 (2005) ("Absent some reason to believe that Congress intended otherwise, therefore, we will conclude that the burden of persuasion lies where it usually falls, upon the party seeking relief."); 5 U.S.C. § 556(d) ("Except as otherwise provided by statute, the

proponent of a rule or order has the burden of proof."). The FDCA creates no exception to the default rule.

Moreover, FDA's approach is fully consistent with the statutory premarket approval scheme for food additives. *Contra* Br.25. The system designed by Congress requires FDA to make a "will be safe" determination *before* the agency authorizes a proposed food-additive use. Congress's objective was to ensure that a substance is not added to the food supply before an interested party can prove that its proposed use is safe. *See* S. Rep. No. 85-2422, at 2. Once FDA authorizes the use of a food additive, however, the new status quo is that the authorized use is "safe" within the meaning of § 348, and a petitioner seeking to repeal that authorization must adduce evidence sufficient to disturb that status quo.[7]

b. FDA's FAP regulations further underscore that FDA applied the correct standard here. Those provisions require repeal petitions to include "[f]ull reports of investigations made with respect to the safety of the food additive," and provide that "[a] petition may be regarded as incomplete unless it includes full reports of adequate tests reasonably applicable to show

[7] This is not to say that FDA necessarily leaves authorizations in place. FDA conducts postmarket surveillance of already-authorized food additives and takes action whenever the agency determines that authorized uses no longer meet the safety standard. *See* FDA, *Food Chemical Safety* (July 30, 2025), https://perma.cc/S78G-23G5.

whether or not the food additive will be safe for its intended use." 21 C.F.R. § 171.1(c); *see id.* § 171.130(b) (applying § 171.1—which governs the requirements for authorization petitions "under the provisions of [§ 348(b)]," 21 C.F.R. § 171.1(a)—to repeal petitions). As this Court has explained, under these regulations, "the petitioner … bear[s] the burden of establishing that an additive is safe or unsafe." *In re Natural Res. Def. Council* (*NRDC*), 645 F.3d 400, 403 (D.C. Cir. 2011).[8]

Petitioners assert to the contrary that the regulations place the burden of proof on parties "contesting withdrawal of approval." Br.27 (quoting 21 C.F.R. § 12.87(d)). But that provision pertains to the burden of proof "[*a*]*t a hearing*" on FDA's repeal of a food-additive regulation. 21 C.F.R. § 12.87(d) (emphasis added). If FDA holds a hearing under § 348(f) after issuing an order under § 348(c) repealing a food-additive regulation, opponents of that order would "ha[ve] the burden of proof in establishing safety" at the

[8] Petitioners misconstrue 21 C.F.R. § 171.130(b). Br.28. That provision provides general descriptions of information that "may justify" repealing a food-additive regulation, and requires repeal petitions to include such information in order to be deemed sufficiently complete to permit substantive review, and thus be officially "filed." *See* 21 C.F.R. § 171.1(d), (g). However, § 171.130(b) does not provide that the mere inclusion of *any* information necessary for filing is sufficient to actually justify the repeal action ultimately requested. Instead, § 171.130(b)'s cross-reference to § 171.1 makes clear that repeal petitions must include "*adequate* supporting information." JA__[FDA-000005] (emphasis added).

hearing. 21 C.F.R. § 12.87(d). But a petitioner who seeks such an order under § 348(c) still bears the burden to justify repealing the regulation in the first instance.

The Ninth Circuit's decision in *League of United Latin American Citizens v. Regan*, 996 F.3d 673 (9th Cir. 2021), is not to the contrary. *See* Br.28-29. That case involved a materially different statutory provision, under which the Environmental Protection Agency (EPA) could "establish *or leave in effect* a tolerance for a pesticide chemical residue in or on a food only if [it] determines that the tolerance is safe." 21 U.S.C. § 346a(b)(2)(A)(i) (emphasis added). Given this statutory command, the court concluded that the petitioners seeking repeal did not have a "burden of persuasion" to offer data "that affirmatively demonstrate that the tolerances are unsafe." 996 F.3d at 695. The court thus interpreted the relevant EPA regulation to be consistent with the statute and only "impose a burden of production." *Id.* The different statutory text requires a different result here. *See* 21 U.S.C. § 348(b)(2), (c)(3), (i).

c. Past agency practice also fails to support petitioners' preferred burden allocation.

Petitioners invoke (Br.29-30) a 2016 FDA decision repealing food-additive regulations involving long-chain perfluorinated chemicals. But

there, FDA required the same showing as in this case: "new data concerning the toxicity of the food additive … must be adequate for FDA to conclude that there is no longer a reasonable certainty of no harm for the intended use of the substance." JA__[FDA-009082-83]; *see* JA__[FDA-009083] (concluding that petition there "raises significant questions as to the safety of the authorized uses" such that "there is no longer a reasonable certainty of no harm"). In that matter, "FDA did *not* state that the … revocation action was being instituted based on a finding of 'significant questions' in isolation." JA__[FDA-000006].

The different outcomes between the cited proceeding and this one arise not from different allocations of evidentiary burdens, but from different levels of evidentiary support for the two petitions. There, for example, certain data gaps could be bridged by other available data, *see* JA__[FDA-009083]; Br.30; but FDA did not find sufficient data to do so in this case, *see, e.g.*, JA__[FDA-002011]; *see also Center for Biological Diversity v. EPA*, 749 F.3d 1079, 1090 (D.C. Cir. 2014) (recognizing that it is "emphatically the province of" the expert agency to determine whether "data gaps were 'of such a significant nature and degree'" to preclude a "'reasoned judgment'"). Overall, FDA thoroughly considered petitioners' arguments

and reasonably explained why a different result was warranted here. *See* JA__[FDA-000006, 13-14]; JA__[FDA-002007].

Nor did FDA acknowledge in another prior proceeding (involving olestra) a "'continuing obligation'" to make a full de novo safety reassessment in response to every repeal petition. *Contra* Br.29 n.8, 32. As an initial matter, the olestra proceeding involved a food-additive approval decision, not a repeal petition. JA__[FDA-021104]. Moreover, FDA imposed an express condition of approval for olestra whereby a petitioner was required to conduct and submit additional studies. JA__[FDA-021153]. Further, FDA committed to review and evaluate the new data within 30 months of the initial approval. JA__[FDA-021153]. No such express condition applies here.

* * *

Petitioners' objection to bearing the burden of proof appears to be founded on frustration with the age of the subject authorizations, *see* Br.31-32, and with the fact that despite continuing research into the safety of phthalates for food-contact use, there has been no corresponding change in the authorizations of the five remaining subject phthalates, *see* Br.33 (citing FDA letter to Congress). But that is the system Congress designed: a stringent procedure to seek food-additive authorizations, and a

"conform[ing]" procedure to seek repeal of such authorizations. 21 U.S.C. § 348(i).

FDA recently sought to add to its knowledge of phthalates' use and safety by seeking data not already in its possession. *See* JA__[FDA-000007]; JA__[FDA-021101-02]. And phthalates remain on FDA's list of substances under review. *See supra* p.9. If new data warrants the conclusion that the food-additive uses are no longer safe, FDA will act to repeal those authorizations. But in exercising its expert judgment on the record here, FDA reasonably did not make that determination.

B. FDA Fairly Evaluated the Record and Reasonably Explained Why It Did Not Raise Sufficiently Significant Safety Questions.

FDA's decision to deny FAP 6B4815 and petitioners' objections was based on a fair evaluation of the record, and the agency's factual conclusions about the lack of sufficient scientific data in the record merit substantial deference.

Under the FDCA's food-additive provisions, "[t]he findings of [FDA] with respect to questions of fact shall be sustained if based upon a fair evaluation of the entire record." 21 U.S.C. § 348(g)(2). This Court has held that this "fair evaluation" standard requires "uphold[ing] the FDA's decision if it reveals that significant evidence on both sides of the question has been

considered and that the agency has explained its conclusions in light of significant objections." *Simpson*, 854 F.2d at 1434. To satisfy this standard, FDA must "state the main reasons for its decision and indicate that it has considered the most important objections," but need not "address every argument advanced." *Id.* at 1434-35.

Moreover, under this standard, this Court has emphasized that "[a] re-weighing … of the mass of scientific evidence presented to the FDA" is inappropriate; rather, the Court's task is limited to considering "whether the agency ignored highly relevant evidence or formed a conclusion for which record support is absent or clearly inadequate to the commonsense observer." *Simpson*, 854 F.2d at 1434. For "highly technical and factual matters," such as the "weight or credence [to give] particular scientific studies," it is appropriate for the Court to defer to the "judgment … of the agency charged with the supervision of the industry." *Young*, 773 F.2d at 1363; *see Rempfer v. Sharfstein*, 583 F.3d 860, 867 (D.C. Cir. 2009) ("[A] scientific judgment within [FDA's] 'area of expertise'" is "the kind of judgment to which this court gives a 'high level of deference.'"). Accordingly, the Court's task is not to "'undertake comparative evaluations of conflicting scientific evidence,'" but instead only "'to discern whether the agency's evaluation was rational.'" *Center for Biological Diversity*, 749 F.3d at 1088.

Here, petitioners' effort to establish sufficiently significant safety questions hinged on three factual assertions: that all 28 phthalates subject to the petition should be grouped together for safety analysis, that a proposed toxicity level for one phthalate should be applied to the entire group, and that the proposed estimated intake for the 28 phthalates exceeds a safe level. FDA reasonably determined that the record failed to adequately support any of those assertions. *See* JA__[FDA-002006-13]. Each one of these conclusions independently sufficed to justify denial of the petition.

1. FDA reasonably concluded that the petition did not adequately support treating all phthalates as a class for purposes of its safety analysis.

Petitioners' first factual assertion was that the 28 phthalates that were the subject of the petition "are a class of chemically- and pharmacologically-related substances for purposes of determining safety." JA__[FDA-012417]; *see* 21 U.S.C. § 348(c)(5) (requiring consideration of "the cumulative effect" of a food additive "taking into account any chemically or pharmacologically related substance"). As FDA observed, this was the petition's "core premise" and served as the predicate for its two subsequent factual assertions. JA__[FDA-000002, 04]. But the petition failed to justify that premise by failing to account for structural differences or demonstrate shared pharmacological effects across the group. JA__[FDA-002006-10].

a. Petitioners now abandon that core premise. Instead, they assert (Br.52-56) that FDA's response to the petition was deficient because FDA did not conduct a new grouping analysis proposed for the first time in petitioners' objections. JA__[FDA-010676-78]. FDA was not obliged to do so. The scope of the objections process is limited to challenges to "an order [FDA] made pursuant to [§ 348(c)]," and objections to "such an order" must "specif[y] with particularity the provisions of the order deemed objectionable, stating reasonable grounds therefor." 21 U.S.C. § 348(f)(1). In faulting FDA's decision not to analyze this new grouping, petitioners essentially "claim that [FDA's] denial order was deficient because it did not address questions [petitioners] failed to ask, and … take actions they failed to request." JA__[FDA-000012]. That does not amount to a "reasonable" challenge to the specific provisions of FDA's denial order addressing the petition's proposed class of 28 phthalates.

Section 348(f)'s objections process does not permit parties to move the goalposts of the administrative proceeding by proposing new actions that were not proposed in the underlying petition and thus reasonably not addressed in a denial order. For good reason: as FDA explained, "[t]he type of information necessary to consider for grouping chemicals for safety assessment is complex." JA__[FDA-000012]. Consequently, "proposing

new groupings at the objection phase—when those groupings were not within the scope of the denial order—does not allow for full consideration of the complex scientific issues involved." JA__[FDA-000012].

Petitioners' contrary approach would short circuit the statute's two-stage administrative structure involving an initial order on a petition followed by an order on objections. *See* 21 U.S.C. § 348(b)-(c), (f). This structure does not allow parties to sandbag FDA by withholding proposals until the objections stage. Moreover, such an approach would undermine Congress's directive for new proposals to be published prior to FDA ruling on them, and would also deprive the public of the opportunity to submit comments on the actions proposed. *See* 21 U.S.C. § 348(b)(5); 21 C.F.R. § 171.1(i)(2); JA__[FDA-002643-45]. Besides being flatly inconsistent with the statutory structure and FDA's regulations, requiring FDA to entertain new proposed actions at the objections phase also calls for the agency to engage in decisionmaking without the benefit of a fully-developed record. As noted above, considering the merits of grouping various chemicals for safety assessment requires resource-intensive analyses involving "complex" information and "scientific issues." JA__[FDA-000012]; *see generally* JA__[FDA-001220-1360] (Organization for Economic Cooperation and Development's (OECD) *Guidance on Grouping of Chemicals*). Nine

phthalates currently remain authorized "pursuant to food additive authorizations, prior sanctions, or both." JA__[FDA-009534]; *see supra* n.4. Petitioners' objections stated that FDA "arbitrarily … fail[ed] to assess whether the nine phthalates … —and/or *any subset* of those substances"—were sufficiently related to be evaluated as a group. JA__[FDA-009556] (emphasis added).[9] Within this set, however, there are over 500 possible groupings consisting of two or more phthalates. Petitioners are not entitled to first specify at the objections stage any number of those hundreds of groupings and demand that FDA evaluate whether each merits class treatment. Rather, it is eminently reasonable for FDA to require that new specific proposed groupings of substances be submitted in a new petition, so that the administrative process can ensure full consideration of whether there is adequate scientific justification for the proposed action.

b. Petitioners contend that FDA was required to analyze a grouping of four substances that they proposed for the first time at the objections stage because although the underlying petition argued that all 28 phthalates were related, it "never asserted that it would be *improper* to group a narrower subset." Br.54 (emphasis added). As explained, *supra* Part II.A, petitioners

[9] Petitioners also specifically requested that FDA evaluate several new groupings, only one of which it raises before this Court. *See* JA__[FDA-010669-80].

bore the burden of justifying their proposed action, which meant that petitioners needed to propose (and then substantiate) that it would be *proper* to group a narrower subset. The burden was not on FDA to identify and conduct a grouping analysis for every conceivable permutation within the only grouping of substances that petitioners actually proposed in their petition. (Nor could it, even if petitioners had asked: for the 28 phthalates, there are over 250 million different potential groupings of two or more substances.) The petition proposed a grouping of 28, and FDA analyzed exactly what the petition proposed.[10]

Petitioners further assert (Br.54) that the FDCA and regulations permit "new evidence and arguments" at the objections stage. But there is a difference between reviewing new scientific information that might demonstrate whether a hearing is warranted—like a "'new exposure analysis,'" Br.54—and proposing a new action that raises fundamentally different factual questions from those analyzed in the order being objected to. The latter must be pursued in a new petition.

Nor did FDA "implicitly recogniz[e]" a "duty" to analyze petitioners' new proposed grouping. Br.54-55. In responding to the petition, FDA

[10] From the beginning, however, FDA expressed concerns about whether there was sufficient evidence to establish the broad 28-phthalate grouping proposed by the petition. *See generally* JA__[FDA-018576-80].

evaluated whether two potential groupings of substances among the five remaining phthalates authorized as food additives should be treated as a class: all five phthalates and four of those phthalates that were approved for the same kind of use (excluding an obvious outlier). JA__[FDA-000017-24]. FDA explained that these were logical alternatives to evaluate, given that it took the petition's "core premise"—that "the subject phthalates should be grouped together as a class for purposes of a safety assessment"—and applied it to the only subject "phthalates that … still have authorized uses" as food additives. JA__[FDA-000018]. By conducting those evaluations regarding the remaining five authorized phthalates—which FDA concluded were not appropriately grouped for purposes of a safety analysis, JA__[FDA-000023]—FDA was considering reasonable alternatives within the scope of the underlying petition. The agency was not committing itself to evaluating different proposals later asserted in petitioners' objections involving a different set of phthalates. *See Center for Auto Safety v. Peck*, 751 F.2d 1336, 1355 n.15 (D.C. Cir. 1985) ("An agency need not address every conceivable issue or alternative, no matter how remote or insignificant."). Petitioners' effort to punish FDA for its flexibility in considering their original petition should be rejected.

The record contained inadequate support for petitioners' assertion that all 28 phthalates authorized under the food-additive regulations were "chemically or pharmacologically related substance[s]." 21 U.S.C. § 348(c)(5)(B). As such, there was no relevant group of chemically or pharmacologically related substances with "cumulative effect" for FDA to account for in considering a cumulative effect. *Id.* If petitioners wish for FDA to evaluate the safety of a different set of substances that they believe are chemically or pharmacologically related, they can file a new petition to substantiate that proposed grouping and any other factual assertions they choose to make.

2. FDA reasonably evaluated the evidence in the record on toxicity.

As noted, the rejection of the petition's core premise by itself provided a sufficient basis to deny the petition. But in any event, the other key factual assertions were also unsubstantiated.

The petition's second factual assertion concerned the levels at which the subject phthalates have toxic effects. FDA explained that the petition had not adequately supported its proposed acceptable daily intake level because it selected a key input for calculating that level—known as a "no observed adverse effect level"—from a study without "evaluat[ing] the underlying evidence supporting the … values listed in [the] publicatio[n]," or providing

the "wide array of information" that is typically considered to "determine appropriate … values … including the results of a comprehensive literature search," or addressing contrary studies on species that are "generally considered more applicable to human risk assessment." JA__[FDA-002011]. The petition thus did not contain "a full report of investigations made with respect to safety," nor did it "provid[e] an adequate scientific rationale to justify the selected" level. JA__[FDA-002011].

In their objections, petitioners contended that FDA's denial order "fail[ed] to address new toxicity information that raises significant questions about the safety of the approved food-additive uses of phthalates." JA__[FDA-010658]. FDA explained, however, that "it is not enough … to simply name health effects linked to the still-authorized [p]hthalates or to list publications and declarations that address the topic"; petitioners failed to "provide meaningful analysis or explanation for why these materials support a finding that there are significant questions about the safety of the still-authorized [p]hthalates." JA__[FDA-000008].

a. Petitioners provide a brief overview of the evidence submitted regarding toxicity, contending that these submissions satisfied their burden of "showing that new data are available as to toxicity of the Phthalate Additives that raise significant questions about their safety." Br.37 (citation

modified). That assertion is premised on petitioners' misapprehension of their burden. *See supra* Part II.A; Br.38-39 (invoking burden allocation). Properly understood, any safety questions raised are only sufficiently "significant" if they demonstrate that there is no longer a reasonable certainty of no harm from the authorized food additives.

As FDA explained, "the existence of toxicity findings, alone, is insufficient to establish" such "significant questions." JA__[FDA-000008]. That is because "[a]ll substances exhibit toxic effects at high enough exposure levels, and most substances exhibit an exposure threshold below which they do not exhibit a toxic effect." JA__[FDA-000008]. Accordingly, "it is not sufficient to cite studies that indicate that a substance is associated with a toxic effect; rather, that effect must be placed in the context of exposure." JA__[FDA-000008].

One way to do so "is to compare the estimated dietary intake of the food additive to an [acceptable daily intake] level established by appropriate toxicological data." JA__[FDA-000009]. Petitioners relied on that approach in their petition. *See* JA__[FDA-002010]; JA__[FDA-012417]. But after FDA explained in the denial order why petitioners' "proposed [acceptable daily intake level] was not supported" by the evidence, petitioners' objections "d[id] not address or otherwise engage with FDA's

identified concerns." JA__[FDA-000009]. Instead, petitioners listed various publications and studies that they claim FDA did not adequately consider, JA__[FDA-010658-62], but they did not explain *how* those studies were relevant to performing an adequate risk assessment. *See* JA__[FDA-000009] (observing that petitioners did not address whether sources were relevant to the specific steps of assessing acceptable dose intake levels, calculating an exposure estimate, or otherwise determining "whether the dietary exposure could result in a toxic effect"). Petitioners' brief continues to make no effort to demonstrate that the evidence supports the safety conclusion they urge.

b. Petitioners' objections to FDA's consideration of specific pieces of evidence are thus inapposite, given their inability to satisfy the overall showing. In any event, FDA adequately considered petitioners' toxicity evidence. Br.34-43.

i. Petitioners erroneously suggest that FDA faulted them for failing to "provid[e] dose-response studies." Br.38. In fact, FDA acknowledged the dose-response studies in the record but concluded they were inadequate. *See* JA__[FDA-000009]. Two of the cited studies, *see* Br.38 (discussing JA__[FDA-012983] and JA__[FDA-011794]), involved the administration of a single phthalate mixed with other substances that were not food-

additive-authorized phthalates. As FDA explained regarding two other examples of dose-response studies exhibiting a similar limitation, "it was not possible to deduce whether the reported adverse effects were caused by a single phthalate or the entire mixture." JA__[FDA-009520]; *see* JA__[FDA-000009] (explaining that such studies "cannot separate adverse effects"). The other three dose-response studies cited in petitioners' brief administered a single subject phthalate, *see* JA__[FDA-015301]; JA__[FDA-009728]; JA__[FDA-009970], and therefore had "limit[ed] … applicability to evaluate the safety of the food contact uses of" the other four subject phthalates, JA__[FDA-009523]. Additionally, those three studies exhibited limitations in design by using either "smaller sample sizes for each testing group … than what is recommended in OECD guidelines" or "doses substantially higher than the expected total human exposure." JA__[FDA-009519-21]. These parameters limited the statistical significance and reproducibility of the reported findings, their applicability to the toxicity of the subject phthalates at commensurate human exposure levels, or both.

In a single sentence, petitioners also invoke "assessments by other governmental authorities synthesizing dose-response data for the Phthalate Additives." Br.38. But petitioners' objections failed to draw any attention to dose-response data discussed therein, or explain how such reports "would be

adequate to assess the safety of the substances' authorized food additive uses." JA__[FDA-000009]; *see* JA__[FDA-009549] (asserting only that they "provide novel insights and weight of evidence analyses that are relevant to the safety reevaluations that FDA must conduct"). That is insufficient. *See Vermont Yankee Nuclear Power Corp. v. NRDC, Inc.*, 435 U.S. 519, 554 (1978) (admonishing that parties cannot merely make "cryptic and obscure reference to matters that 'ought to be' considered"). In any event, FDA's response to the objections shows that the agency properly considered exposure information addressed by the cited assessments. For example, FDA observed that one of these reports indicated "that the general population is exposed to [the relevant phthalate] at levels that are 3-4 orders of magnitude lower than those observed to cause adverse health effects in animal studies." JA__[FDA-000014] (discussing Agency for Toxic Substances and Disease Registry (ATSDR) report). Accordingly, FDA reasonably concluded that the cited report did "not justify resolution of the factual question about unsafe exposure in [petitioners'] favor." JA__[FDA-000014].

ii. Petitioners also take issue with the discussion in FDA's supplementary memorandum of limitations in 48 referenced studies that "included data from *in vivo* rodent studies," JA__[FDA-009519].

Petitioners assert that FDA acted arbitrarily in faulting the studies for being "insufficient to assess chronic toxicity," JA__[FDA-009520], because in 1973 "FDA had no chronic studies to support its authorizatio[n]" for one of the remaining authorized phthalates, diisodecyl phthalate (DIDP). Br.39. Notably, petitioners ignore the "multiple [other] limitations" that FDA identified in the studies, which are themselves a sufficient basis for rejecting this argument. JA__[FDA-009519].

Regardless, petitioners do not seek to demonstrate that "chronic toxicity studies" are not "'essential,'" or to introduce new data demonstrating the chronic toxicity of DIDP. Br.39. Instead, they assert that FDA's safety assessment for DIDP was "deficien[t]" decades ago. Br.39. But FDA's original actions authorizing food-additive use of the five subject phthalates are not under review here. *Cf. NLRB Union v. FLRA*, 834 F.2d 191, 196 (D.C. Cir. 1987) ("An appellate court's review in cases of this kind, however, is limited to the 'narrow issues as defined by the denial of the petition for rulemaking,' and does not extend to a challenge of the agency's original action in promulgating the disputed rule." (emphasis omitted)). Petitioners' references to FDA's original authorization decisions (Br.32, 35-36, 39-40, 42) again reflect their misunderstanding of the allocation of burdens in a FAP repeal proceeding: the legal status quo is that the authorized uses of the

subject phthalates are safe under § 348, and it is petitioners' burden to demonstrate that new toxicity evidence in the record is sufficient to disturb that status quo. In other words, the inquiry is not whether the original authorizations were correct and the record sufficient to support them when made; it is whether the record before the agency now is sufficient to justify repealing those authorizations. Petitioners have not made this required showing.

Petitioners also assert that FDA's memorandum "ignor[es]" studies "that do not exhibit the asserted 'limitations.'" Br.40. The fact that the memorandum does not expressly discuss every study does not mean that FDA failed to consider them. To the contrary, the memorandum explains that FDA "evaluat[ed the] studies individually," considering "the suitability of [its] design" and whether its "results are statistically significant and/or treatment-related, and reproducible." JA__[FDA-009518]. FDA "identified several limitations" in the studies, discussing limitations that applied to various categories of studies. *See* JA__[FDA-009519-23]. FDA was not required to undertake the box-checking exercise of specifically identifying which limitation(s) applied to each study. *See Simpson*, 854 F.2d at 1434 (FDA need only consider "significant evidence on both sides of the question" and "explai[n] its conclusions in light of significant objections").

In tension with this critique, petitioners simultaneously fault FDA for "consider[ing] the evidence piecemeal" instead of "'weigh[ing] the entire record.'" Br.41-42. But FDA specifically explained that it "considered whether the studies *collectively* supported the reported adverse health outcomes … by considering study types, methodological quality, quantity of evidence for and against the adverse health outcome … and overall consistency of the evidence." JA__[FDA-009518-19] (emphasis added). FDA concluded "that the objection and its referenced articles, individually and collectively, do not provide support for the claim that there are significant safety questions for the food additive uses of" the five phthalates, "nor does it provide sufficient support to alter [FDA's] decision on the arguments made in FAP 6B4815." JA__[FDA-009523-24]. Moreover, FDA considered the record as a whole in concluding that, "based on the information currently available," it did "not have a basis to conclude that dietary exposure levels from approved [p]hthalates exceed a safe level." JA__[FDA-002013]; *see* JA__[FDA-000006].

iii. Petitioners further contend that FDA "irrationally dismissed" epidemiological studies in the record. Br.40. As FDA reasonably explained, however, "[w]hile epidemiological studies may suggest a possibility of occurrence of an effect, they are generally not useful for risk assessment due

to a lack of control of confounders such as dietary, medical, and lifestyle factors, socioeconomic status, and characterization of past exposures." JA__[FDA-000009]; *see* JA__[FDA-000009] (noting that such studies may include "self-reported data by the test subjects which increases the potential for biases and inaccuracies"). Accordingly, "although epidemiological studies may be considered supplementary to the available toxicological data for conducting a safety evaluation, in general" data from such studies are "not suitable to provide primary or sufficient basis for performing a risk assessment." JA__[FDA-000009]. That was ample justification for FDA's conclusion that such studies had limited weight.

Petitioners further contend (Br.40-41) that FDA "contravene[d]" the approach of the Consumer Product Safety Commission (CPSC), but they demonstrate no inconsistency. In concluding that "[e]stablishing cause and effect in epidemiological studies [wa]s not required" in a particular matter, CPSC was discussing an assessment that was "based primarily on animal studies" and for which "there [wa]s sufficient evidence in animal studies to conclude that certain phthalates are probably toxic to humans." JA__[FDA-020772]. That does not conflict with FDA's inability to reach a similar conclusion based on the record here, or FDA's conclusion that epidemiological studies are "not suitable" as a "primary or sufficient basis"

for food-additive risk assessment. JA__[FDA-000009]; *see* JA__[FDA-000009] ("epidemiological studies *may be considered supplementary* to the available toxicological data" (emphasis added)).

Moreover, FDA thoroughly considered the cited report to the CPSC, which FDA acknowledged was the "result of significant scientific analysis." JA__[FDA-002014]; *see* JA__[FDA-000014]. However, that report and CPSC's conclusions based thereon apply to certain phthalates in products within CPSC's jurisdiction, such as "children's toys and child care articles." *See* JA__[FDA-020758]; JA__[FDA-001375]. This meant that CPSC's conclusions did not "directly determine the safety" of phthalates' intended use in food-contact applications under the FDCA, requiring FDA to independently evaluate the data before it. JA__[FDA-002014]; *see* 21 U.S.C. § 348(b)(1). That two agencies operating under distinct sources of statutory authority to regulate different products might analyze the evidentiary records before them and reach differing factual conclusions regarding a particular set of substances is not surprising.

Finally, petitioners assert that FDA's analysis here was inconsistent with its own guidance document recommending against the use of one of the subject phthalates in pharmaceuticals. Br.41 (citing JA__[FDA-013336]). That recommendation was limited to addressing the use in drugs and

biological products regulated under different statutory authorities. *See* 21 U.S.C. § 321(g)(1); 42 U.S.C. § 262. And as FDA explained, that guidance involved "safety considerations and assessments" different from those under "food additive safety standards," and expressly did not "address the use of [those phthalates] in other types of FDA-regulated products." JA__[FDA-002014-15]; JA__[FDA-013333]. Additionally, there is no indication that epidemiological studies were the "primary or sufficient basis" for FDA's recommendation in the guidance document, and thus no reason to think FDA's approach to such studies differed in that context. *See* JA__[FDA-000009]; JA__[FDA-013334-35].

3. FDA reasonably evaluated the evidence in the record on exposure.

Petitioners' third factual assertion related to exposure to phthalates. FDA concluded that the petition did not "adequately support its proposed exposure estimates." JA__[FDA-002013]. In particular, the agency identified three issues that the petition failed to account for:

> (1) The imprecision of relying on exposur[e] estimates derived from biomonitoring studies to assess dietary exposure; (2) the diverse parameters used in the cited dietary exposure analyses to determine which analysis, if any, most accurately reflects true U.S. dietary exposure; and (3) the contradiction in reported dietary exposure values between those analyses.

JA__[FDA-002013].

In their objections, petitioners switched tack and asserted that they had no obligation to submit *any* evidence regarding exposure, JA__[FDA-010681-84]; and alternatively, that their exposure data alone raises serious safety questions, JA__[FDA-010684-90]. FDA overruled those objections, explaining that a petition must provide adequate support for the requested changes to food-additive regulations—including exposure data—and that the denial order properly evaluated petitioners' "dietary exposure estimates" and "explained why they were lacking." JA__[FDA-000013-14].

FDA thus reasonably considered phthalate exposure and concluded based on a fair and thorough evaluation of the record that significant safety questions have not been raised. This Court should deny the petition for review on this issue.

a. Petitioners assert (Br.44) that even though FDA "must consider the level of human exposure to an additive in assessing safety," a petitioner has no obligation under the FDCA or regulations to submit information "quantif[ying] exposure to the additives" whose authorizations the petitioner proposes to repeal. Petitioners again misunderstand their burden. As explained, *supra* Part II.A, petitioners must provide adequate evidence to demonstrate significant safety questions to show that it is no longer reasonably certain that the approved food-additive uses are not harmful.

Estimating exposure to an additive is a crucial factor in evaluating its safety. 21 U.S.C. § 348(c)(5) ("In determining … whether a proposed use of a food additive is safe, the Secretary shall consider … the probable consumption of the additive[.]"); s*ee* JA__[FDA-000008-9]; JA__[FDA-002010].

Petitioners contend that the regulations only require them to provide new toxicity data. Br.44 (citing 21 C.F.R. § 171.130(b)). But again, § 171.130(b) requires only that a petition contain certain broad categories of information that "*may* justify" repeal as a condition for filing and substantive review. 21 C.F.R. § 171.130(b) (emphasis added); *see supra* n.8. It does not mean that a petitioner satisfies its burden merely by providing some information within any of those broad categories.

Petitioners also posit that 21 C.F.R. § 171.1 only governs the "'form'" in which data must be submitted for a repeal petition, but not its substance. Br.44 (emphasis omitted). That "form" established in § 171.1, however, lists the specific "data" that must be "[a]ttached [t]hereto" and "constitut[e] a part of [the] petition." 21 C.F.R. § 171.1(c). And such data includes "full information on each proposed change" and "[f]ull reports of investigations made with respect to the safety of the food additive." *Id.* ("A petition may be regarded as incomplete unless it includes full reports of adequate tests reasonably applicable to show whether or not the food additive will be safe

for its intended use."); *see In re NRDC*, 645 F.3d at 403 ("When a food additive petition seeks to amend an existing regulation, the petitioner must include 'full information on each proposed change[.]'" (quoting 21 C.F.R. § 171.1(c))). As noted, exposure is a necessary factor to consider in evaluating safety.

Finally, contrary to petitioners' suggestion, FDA has not affirmed that "it may grant revocation petitions 'based upon new data concerning the toxicity of the food additive'" only. Br.44 (emphasis omitted) (quoting JA__[FDA-009082]). The decision that petitioners invoke did not rely exclusively on toxicity information. Rather, in the quoted decision, FDA concluded that the record contained "adequate migration data to determine dietary exposure to [the relevant substances], and sufficient data to account for a consumer's systemic exposure resulting from chronic dietary exposure to [those substances]." JA__[FDA-009083]; *see* JA__[FDA-000014].

b. Petitioners assert that FDA improperly found their exposure data to be insufficient. Br.45-51. But petitioners' explanation of their own data demonstrates their inadequacy. Petitioners essentially posit that the evidence shows that: (1) "diet is the primary source of exposure" for three of the phthalates, Br.45; (2) overall exposure (dietary and non-dietary) to one of those phthalates exceeds safe levels, Br.46; and (3) other phthalates

"contribute to the same health harms," Br.46. Those premises do not support the conclusion that the "specific food additive uses" of the five subject phthalates, JA__[FDA-000014], result in unsafe levels of exposure.

i. Petitioners again invoke the same panel report to the CPSC, contending that FDA unreasonably "dismissed" that report as "not relevant" because it was not dispositive of FDA's consideration of phthalates as food additives. Br.46-47. To the contrary, FDA considered the report's information on phthalate exposure, including "dietary exposure estimates," as part of FDA's own analysis in the denial order and supporting memoranda. *See* JA__[FDA-002012]; JA__[FDA-000321-31, 349-50]. FDA explained, however, that this report "was not designed to assess the safety of food additive uses." JA__[FDA-002011]. Indeed, the report considered total exposure to all sources of phthalates, JA__[FDA-020763], and was not specifically focused on dietary exposure. Accordingly, there were multiple "data gaps" that limited the support the report provided for the petition's factual claims regarding "U.S. dietary exposures." JA__[FDA-002012] (noting that report relied on only one study "conducted in the United Kingdom"). Not only did the petition not try to fill those gaps, but it failed to address "contradictory" dietary exposure values provided by another study and explain "which … of these contradictory values is suitable

for the purpose of a safety assessment." JA__[FDA-002013]. FDA thus thoroughly considered the report. And although relevant to the CPSC in its regulation of a different field, FDA reasonably declined to give the report greater weight in the food-additive context.

ii. Petitioners next assert (Br.47-48) that FDA "irrationally dismissed" the exposure findings in the ATSDR report by considering them in isolation. But FDA considered this report alongside the report to the CPSC and reasonably explained that even if it "were to reach the general conclusion that the diet is a major source of exposure to approved [p]hthalates"—as petitioners urged based on the ATSDR report—"that would not answer the question of whether or not a specific approved food additive use is safe." JA__[FDA-000014]; *see also supra* Part II.B.2.b.i (addressing ATSDR report regarding toxicity evidence).

Petitioners state that ATSDR "calculated the exposure level at which [di-(2-ethylhexyl) phthalate] may cause harm *to humans* and found that exposures in the U.S. exceed that level." Br.48. However, the ATSDR report made no such comparison. Instead, the ATSDR report supplied a "minimal risk level" for "oral exposure," JA__[FDA-010677], based on toxicological data. FDA reasonably explained that the ATSDR "minimal risk level" was not adequately supported. *See* JA__[FDA-000015] (explaining that level

was "determined based on a single study that used only one dose level and only a limited number of animals," thus "there is not enough supporting information to rely on this value for the purposes of a safety assessment"). Petitioners do not contest that conclusion.

iii. Petitioners take issue with FDA's response to their reliance on biomonitoring data. Br.48-49. But as FDA explained, "[r]elying on biomonitoring data alone does not differentiate the amount of exposure that results from the diet compared to environmental and other sources." JA__[FDA-000015]. Biomonitoring studies can "provide insight into the total exposure to a substance from multiple routes such as inhalation, ingestion, and dermal contact," but that "overall exposure value overestimates the probable *dietary* exposure value." JA_[FDA-000328] (emphasis added); *see* JA__[FDA-002013]. And safety evaluations for food-additive petitions must consider "the cumulative effect of such additive in the *diet* of man." 21 U.S.C. § 348(c)(5)(B) (emphasis added).

To be clear, FDA acknowledged that biomonitoring data may be "relevant," but took issue with how the petition was specifically attempting to use that data. JA__[FDA-002013]; *see* JA__[FDA-000015]. Because the petition "did not account for these limitations by addressing how the biomonitoring data accounts for dietary exposure" specifically, FDA

concluded the petition's proposed "direct comparison of biomonitoring-based exposure values to the purported [acceptable daily intake level] was scientifically flawed." JA__[FDA-000015]; JA__[FDA-002013]. And FDA reasonably determined that the petition did not provide an evidentiary basis for qualitatively assessing dietary exposure. *See* JA__[FDA-000014] (explaining possibility of qualitative assessment given "biopersistence" data in other proceeding, and lack of "comparable evidence" in this record).

Petitioners also assert that FDA improperly focused only on dietary exposure to the five phthalates, rather than total exposure. Br.50-51. As FDA explained, the FDCA "does not impose a 'legal obligation' for FDA to consider exposure from non-dietary sources in determining safety." JA__[FDA-000016]. Rather, the statute requires FDA to consider dietary exposure and provides "discretion to decide, in [its] scientific expertise, whether there are other factors that are 'relevant' to the safety of a food additive in the context of a particular petition." JA__[FDA-000016] (citing 21 U.S.C. § 348(c)(5)).

Petitioners contend that total exposure to a food-additive including from non-dietary sources is necessarily always a "'relevant facto[r]'" that the agency is required to consider under § 348(c)(5). Br.50. If Congress had meant to impose an additional mandatory consideration on FDA's safety evaluations in regulating food additives, on top of the three mandatory

considerations listed in the statute, it would have done so expressly. Especially in these circumstances where petitioners had not established two independent, antecedent premises of the petition (proposing a class of phthalates and assigning a proposed toxicity level to that class), it was appropriate for FDA to exercise its discretion to limit its review to information mandated by statute related to dietary exposure.

III. FDA Was Not Required To Hold An Administrative Hearing Before Denying Petitioners' Objections.

Petitioners are also incorrect to contend that FDA was required to hold an evidentiary hearing before overruling their objections to FDA's denial of the food-additive petition.

This Court has recognized that the statutory provision authorizing FDA to hold public hearings on objections to its decision granting or denying food-additive petitions, 21 U.S.C. § 348(f)(1), does not require a hearing in all circumstances. *See Young*, 773 F.2d at 1364. Instead, to warrant a hearing, a party's request must "contain evidence that raises a material issue of fact on which a meaningful hearing might be held" and that "go[es] to the legality of the agency's order." *Id.* FDA will deny a hearing request unless the request shows: (1) "the existence of a genuine and substantial issue of fact to be resolved"; that (2) "can be resolved by available reliable evidence"; (3) that the objector's "data and information, if proved, would be sufficient

to resolve the factual issue in the way sought"; and (4) that "resolution of the factual issue in that way would suffice to warrant the relief requested." *Id.* (citing 21 C.F.R. § 12.24(b)).

This Court's review of the decision whether to hold such a hearing is "necessarily deferential," "limited to an evaluation of whether the agency has given adequate consideration to all relevant evidence in the record." *National Corn Growers Ass'n*, 613 F.3d at 271-72 (alteration omitted) (quoting *Young*, 773 F.2d at 1362-63). The Court has emphasized that "[m]ere differences in the weight or credence given to particular scientific studies, or in the numerical estimates of the average daily intake of a substance, are insufficient," and that it "will not substitute [its] judgment on highly technical and factual matters for that of the agency charged with the supervision of the industry." *Id.* (alteration omitted) (quoting *Young*, 773 F.2d at 1363).

A. FDA denied petitioners' requests for an administrative hearing after thoroughly considering all of their submissions and not finding any issues of material fact that could be resolved in their favor at a hearing and justify granting the petition.

As to petitioners' request to analyze a new grouping of four phthalates as a class for purposes of the safety analysis, *see supra* Part II.B.1, FDA

determined that a hearing was not required on the question of the substances' relatedness. *See* JA__[FDA-000011-12]. The agency explained that, because petitioners' request improperly exceeded the scope of the objections process to request action not addressed in the denial order, resolution of any factual issues would not "justify the action requested." JA__[FDA-000012] (citing 21 C.F.R. § 12.24(b)(4)); *see* JA__[FDA-000012] ("Because [petitioners] seek determinations regarding issues that are outside the scope of the provisions of FDA's denial order, the objection and hearing request are improper.").

Regarding petitioners' toxicity evidence, FDA explained that despite discussing health effects and listing various publication, petitioners "failed to demonstrate how the cited studies, publications, declarations, and facts asserted would be sufficient to justify resolution of the safety question in the objectors' favor." JA__[FDA-000008-09]. Because "the information in the record is [not] adequate to justify their factual assertion regarding safety," denial was warranted under 21 C.F.R. § 12.24(b)(3). JA__[FDA-000009].

And for exposure data, petitioners requested a hearing to address whether biomonitoring data and other information collectively establish significant safety questions. JA__[FDA-010690]. FDA explained, however, that even if established, the data identified "would not be adequate to justify

the factual determination about unsafe exposure urged by [petitioners]," JA__[FDA-000014], because they "do not provide a factual basis for determining that … there are significant safety questions regarding the *dietary* exposure levels because these claims do not proffer evidence of unsafe *dietary* exposure levels for any [p]hthalates with authorized uses," JA__[FDA-000015] (emphases added).

More generally, FDA also explained that certain individual factual assertions on which petitioners sought a hearing would not be outcome-determinative, because petitioners had failed to establish the other antecedent premises in the petition. *See* JA__[FDA-000009-10] (explaining that petitioners' objections regarding toxicity data would not affect FDA's conclusion that the petition failed to justify its premise of treating all 28 phthalates as a class); JA__[FDA-000014] (explaining that a different conclusion regarding exposure data would not be "determinative" given failure to adequately support the two antecedent premises regarding class-treatment and toxicity). An evidentiary hearing on those points was thus also unwarranted under 21 C.F.R. § 12.24(b)(4).

B. Petitioners assert generally (Br.57-59) that they raised factual issues as to toxicity, exposure, and cumulative effects that are "material." This argument again hinges on petitioners' view regarding their burden in

seeking to repeal a food-additive authorization, and what it means in that context to raise a sufficiently "significant" safety question. *See* Br.58; Br.59 (discussing exposure evidence). Under the correct understanding of a petitioner's obligations in this kind of proceeding, *see supra* Part II.A, FDA properly denied the hearing requests. And contrary to petitioners' suggestion (Br.59), FDA did not require definitive proof that "dietary exposure" exceeds safe levels as a "'predicate'" for granting a hearing. *See* JA__[FDA-000014] (explaining that "the data and information identified … *even if established at a hearing*, would not be adequate to justify the factual determination about unsafe exposure urged by the objectors" (emphasis added)).

Petitioners contend (Br.58-59) that in denying the hearing requests, FDA irrationally invoked the fact that the petition failed to support its core premise that all 28 phthalates could be grouped into a single safety analysis. But as explained, that was the conclusion in the order under review to which petitioners needed to specifically object. *See supra* Part II.B.1.a. To abandon that premise at the objections stage, and seek a hearing on a new basis not presented in the underlying petition, falls outside the scope of the objections process. *See* JA__[FDA-000010]; 21 U.S.C. § 348(f)(1). A hearing on an assertion cannot be properly considered outcome-determinative of the

proceeding at issue when it raises "questions [petitioners] failed to ask," and seeks "actions they failed to request, in the petition that is the subject of [the] proceeding." JA__[FDA-000010].

CONCLUSION

For the foregoing reasons, the petition for review should be dismissed for lack of jurisdiction or denied on the merits.

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limit of Federal Rule of Appellate Procedure 32(a)(7)(B) because it contains 12,964 words. This brief also complies with the typeface and type-style requirements of Federal Rule of Appellate Procedure 32(a)(5)-(6) because it was prepared using Word for Microsoft 365 in Georgia 14-point font, a proportionally spaced typeface.

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CERTIFICATE OF SERVICE

I hereby certify that on August 13, 2025, I electronically filed the foregoing brief with the Clerk of the Court for the United States Court of Appeals for the District of Columbia Circuit by using the appellate CM/ECF system.

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ADDENDUM

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21 U.S.C. § 321

§ 321. Definitions; generally

For the purposes of this chapter—

* * *

(s) The term "food additive" means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; * * *

* * * *

21 U.S.C. § 342

§ 342. Adulterated food

A food shall be deemed to be adulterated--

(a) Poisonous, insanitary, etc., ingredients

> * * * (2) * * * (C) if it is or if it bears or contains (i) any food additive that is unsafe within the meaning of section 348 of this title * * *

* * * *

21 U.S.C. § 348

§ 348. Food additives

(a) Unsafe food additives; exception for conformity with exemption or regulation

A food additive shall, with respect to any particular use or intended use of such additives, be deemed to be unsafe for the purposes of the application of clause (2)(C) of section 342(a) of this title, unless--

(1) it and its use or intended use conform to the terms of an exemption which is in effect pursuant to subsection (j) of this section;

(2) there is in effect, and it and its use or intended use are in conformity with, a regulation issued under this section prescribing the conditions under which such additive may be safely used; or

(3) in the case of a food additive as defined in this chapter that is a food contact substance, there is--

(A) in effect, and such substance and the use of such substance are in conformity with, a regulation issued under this section prescribing the conditions under which such additive may be safely used; or

(B) a notification submitted under subsection (h) that is effective.

While such a regulation relating to a food additive, or such a notification under subsection (h)(1) relating to a food additive that is a food contact substance, is in effect, and has not been revoked pursuant to subsection (i), a food shall not, by reason of bearing or containing such a food additive in accordance with the regulation or notification, be considered adulterated under section 342(a)(1) of this title.

(b) Petition for regulation prescribing conditions of safe use; contents; description of production methods and controls; samples; notice of regulation

(1) Any person may, with respect to any intended use of a food additive, file with the Secretary a petition proposing the issuance of a regulation prescribing the conditions under which such additive may be safely used.

(2) Such petition shall, in addition to any explanatory or supporting data, contain--

(A) the name and all pertinent information concerning such food additive, including, where available, its chemical identity and composition;

(B) a statement of the conditions of the proposed use of such additive, including all directions, recommendations, and suggestions proposed for the use of such additive, and including specimens of its proposed labeling;

(C) all relevant data bearing on the physical or other technical effect such additive is intended to produce, and the quantity of such additive required to produce such effect;

(D) a description of practicable methods for determining the quantity of such additive in or on food, and any substance formed in or on food, because of its use; and

(E) full reports of investigations made with respect to the safety for use of such additive, including full information as to the methods and controls used in conducting such investigations.

(3) Upon request of the Secretary, the petitioner shall furnish (or, if the petitioner is not the manufacturer of such additive, the petitioner shall have the manufacturer of such additive furnish, without disclosure to the petitioner) a full description of the methods used in, and the facilities and controls used for, the production of such additive.

(4) Upon request of the Secretary, the petitioner shall furnish samples of the food additive involved, or articles used as components thereof, and of the food in or on which the additive is proposed to be used.

(5) Notice of the regulation proposed by the petitioner shall be published in general terms by the Secretary within thirty days after filing.

(c) Approval or denial of petition; time for issuance of order; evaluation of data; factors

(1) The Secretary shall--

(A) by order establish a regulation (whether or not in accord with that proposed by the petitioner) prescribing, with respect to one or more proposed uses of the food additive involved, the conditions under which such additive may be safely used (including, but not limited to, specifications as to the particular food or classes of food in or in which such additive may be used, the maximum quantity which may be used or permitted to remain in or on such food, the manner in which such additive may be added to or used in or on such food, and any directions or other labeling or packaging requirements for such additive deemed necessary by him to assure the safety of such use), and shall notify the petitioner of such order and the reasons for such action; or

(B) by order deny the petition, and shall notify the petitioner of such order and of the reasons for such action.

(2) The order required by paragraph (1)(A) or (B) of this subsection shall be issued within ninety days after the date of filing of the petition, except that the Secretary may (prior to such ninetieth day), by written notice to the petitioner, extend such ninety-day period to such time (not more than

one hundred and eighty days after the date of filing of the petition) as the Secretary deems necessary to enable him to study and investigate the petition.

(3) No such regulation shall issue if a fair evaluation of the data before the Secretary--

(A) 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: *Provided*, That no additive shall be deemed to be 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, except that this proviso shall not apply with respect to the use of a substance as an ingredient of feed for animals which are raised for food production, if the Secretary finds (i) that, under the conditions of use and feeding specified in proposed labeling and reasonably certain to be followed in practice, such additive will not adversely affect the animals for which such feed is intended, and (ii) that no residue of the additive will be found (by methods of examination prescribed or approved by the Secretary by regulations, which regulations shall not be subject to subsections (f) and (g)) in any edible portion of such animal after slaughter or in any food yielded by or derived from the living animal; or

(B) shows that the proposed use of the additive would promote deception of the consumer in violation of this chapter or would otherwise result in adulteration or in misbranding of food within the meaning of this chapter.

(4) If, in the judgment of the Secretary, based upon a fair evaluation of the data before him, a tolerance limitation is required in order to assure that the proposed use of an additive will be safe, the Secretary--

(A) shall not fix such tolerance limitation at a level higher than he finds to be reasonably required to accomplish the physical or other technical effect for which such additive is intended; and

(B) shall not establish a regulation for such proposed use if he finds upon a fair evaluation of the data before him that such data do not establish that such use would accomplish the intended physical or other technical effect.

(5) In determining, for the purposes of this section, whether a proposed use of a food additive is safe, the Secretary shall consider among other relevant factors--

(A) the probable consumption of the additive and of any substance formed in or on food because of the use 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 which in the opinion of experts qualified by scientific training and experience to evaluate the safety of food additives are generally recognized as appropriate for the use of animal experimentation data.

(d) Regulation issued on Secretary's initiative

The Secretary may at any time, upon his own initiative, propose the issuance of a regulation prescribing, with respect to any particular use of a food additive, the conditions under which such additive may be safely used, and the reasons therefor. After the thirtieth day following publication of such a proposal, the Secretary may by order establish a regulation based upon the proposal.

(e) Publication and effective date of orders

Any order, including any regulation established by such order, issued under subsection (c) or (d) of this section, shall be published and shall be effective upon publication, but the Secretary may stay such effectiveness if, after issuance of such order, a hearing is sought with respect to such order pursuant to subsection (f).

(f) Objections and public hearing; basis and contents of order; statement

(1) Within thirty days after publication of an order made pursuant to subsection (c) or (d) of this section, any person adversely affected by such an order may file objections thereto with the Secretary, specifying with particularity the provisions of the order deemed objectionable, stating reasonable grounds therefor, and requesting a public hearing upon such objections. The Secretary shall, after due notice, as promptly as possible hold such public hearing for the purpose of receiving evidence relevant and material to the issues raised by such objections. As soon as

practicable after completion of the hearing, the Secretary shall by order act upon such objections and make such order public.

(2) Such order shall be based upon a fair evaluation of the entire record at such hearing, and shall include a statement setting forth in detail the findings and conclusions upon which the order is based.

(3) The Secretary shall specify in the order the date on which it shall take effect, except that it shall not be made to take effect prior to the ninetieth day after its publication, unless the Secretary finds that emergency conditions exist necessitating an earlier effective date, in which event the Secretary shall specify in the order his findings as to such conditions.

(g) Judicial review

(1) In a case of actual controversy as to the validity of any order issued under subsection (f), including any order thereunder with respect to amendment or repeal of a regulation issued under this section, any person who will be adversely affected by such order may obtain judicial review by filing in the United States Court of Appeals for the circuit wherein such person resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a petition praying that the order be set aside in whole or in part.

(2) A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall file in the court the record of the proceedings on which he based his order, as provided in section 2112 of Title 28. Upon the filing of such petition the court shall have jurisdiction, which upon the filing of the record with it shall be exclusive, to affirm or set aside the order complained of in whole or in part. Until the filing of the record the Secretary may modify or set aside his order. The findings of the Secretary with respect to questions of fact shall be sustained if based upon a fair evaluation of the entire record at such hearing.

(3) The court, on such judicial review, shall not sustain the order of the Secretary if he failed to comply with any requirement imposed on him by subsection (f)(2) of this section.

(4) If application is made to the court for leave to adduce additional evidence, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and

upon such terms and conditions as to the court may seem proper, if such evidence is material and there were reasonable grounds for failure to adduce such evidence in the proceedings below. The Secretary may modify his findings as to the facts and order by reason of the additional evidence so taken, and shall file with the court such modified findings and order.

(5) The judgment of the court affirming or setting aside, in whole or in part, any order under this section shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of Title 28. The commencement of proceedings under this section shall not, unless specifically ordered by the court to the contrary, operate as a stay of an order.

(h) Notification relating to food contact substance

* * *

(6) In this section, the term "food contact substance" means any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have any technical effect in such food.

(i) Amendment or repeal of regulations

The Secretary shall by regulation prescribe the procedure by which regulations under the foregoing provisions of this section may be amended or repealed, and such procedure shall conform to the procedure provided in this section for the promulgation of such regulations. The Secretary shall by regulation prescribe the procedure by which the Secretary may deem a notification under subsection (h) to no longer be effective.

* * * *

21 C.F.R. § 12.24

§ 12.24. Ruling on objections and requests for hearing

(a) As soon as possible the Commissioner will review all objections and requests for hearing filed under § 12.22 and determine—

(1) Whether the regulation should be modified or revoked under § 12.26;

(2) Whether a hearing has been justified; and

(3) Whether, if requested, a hearing before a Public Board of Inquiry under part 13 or before a public advisory committee under part 14 or before the Commissioner under part 15 has been justified.

(b) A request for a hearing will be granted if the material submitted shows the following:

(1) There is a genuine and substantial issue of fact for resolution at a hearing. A hearing will not be granted on issues of policy or law.

(2) The factual issue can be resolved by available and specifically identified reliable evidence. A hearing will not be granted on the basis of mere allegations or denials or general descriptions of positions and contentions.

(3) The data and information submitted, if established at a hearing, would be adequate to justify resolution of the factual issue in the way sought by the person. A hearing will be denied if the Commissioner concludes that the data and information submitted are insufficient to justify the factual determination urged, even if accurate.

(4) Resolution of the factual issue in the way sought by the person is adequate to justify the action requested. A hearing will not be granted on factual issues that are not determinative with respect to the action requested, e.g., if the Commissioner concludes that the action would be the same even if the factual issue were resolved in the way sought, or if a request is made that a final regulation include a provision not reasonably encompassed by the proposal. A hearing will be granted upon proper objection and request when a food standard or other regulation is shown to have the effect of excluding or otherwise affecting a product or ingredient.

(5) The action requested is not inconsistent with any provision in the act or any regulation in this chapter particularizing statutory standards. The proper procedure in those circumstances is for the person requesting the hearing to petition for an amendment or waiver of the regulation involved.

(6) The requirements in other applicable regulations, e.g., §§ 10.20, 12.21, 12.22, 314.200, 514.200, and 601.7(a), and in the notice promulgating the final regulation or the notice of opportunity for hearing are met.

(c) In making the determination in paragraph (a) of this section, the Commissioner may use any of the optional procedures specified in §

10.30(h) or in other applicable regulations, e.g., §§ 314.200, 514.200, and 601.7(a).

(d) If it is uncertain whether a hearing has been justified under the principles in paragraph (b) of this section, and the Commissioner concludes that summary decision against the person requesting a hearing should be considered, the Commissioner may serve upon the person by registered mail a proposed order denying a hearing. The person has 30 days after receipt of the proposed order to demonstrate that the submission justifies a hearing.

21 C.F.R. § 12.26

§ 12.26. Modification or revocation of regulation or order

If the Commissioner determines upon review of an objection or request for hearing that the regulation or order should be modified or revoked, the Commissioner will promptly take such action by notice in the Federal Register. Further objections to or requests for hearing on the modification or revocation may be submitted under §§ 12.20 through 12.22 but no further issue may be taken with other provisions in the regulation or order. Objections and requests for hearing that are not affected by the modification or revocation will remain on file and be acted upon in due course.

21 C.F.R. § 12.87

§ 12.87. Purpose; oral and written testimony; burden of proof

* * *

(d) At a hearing involving issuing, amending, or revoking a regulation or order relating to the safety or effectiveness of a drug, device, food additive, or color additive, the participant who is contending that the product is safe or effective or both and who is requesting approval or contesting withdrawal of approval has the burden of proof in establishing safety or effectiveness or both and thus the right to approval. The burden of proof remains on that participant in an amendment or revocation proceeding.

* * * *

21 C.F.R. § 170.3

§ 170.3. Definitions

* * *

(i) Safe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the conditions of its intended use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined by scientific procedures or by general recognition of safety. In determining safety, the following factors shall be considered:

(1) The probable consumption of the substance and of any substance formed in or on food because of its use.

(2) The cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet.

(3) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate.

* * * *

21 C.F.R. § 171.1

§ 171.1. Petitions

* * *

(c) Petitions shall include the following data and be submitted in the following form:

* * *

E. Full reports of investigations made with respect to the safety of the food additive.

(A petition may be regarded as incomplete unless it includes full reports of adequate tests reasonably applicable to show whether or not the food additive will be safe for its intended use. The reports ordinarily should include detailed data derived from appropriate animal and other biological experiments in which the methods used and the results obtained are clearly set forth. The petition shall not omit without explanation any reports of investigations that would bias an evaluation of the safety of the food additive.)

F. Proposed tolerances for the food additive, if tolerances are required in order to insure its safety. A petitioner may include a proposed regulation.

G. If submitting petition to modify an existing regulation issued pursuant to section 409(c)(1)(A) of the Act, full information on each proposed change that is to be made in the original regulation must be submitted. The petition may omit statements made in the original petition concerning which no change is proposed. A supplemental petition must be submitted for any change beyond the variations provided for in the original petition and the regulation issued on the basis of the original petition.

* * *

(d) The petitioner will be notified of the date on which his petition is filed; and an incomplete petition, or one that has not been submitted in triplicate, will usually be retained but not filed as a petition under section 409 of the Act. The petitioner will be notified in what respects his petition is incomplete.

* * *

(g) A petition shall be retained but shall not be filed if any of the data prescribed by section 409(b) of the Act are lacking or are not set forth so as to be readily understood.

* * * *

21 C.F.R. § 171.130

§ 171.130. Procedure for amending and repealing tolerances or exemptions from tolerances

(a) The Commissioner, on his own initiative or on the petition of any interested person, pursuant to part 10 of this chapter, may propose the issuance of a regulation amending or repealing a regulation pertaining to a food additive or granting or repealing an exception for such additive.

(b) Any such petition shall include an assertion of facts, supported by data, showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption may justify its amendment or repeal. New data shall be furnished in the form specified in §§ 171.1 and 171.100 for submitting petitions.