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Tenth Circuit

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PUBLISH

UNITED STATES COURT OF APPEALS

FOR THE TENTH CIRCUIT

ELECTRIC CLOUDS, INC. and CLOUD 9 VAPOR PRODUCTS, L.L.C.,

Petitioners,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,

Respondent.

AMERICAN ACADEMY OF FAMILY PHYSICIANS; AMERICAN ACADEMY OF PEDIATRICS; AMERICAN CANCER SOCIETY CANCER ACTION NETWORK; AMERICAN HEART ASSOCIATION; AMERICAN LUNG ASSOCIATION OF OKLAHOMA; AMERICAN MEDICAL ASSOCIATION; CAMPAIGN FOR TOBACCO-FREE KIDS; COLORADO MEDICAL SOCIETY; PARENTS AGAINST VAPING E-CIGARETTES; TRUTH INITIATIVE,

Amici Curiae.

Nos. 21-9577 & 21-9578

PETITION FOR REVIEW FROM AN ORDER OF THE U.S. FOOD AND DRUG ADMINISTRATION (FDA Nos. PM0002382 & PM002523)

Jerad Wayne Najvar, Najvar Law Firm, PLLC, Houston, Texas, for Petitioners.

Joshua M. Koppel, Appellate Staff Attorney, U.S. Department of Justice, Washington D.C. (Bryan M. Boynton, Principal Deputy Assistant Attorney General, and Alisa B. Klein, Appellate Staff Attorney, with him on the briefs), for Respondent.

William B. Schultz, Andrew N. Goldfarb, and Trillium Chang of Zuckerman Spaeder LLP, Washington D.C., and Dennis A. Henigan and Connor Fuchs, Campaign for Tobacco-Free Kids, Washington, D.C., filed an amicus curiae brief in support of Respondent.

Before **BACHARACH**, **BALDOCK**, and **MURPHY**, Circuit Judges.

BACHARACH, Circuit Judge.

This case arose from concern over the spread of nicotine. Traditionally, nicotine had come mainly from cigarettes. But nicotine now comes from other sources, such as *e-cigarettes*. With e-cigarettes, users inhale vaporized liquid rather than smoke; the vapor comes from heated liquids called *e-liquids*.

E-liquids contain nicotine, which harms human health. So the Food and Drug Administration began requiring manufacturers to apply for approval before they could continue selling e-liquids. Because the

application process would be new, the FDA issued guidance for manufacturers.

With this guidance, manufacturers blitzed the FDA with applications to market e-liquids bearing attractive flavors. Our petitions for review involve applications from two of these manufacturers: Electric Clouds, Inc. and Cloud 9 Vapor Products, L.L.C. With their applications, Electric Clouds and Cloud 9 submitted scientific data and marketing proposals to restrict access for children. The FDA rejected the applications without reviewing the proposed restrictions on access, and Electric Clouds and Cloud 9 seek judicial review on two main issues:

1. **Notice**: Because the application process was new, the FDA provided manufacturers with guidance. For example, the FDA suggested to manufacturers that they would need to show enough benefits to adult users to offset the risk of attracting children to e-liquids. Did this suggestion mislead manufacturers to believe that they wouldn't need long-term clinical studies or comparisons involving flavored and non-flavored e-liquids? We answer *no*.

2. **Harmless error**: The FDA studied existing access restrictions based on age and found that they had generally proved ineffective. Electric Clouds and Cloud 9 proposed age restrictions like those that the FDA had regarded as ineffective. Did the FDA prejudice Electric Clouds or Cloud 9 by rejecting their applications without reviewing their proposed age-restrictions? We again answer *no*.

1. FDA approval is required to manufacture e-liquids.

The FDA considered the applications against the backdrop of federal law, which permits approval only if the availability of the e-liquid "would

be appropriate" to protect public health. 21 U.S.C. § 387j(c)(2)(A). To apply this standard, the FDA must balance

- the chance that more adult users will transition away from tobacco use and
- the risk that more children will start using e-liquids.

21 U.S.C. § 387j(c)(4)(A)–(B).

In balancing these factors, the FDA has considered the advantages and disadvantages of e-liquids. The disadvantages mainly involve the presence of nicotine. *See* Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31, § 2(3), 123 Stat. 1776, 1777 (2009); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 414–15 (4th Cir. 2022). So the FDA has set out to encourage adult users to transition to e-liquids without making them attractive to children. *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 504–05 (6th Cir. 2021). This task was complicated by the growing use of flavors in e-liquids. These flavors attract children by making the e-liquids taste like fruit, mint, candy, desserts, and other sweets. *See Avail Vapor*, 55 F.4th at 415.

2. The FDA denied the applications by Electric Clouds and Cloud 9 to market flavored e-liquids.

With this regulatory framework in place, Electric Clouds and Cloud 9 applied for approval to manufacture flavored e-liquids bearing names like

Ice Cream Dream, *Berries Gone Wild*, *Cap'n Berry Crack*, *Banana Colada*, *Apple Pie*, and *Candy Man*. ER6–10, 306–23.

The FDA denied the applications, finding that Electric Clouds and Cloud 9 hadn't shown that their flavored e-liquids would help adult smokers enough to offset the risk to youth. ER14–15, ER325–26. The FDA considered the manufacturers' scientific evidence, but regarded it as deficient based on the absence of

- long-term, product-specific studies of cigarette reduction or comparisons to tobacco-flavored e-liquids (such as a randomized controlled trial or longitudinal cohort study) or
- other evidence that had reliably evaluated the effect of flavoring on adults reducing their use of cigarettes or transitioning to e-liquids.

ER14–15, 325–26.

Given these deficiencies, the FDA rejected the applications without reviewing the proposed marketing plans. ER15, 325. The FDA acknowledged that marketing plans might theoretically reduce the risk to youth. ER35 n.xix, 352 n.xix. But the FDA pointed out that it hadn't yet seen any marketing plans that would sufficiently offset the risk of attracting young consumers. *Id.*

3. The FDA didn't mislead Electric Clouds or Cloud 9 by ambushing them with a new, undisclosed evidentiary standard.

Electric Clouds and Cloud 9 argue in part that the FDA misled them by imposing rigid requirements after suggesting a more flexible approach.

The changes, according to Electric Clouds and Cloud 9, involved requirements for long-term clinical studies and comparisons between e-liquids based on the presence of flavoring.

An agency must explain changes in its position, particularly when a regulated party has relied on the earlier position. *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515–16 (2009). Electric Clouds and Cloud 9 argue that the FDA changed its position after fostering reliance on its written guidance, proposed rule, and statements in a public meeting. We disagree, concluding that the FDA didn't deviate from its earlier statements. *See Prohibition Juice Co. v. FDA*, 45 F.4th 8, 20–21 (D.C. Cir. 2022) (rejecting a similar challenge because the FDA's final determinations were consistent with the FDA's 2019 Guidance).

3.1 The FDA's statements didn't mislead Electric Clouds or Cloud 9 on the need for long-term clinical studies or the equivalent.

Electric Clouds and Cloud 9 argue that three of the FDA's statements had suggested to manufacturers that they could forgo long-term clinical studies:

1. the Guidance in 2019 for e-liquid manufacturers, FDA, Guidance for Industry, Premarket Tobacco Applications for Electronic Nicotine Delivery Systems (June 2019),

2. a 2019 proposed rule, Premarket Tobacco Product Applications and Recordkeeping Requirements, 84 Fed. Reg. 50,566 (Sept. 25, 2019), and

3. an FDA public meeting on October 22–23, 2018.

3.1.1 The 2019 Guidance didn't mislead the manufacturers.

Electric Clouds and Cloud 9 argue that they were misled by the FDA's guidance. Granted, "[t]he fair-notice requirement extends to informal guidance." *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 504 (6th Cir. 2021). But the guidance itself stressed that

- it was not binding,
- the FDA would continue to adapt to new information, and
- manufacturers would need to show empirical data at multiple points in time.

In both 2019 and 2020, the FDA issued guidance, beginning both times with warnings that they "represent[] the *current* thinking of the [FDA] on this topic" and are "not binding on the FDA or the public." ER47, ER115 (emphasis added). The 2019 Guidance added that "guidances . . . should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited." ER117. To emphasize the nonbinding nature of the guidance, the FDA included a bolded disclaimer on every page saying that it "[c]ontains nonbinding recommendations." *See Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 65 n.6 (5th Cir. 2024) (en banc) (Haynes, J., dissenting) ("The conditional language used

by the FDA in its nonbinding guidance documents indicates that it never guaranteed that a certain type of evidence would be sufficient.").[1]

With these disclaimers, the FDA emphasized in the 2020 Guidance that the requirements would change based on new information: "Manufacturers cannot have settled expectations to market unlawful products, especially in the face of evolving public health concerns." ER72, *Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised): Guidance for Industry* (Apr. 2020). Given the development of new information, the FDA reminded manufacturers that they

- would need to adapt their compliance policies based on "changed circumstances" and

[1] The Fifth Circuit disagreed, reasoning that the D.C. Circuit had declined to consider cautionary language in two opinions: *Southwest Airlines Co. v. FERC*, 926 F.3d 851 (D.C. Cir. 2019), and *Physicians for Social Responsibility v. Wheeler*, 956 F.3d 634 (D.C. Cir. 2020). *Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 27–40 (5th Cir. 2024) (en banc). But in these opinions, the D.C. Circuit hadn't addressed the impact of an agency's cautionary language. For example, in *Southwest Airlines Co.*, the D.C. Circuit had examined an agency's sudden departure from longstanding procedures for making determinations. *See Sw. Airlines Co.*, 926 F.3d at 856–58. The case hadn't involved guidance or a suggestion that the agency's statements weren't binding. *See id.* The same is true of *Physicians for Social Responsibility*. This case had involved an agency directive departing from a policy established by a handbook and a report. *Physicians for Soc. Respon.*, 956 F.3d at 645. There the court again had no occasion to discuss administrative guidance or a suggestion that the agency's statements weren't binding. *See id.*

- couldn't reasonably rely "on a . . . policy subject to change at any time."

ER79–80.[2]

Regardless of these reminders, the 2019 Guidance shouldn't have induced Electric Clouds or Cloud 9 to omit long-term clinical studies or the equivalent. In the guidance, the FDA regarded long-term clinical studies as the strongest type of evidence; however, the FDA also acknowledged that existing data might suffice. For example, the FDA said that it would consider "established bod[ies] of evidence," such as "existing

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[2] In their reply brief, Electric Clouds and Cloud 9 urge judicial estoppel for the first time, arguing that the FDA made contrary arguments in other federal cases. Petitioners' Reply Br. at 12–13. We generally decline to address issues raised for the first time in a reply brief. *See, e.g.*, *Belnap v. Iasis Healthcare*, 844 F.3d 1272, 1293 n.16 (10th Cir. 2017).

But we would reject this argument even if it had come earlier because the FDA hadn't taken a different position in the prior cases. In those cases, the FDA emphasized that

- "the guidance [was] 'not binding on FDA or the public'" and
- manufacturers could submit alternative forms of evidence, but only "if [the evidence] satisfie[d] the requirements of the applicable statutes and regulations."

Defendants' Response to Industry Amicus Br. at 4, *Am. Acad. of Pediatrics v. FDA*, No. 18-883 (D. Md. June 26, 2019) (quoting the 2019 Guidance); *see also* Final Br. for Appellees at 26, *Nicopure Labs, LLC v. FDA*, No. 17-5196 (D.C. Cir. June 5, 2018) ("FDA has stated in draft guidance that scientific-literature reviews *may be acceptable in some circumstances*, and has discussed alternatives to randomized, controlled trials." (emphasis added)). The FDA took the same position here. *See* pp. 10–11, below.

longer duration studies in the public literature." ER160, ER127. But the manufacturer would still need to "bridg[e]" its own e-liquid to the existing data by showing why the existing data would apply to the new product. ER127; *see* ER160.

The 2019 Guidance also clarified that

- the FDA would review "'other valid scientific evidence'" to determine whether it was "sufficient to evaluate the tobacco product," ER126 (quoting 21 U.S.C. § 387j(c)(5)(B)),
- "[n]onclinical studies alone [were] generally not sufficient," ER126, and
- "[p]ublished literature reviews . . . [were] considered a less robust form of support." ER161.

Given these qualifications, seven federal appellate courts have rejected similar challenges, reasoning that the 2019 Guidance had not guaranteed approval without long-term clinical studies. *Magellan Tech., Inc. v. FDA*, 70 F.4th 622, 629 (2d Cir. 2023); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 541 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 422–23 (4th Cir. 2022); *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 505–07 (6th Cir. 2021); *Gripum, LLC v. FDA*, 47 F.4th 553, 559–60 (7th Cir. 2022); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 672 (9th Cir. 2022); *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 23 (D.C. Cir. 2022).

For example, the D.C. and Seventh Circuits addressed similar reliance on the 2019 Guidance. In these cases, manufacturers of e-liquids argued that they had skipped long-term studies because of the 2019

Guidance. *See Prohibition Juice Co.*, 45 F.4th at 23–24; *Gripum*, 47 F.4th at 559. The D.C. Circuit rejected this argument, explaining that the FDA hadn't "guaranteed that unspecified other forms of evidence would necessarily be sufficient—only that they might be, so the FDA would consider them." *Prohibition Juice Co.*, 45 F.4th at 21 (citing the 2019 Guidance at 12–13). The Seventh Circuit also rejected the argument, pointing out that the 2019 Guidance had "consistently reflected" the need for "product-specific long-term data . . . only if existing studies [had been] inadequately related to the proposed product." *Gripum*, 47 F.4th at 559.

These opinions are persuasive.[3] Unlike Electric Clouds and Cloud 9, the D.C. and Seventh Circuits relied on the entirety of the FDA's guidance. Even if that guidance could have fostered reliable expectations, the entirety of the documents would have informed manufacturers of the need to

- tie their own e-liquids to the existing data or
- present new studies.

[3] One circuit disagrees, pointing out that "law is not a nose-counting exercise." *Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 20, 28–30 (5th Cir. 2024) (en banc). We agree, but we're persuaded by the reasoning of the seven other circuit courts.

3.1.2 The proposed rule didn't mislead the manufacturers.

The manufacturers rely not only on the 2019 Guidance, but also on a proposed rule. There the FDA said that it didn't expect each applicant to include a new long-term clinical study. But the FDA explained that with or without such a study, applicants would need to provide "both clinical and nonclinical investigations" offering "comprehensive information about the product's likely health effects in the U.S. market." 84 Fed. Reg. 50,566; 50,619 (Sept. 25, 2019). The FDA added that an applicant might be able to forgo new studies by "bridging" its own e-liquid to existing studies. *Id.* And even then, the FDA cautioned, "information from nonclinical studies alone" would generally not suffice. *Id.*

Given the whole of the proposed rule, it shouldn't have misled Electric Clouds or Cloud 9 to think that it could forgo a new long-term clinical study or an effort to bridge the new e-liquids to an existing study.

3.1.3 The 2018 public meeting didn't mislead the manufacturers.

Electric Clouds and Cloud 9 also argue that the FDA misled them at a public meeting in 2018. At that meeting, an FDA representative stated: "[I]t may be possible to support a marketing order for an [electronic nicotine delivery system], as an example, without conducting new non-clinical or clinical studies, given other data sources can support the [marketing application]." Transcript, Tobacco Product Application Review Public Meeting at 133–34 (Oct. 23, 2018).

This statement shouldn't have misled Electric Clouds or Cloud 9. The representative said only that "it may be possible" to rely on existing studies. From that statement, Electric Clouds and Cloud 9 shouldn't have assumed that they could forgo either a new long-term clinical study or any effort to bridge the new e-liquids to an existing study.[4]

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The FDA didn't mislead Electric Clouds or Cloud 9 about the need to present either a new long-term clinical study or to bridge the new e-liquid to an existing study.[5]

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[4] The Fifth Circuit concluded that the public meetings had misled tobacco manufacturers. There the Fifth Circuit relied on the FDA's slides that

- included this statement and
- disclaimed a requirement for "specific studies."

Wages & White Lion Invs., LLC v. FDA, 90 F.4th 357, slip op. at 5–7 (5th Cir. 2024) (en banc). It's unclear whether Electric Clouds and Cloud 9 are relying on the FDA's statement at the public meeting or the slides.

The slides themselves are not in our record. From the petitioners' description, however, the slides shouldn't have misled anyone. Just because the FDA didn't require a specific type of study doesn't mean that Electric Clouds and Cloud 9 could omit any new studies or bridging efforts. After all, the FDA had repeatedly stressed that applicants would need to bridge their own products to valid scientific evidence. *See* Parts 3.1.1–3.1.2, above.

[5] Electric Clouds and Cloud 9 also cite the final rule, arguing that the FDA never said that it would require long-term studies. *Premarket Tobacco Product Applications and Recordkeeping Requirements*, *Final Rule*, 86

3.2 The FDA didn't mislead manufacturers about the need to compare e-liquids with and without flavoring.

Electric Clouds and Cloud 9 also argue that the FDA misled them about the need to compare flavored and unflavored e-liquids. But the FDA repeatedly explained that manufacturers would need to present comparative data on the impact of flavors.

3.2.1 The Tobacco Control Act should have flagged the need for comparative evidence.

The Tobacco Control Act itself would have informed manufacturers that they needed to compare flavored e-liquids with other e-liquids. *See Abhe & Swoboda, Inc. v. Chao*, 508 F.3d 1052, 1060–61 (D.C. Cir. 2007) (stating that the underlying statute provided fair notice of regulatory requirements). For example, the Act requires manufacturers to show whether the new e-liquid "presents *less risk* than other tobacco products."

Fed. Reg. 55,300 (Oct. 5, 2021). But the final rule came after the application deadline, so the petitioners could not have relied on it.

The final rule was consistent with the FDA's prior statements, saying only that the FDA would consider evidence besides long-term studies:

> While this [Final Rule] does not necessarily require applicants to conduct new studies . . . FDA expects that it could not issue a marketing granted order unless an application contains data from a variety of sources, including both clinical and nonclinical investigations that give FDA comprehensive information about the product's likely health effects.

Id. at 55,387. With this language, the FDA warned that "information from nonclinical studies alone [was] generally not sufficient" for approval. *Id.*

21 U.S.C. § 387j(b)(1)(A) (emphasis added). To evaluate that showing, the FDA must consider "the *increased or decreased likelihood* that existing users of tobacco will stop using such products." 21 U.S.C. § 387j(c)(4)(A) (emphasis added).

Given the statutory language, five federal appellate courts have concluded that the Act supplied adequate notice of the need to compare flavored and unflavored e-liquids. *Magellan Tech., Inc. v. FDA*, 70 F.4th 622, 632 (2d Cir. 2023); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 542–43, 543 n.12 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 427–28 (4th Cir. 2022); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 670–71 (9th Cir. 2023); *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 23 (D.C. Cir. 2022).[6] For example, the Second and Fourth Circuits addressed similar challenges based on the FDA's guidance. In these cases, the courts rejected the challenges, reasoning in part that the Tobacco Control Act "explicitly contemplates that FDA must embark on a comparative inquiry." *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 427 (4th Cir. 2022); *see Magellan Tech., Inc. v. FDA*, 70 F.4th 622, 632 (2d Cir. 2023) (following the Fourth Circuit's analysis involving the Act).

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[6] Only one circuit court has found inadequate notice of the FDA's scientific requirements. *Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 22–42 (5th Cir. 2024) (en banc). But that court did not discuss notice from the statute itself. *See id.*

This reasoning is persuasive. The Tobacco Control Act uses clear comparative language and should have expressly alerted manufacturers to the need to compare e-liquids based on flavoring.

3.2.2 The FDA flagged the need for comparative evidence.

Before the application process unfolded, the FDA had told manufacturers that they would need to compare products within the same category. For example, the 2019 Guidance recommended comparisons to "other . . . tobacco products *within the same product category*." ER138 (emphasis added). And in the proposed rule, the FDA encouraged manufacturers to "compare the health risks of [their] products to both products within *the same category and subcategory*, as well as [other] products." 84 Fed. Reg. 50,566, 50,600 (Sept. 25, 2019) (emphasis added).

Electric Clouds and Cloud 9 argue that the term *category* was too vague. But the FDA had repeatedly explained the youthful appeal of flavoring. For example, the 2019 Guidance stressed the importance of "scientific reviews of flavors" because of "the potential impact of flavors on . . . appeal to youth and young adults." ER155. Given the potential effect on youthful consumers, the 2019 Guidance urged applicants to compare the risks from new products with the risks from "other tobacco products." ER156.

The FDA repeated these recommendations in guidance published in 2020. ER45. There the FDA again interpreted the data to "show that flavors are a strong driver for youth use." ER65.

The public meetings contained similar admonitions. In these meetings, the FDA encouraged manufacturers to show how

- "appeal of a specific product might be generalized to other products within the same brand family, or to similar products of other brands" and
- "consumers perceive the product and its flavor, as well as [the flavor's] impact on intention to use the product, as well as actual use."

Transcript, Tobacco Product Application Review Public Meeting at 123–24 (Oct. 23, 2018).

The FDA thus repeatedly notified manufacturers of the need to compare the risks of e-liquids with and without flavoring. Without these comparisons, the FDA explained that it couldn't adequately assess the increased risk of attracting children from the presence of flavoring. Given these explanations, the FDA didn't mislead Electric Clouds and Cloud 9; they had adequate notice of the need to compare their flavored e-liquids with unflavored e-liquids. *See Prohibition Juice Co. v. FDA*, 45 F.4th 8, 23 (D.C. Cir. 2023) ("Petitioners' own unflavored or tobacco-flavored e-liquids were an obvious, otherwise-similar comparator against which to gauge whether the added risk of their flavored e-liquids are overcome by

those products' added benefits to adult smokers."); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 671 (9th Cir. 2023) (same).

4. The FDA's internal documents don't show reliance on a new evidentiary standard.

Electric Clouds and Cloud 9 argue not only that they were misled, but also that the FDA secretly planned to deny any application omitting long-term clinical studies (even if the application contained the equivalent information). For this argument, Electric Clouds and Cloud 9 rely on

- a July 2021 internal memorandum, which the FDA later superseded,
- an August 2021 internal memorandum, which the FDA later rescinded, and
- the review forms attached to each denial letter.

These documents don't suggest a plan to automatically reject applications lacking long-term clinical studies, and the internal memoranda had lapsed before Electric Clouds and Cloud 9 applied.[7]

In July 2021, the FDA internally circulated a memorandum on how to assess applications lacking long-term clinical studies. ER167–68. In the memorandum, an employee suggested that the FDA should deny any

[7] Electric Clouds and Cloud 9 wouldn't have seen these documents until after they had applied. So Electric Clouds and Cloud 9 couldn't have relied on these documents. *See Avail Vapor, LLC v. FDA*, 55 F.4th 409, 424 (4th Cir. 2022) (reasoning that the memoranda were "internal documents unlikely to create reliance interests").

application lacking either a randomized controlled trial or long-term clinical studies. *Id.* The FDA superseded this memorandum a month later, and there's no evidence that the FDA ever applied the earlier memorandum.

Electric Clouds and Cloud 9 also rely on another FDA memorandum from August 2021, which suggested that applications for flavored e-liquids show "that the flavored products have an added benefit relative to that of tobacco-flavored" e-liquids. ER180. But the FDA rescinded this memorandum before accepting applications.

Even if the memoranda hadn't become obsolete, they didn't suggest a plan to require long-term clinical studies. The first memorandum didn't foreclose "reliance on other forms of rigorous evidence," and the second memoranda "expressly required the agency to consider other forms of evidence if sufficiently robust." *Prohibition Juice Co. v. FDA*, 45 F.4th at 22; *Liquid Labs v. LLC v. FDA*, 52 F.4th 533, 541 (3d Cir. 2022) (quoting *Prohibition Juice*, 45 F.4th at 22).

No matter what the memoranda had said, they were superseded or rescinded before the FDA opened the application process. So four federal appellate courts have concluded that the memoranda in July and August 2021 couldn't have supported the existence of an internal plan. *Magellan Tech., Inc. v. FDA*, 70 F.4th 622, 630 (2d Cir. 2023); *Liquid Labs*, 52 F.4th at 540 n.7, 541 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 424

(4th Cir. 2022); *Prohibition Juice Co.*, 45 F.4th at 22. For example, the Fourth Circuit explained that "these internal documents were just that: internal." *Avail Vapor*, 55 F.4th at 424.

We agree with these courts: the memoranda don't reveal a secret plan, and they weren't even in effect when Electric Clouds and Cloud 9 applied.

Electric Clouds and Cloud 9 rely not only on the internal memoranda, but also on the FDA's review forms. These forms tell the reviewer to consider not only long-term clinical studies, but also other evidence. Reviewers had to note "whether the [applications] contain evidence from a randomized controlled trial, longitudinal cohort study, *and/or other evidence*." ER20, 333 (emphasis added). So the review forms didn't suggest a secret plan to nix any application omitting a long-term clinical study.

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The FDA's documents don't show a secret change in position after the FDA's issuance of informal guidance to manufacturers because

- the FDA superseded the July 2021 memorandum,
- the FDA rescinded the August 2021 memorandum, and
- the review forms showed the opportunity for manufacturers to rely on evidence besides long-term clinical studies.

5. The FDA didn't act arbitrarily and capriciously by finding insufficient scientific evidence for approval.

Electric Clouds and Cloud 9 also argue that the denials were arbitrary and capricious based on the administrative record. *See* 5 U.S.C. § 706(2)(A) (arbitrary-and-capricious standard). We disagree.

Congress designated the FDA as the agency with scientific expertise. Family Smoking Prevention and Tobacco Control Act, Pub. L. 111-31, § 2(44)–(45), § 3(1), (7), 123 Stat. 1776, 1780, 1782 (2009). So we conduct a "narrow" review and can't substitute our judgment for the FDA's. *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

In our view, the denials weren't arbitrary and capricious. The FDA considered the evidence and acted reasonably in concluding that the applications didn't merit approval under the statutory standard.

Under that standard, Electric Clouds and Cloud 9 needed to show that the benefit to adult smokers would outweigh the risk of attracting children to tobacco. 21 U.S.C. § 387j(c)(4)(A)–(B). In trying to satisfy this standard, Electric Clouds and Cloud 9 submitted two kinds of evidence:

1. Literature reviews summarizing existing scientific studies and
2. surveys of current customers.

The FDA acted reasonably when it regarded the literature reviews as insufficient for approval. The literature reviews acknowledged

- the need for more long-term studies comparing the harms from e-cigarettes and traditional cigarettes and

- the presence of mixed results involving the impact of e-liquids on young individuals' use of cigarettes.[8]

And in the literature reviews submitted by Electric Clouds and Cloud 9, there was no discussion about the impact of flavoring on underage use. *See* ER278–84. So the FDA had no evidence to compare the risks of

- flavored e-liquids and

- unflavored or tobacco-flavored e-liquids.

When faced with similar literature reviews, six federal appellate courts have concluded that the FDA didn't act arbitrarily and capriciously by rejecting applications based on insufficient evidence arising from the

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[8] The literature reviews stated:

> The evolving nature of [electronic nicotine delivery systems] presents challenges for the gathering of recent relevant studies of current methods of use. Current studies find that [electronic nicotine delivery systems] are much less harmful to the user than traditional combustible cigarettes, but more long term studies are needed.
>
> * * * *
>
> Some studies have found that for youth and young adults, [electronic nicotine delivery systems] may increase the use of ever using combustible cigarettes; however, other studies found that the reverse is true—that e-cigarette use in youth is limited primarily to individuals who already smoke combustible cigarettes.

ER207.

presence of mixed results or the absence of studies addressing the impact of flavors on youth. *Magellan Tech., Inc. v. FDA*, 70 F.4th 622, 629 (2d Cir. 2023); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 541 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 420–21 (4th Cir. 2022); *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 506 (6th Cir. 2022); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 672–73 (9th Cir. 2022); *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 21–22 (D.C. Cir. 2022).[9]

For example, the D.C. Circuit said that a literature review was "insufficiently rigorous" because of the dearth of "evidence from well-designed studies to determine whether e-cigarette flavors aid in smoking cessation." *Prohibition Juice Co.*, 45 F.4th at 21 (quoting the petitioners' literature review). Similarly, the Third Circuit concluded that the FDA had acted properly in denying an application based on uncertainty in the literature on the value of flavors in helping smokers to quit. *Liquid Labs*, 52 F.4th at 541. This reasoning is persuasive here because Electric Clouds and Cloud 9 submitted literature reviews with equally mixed results.

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[9] The Fifth Circuit disagreed, concluding that the agency should have credited the tobacco manufacturers' literature review. *Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 33–34 (5th Cir. 2024) (en banc). But the Fifth Circuit did not discuss the mixed nature of the literature reviews. *Cf. id.*, slip op. at 68, 75 n.12 (en banc) (Haynes, J., dissenting) (noting that the majority didn't address statements in the literature reviews that there was "not enough evidence . . . to determine whether e-cigarette flavors aid in smoking cessation" (quoting the petitioners' literature reviews)).

Electric Clouds and Cloud 9 also presented surveys, but the FDA identified four defects:

1. The surveys hadn't compared flavored and unflavored e-cigarettes.

2. The surveys had captured only a single point in time, so they couldn't help to assess product switching or cigarette reduction from the "use of these [flavored] products over time." ER326.

3. The customer surveys had been online and voluntary, which restricted participation to existing customers.

4. One survey had included only 314 participants, and another survey had included only 30 participants.

We're not the first court to address similar survey results: Six federal appellate courts have already concluded that similar surveys weren't rigorous enough to support approval. *Magellan Tech., Inc. v. FDA*, 70 F.4th 622, 628 (2d Cir. 2023); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 541 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 421, 425 (4th Cir. 2022); *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 506 (6th Cir. 2021); *Gripum, LLC v. FDA*, 47 F.4th 553, 557 (7th Cir. 2022); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 673 (9th Cir. 2023).

For example, the Ninth Circuit considered customer surveys measuring a single point in time. *Lotus Vaping Techs.*, 75 F.4th at 666. Measurement of a single point in time posed a problem, the Ninth Circuit explained, because the surveys hadn't enabled "reliable evaluation of behavior change over time." *Id.* at 673 (quoting the FDA's denial order).

The Third Circuit also considered a survey that hadn't compared all the manufacturer's flavored e-cigarettes with unflavored e-cigarettes, concluding that the results hadn't shown "a benefit to flavoring" or provided "meaningful information regarding actual switching or reduction." *Liquid Labs*, 52 F.4th at 541. The same is true of the customer surveys submitted by Electric Clouds and Cloud 9.

The FDA also rejected the literature reviews and surveys because they didn't relate to the e-liquids made by Electric Clouds and Cloud 9. In response, Electric Clouds and Cloud 9 argue that the FDA

- used a double-standard by relying on a scientific consensus to regard flavors as dangerous to children,
- failed to consider whether these dangers had applied to the e-liquids that Electric Clouds and Cloud 9 were making, and
- relied on a consensus involving closed systems even though Electric Clouds and Cloud 9 used open systems.

We reject these arguments and conclude that the FDA acted reasonably in relying on a scientific consensus. The Tobacco Control Act requires the FDA to consider all available information. *See* 21 U.S.C. § 387j(c)(2)(A); *see also Avail Vapor, LLC v. FDA*, 55 F.4th 409, 419 (4th Cir. 2022) (recognizing the "FDA's broad statutory mandate to determine from the totality of the evidence"). In considering such information, the FDA legitimately found a consensus showing the dangers from flavoring regardless of the type of device. ER31.

The FDA found no such consensus on the value of flavoring on adults trying to quit. *See* ER35 ("Although . . . bridged data from the literature may still be appropriate for many new products, including tobacco-flavored [electronic nicotine delivery systems], robust and direct evidence . . . has been needed when the known risks are high as with all flavored [electronic nicotine delivery systems]."). The difference led the Fourth Circuit to reject a similar challenge:

> Whereas the evidence on the role of flavors in promoting youth use of [electronic nicotine delivery systems] was established as a matter of scientific consensus, there was no comparable showing of the benefits that flavored [electronic nicotine delivery systems] have for adult smokers in promoting switching or cessation. Moreover, evidence showed that tobacco-flavored [electronic nicotine delivery systems] may offer the same type of public health benefits as flavored [electronic nicotine delivery systems], in encouraging adult cigarette smokers to switch to [electronic nicotine delivery systems] and decreasing the use of combustible cigarettes. Such tobacco-flavored products, however, do not pose the same degree of risk of youth uptake as fruit or dessert-flavored products. As such, FDA required [the manufacturer] to provide strong, product-specific evidence demonstrating its products would provide an extra benefit to current smokers over that of other lower-risk products.

Avail Vapor, LLC v. FDA, 55 F.4th 409, 421 (4th Cir. 2022) (cleaned up); *see also Prohibition Juice Co. v. FDA*, 45 F.4th 8, 22 (D.C. Cir. 2022) (rejecting a similar challenge based on the consensus as to the risks from flavored products and inconclusive information as to the benefits).

Electric Clouds and Cloud 9 disagree with the FDA, arguing that the existing information involves systems that were closed rather than open.

But the FDA could reasonably regard the role of flavor as consistent between closed systems and open systems. *See Avail Vapor, LLC*, 55 F.4th at 427 (rejecting a similar challenge based on the FDA's conclusion that the risks of flavoring were consistent between open and closed systems); *Prohibition Juice Co.*, 45 F.4th at 26 (rejecting a similar challenge based on the FDA's assessment that the risks from flavoring were consistent and equally applicable to open and closed systems).

Electric Clouds and Cloud 9 point to a 2021 study, which they characterize as proof that few children use open-system devices. But the administrative record doesn't include this study, and it didn't exist when the FDA decided the applications submitted by Electric Clouds and Cloud 9.[10] *See* note 11, below (discussing our inability to stray beyond the administrative record).

At that time, the FDA could reasonably conclude that children preferred flavored e-liquids regardless of device type. The FDA thus

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[10] Electric Clouds and Cloud 9 also cite an article, which quoted a former FDA commissioner. Petitioners' Opening Br. at 44. When the individual made the quoted statement, he had left the FDA and was serving as a resident fellow at the American Enterprise Institute and as a special partner at a venture capital firm. Nicholas Florko, *Former FDA Commissioner Calls for a Full Ban on Pod-Based E-Cigarettes*, Stat News (Nov. 12, 2019) https://tinyurl.com/mdrjpyhw, quoted in Petitioners' Opening Br. at 44. So his comments didn't represent the FDA's position, and Electric Clouds and Cloud 9 do not point to evidence supporting his statement.

explained that it had learned that "the removal of one flavored product option prompted youth to migrate to another [electronic nicotine delivery system] type that offered the desired flavor options, underscoring the fundamental role of flavor in driving appeal." ER32.

This explanation doesn't suggest that the FDA ignored the distinctions between products. To the contrary, the FDA relied on new evidence showing that children care more about flavors than the devices. *See, e.g.*, ER31–32 (explaining the data showing the consistent role of flavor in youth use of all tobacco products).[11]

The FDA used the new information to carry out the statutory mandate to balance

- the known risks that flavored e-liquids posed to children and
- the potential benefit to adults wanting to quit.

The FDA didn't act arbitrarily or capriciously by regarding flavors as attractive to children even when using open systems. *See Prohibition Juice*

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[11] The petitioners argue that open-system devices are big and clunky, making them unappealing to youth. The Fifth Circuit credited this argument, pointing to photographs of large open-system devices. *Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 12 (5th Cir. 2024) (en banc). In our case, the FDA said that new open-system devices are often small, pointing to pictures submitted by the amici. Brief of Amici Curiae Medical, Public Health, and Community Groups in Support of Respondent at 11. But none of these photographs or pictures are in our record. So we don't rely on them. *See, e.g.*, *Atteberry v. Finch*, 424 F.2d 36, 39 (10th Cir. 1970) (stating that judicial review is limited to evidence in the administrative record).

Co. v. FDA, 45 F.4th 8, 22, 26 (D.C. Cir. 2022) (rejecting the double-standard argument and upholding the FDA's denial of approval to market an open-system e-liquid); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 544–45 (3d Cir. 2022) (upholding the FDA's denial of approval to market an open-system e-liquid because flavors appealed to children regardless of the device type); *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 506, 508 (6th Cir. 2021) (upholding the FDA's determination that generalized evidence included in an open-system e-liquid application could not overcome the clear preference of children for flavored e-cigarettes); *Gripum, LLC v. FDA*, 47 F.4th 553, 559–60 (7th Cir. 2022) (concluding that without product-specific evidence, the manufacturer of an open-system e-liquid hadn't satisfied its burden of proof); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 671 n.14 (9th Cir. 2023) (concluding that the FDA didn't arbitrarily disregard device types because the scientific consensus had shown that children preferred flavored e-liquids).[12]

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[12] In their reply brief, Electric Clouds and Cloud 9 argue that the FDA's studies show that open systems are less popular with youth than tobacco-flavored e-cigarettes. Petitioners' Reply Br. at 19. For this argument, Electric Clouds and Cloud 9 cite a statement by the FDA; but this statement doesn't discuss open systems. *Id.* (citing ER30). To the contrary, the cited page suggests that youthful consumers prefer fruit flavors over tobacco flavors without any mention of the devices being used. ER30 (stating that "66.8% of youth [electronic nicotine delivery system] users aged 13 to 17 reported using fruit, followed by . . . 13.3% for tobacco flavor"). When open systems were incorporated, the FDA

According to Electric Clouds and Cloud 9, the FDA reached different results for similarly situated manufacturers. But Electric Clouds and Cloud 9 present no support for this claim, and we see no evidence of different standards for manufacturers of similar e-liquids. *See Prohibition Juice Co.*, 45 F.4th at 26 (rejecting this argument). To the contrary, the FDA consistently rejected evidence involving literature reviews and surveys:

Circuit Case Affirming FDA Denial	**Manufacturers' Scientific Evidence**
Prohibition Juice Co. v. FDA, 45 F.4th 8, 21–22 (D.C. Cir. 2022)	Online, one-time voluntary studies; mixed literature review.
Magellan Tech., Inc. v. FDA, 70 F.4th 622, 627–29 (2d Cir. 2023)	Focus group of only 24 participants; 2-week online study of 18 existing customers; a study of 15 participants; an online survey of 400 smokers and over 1,000 non-smokers; insufficient literature review.
Liquid Labs, LLC v. FDA, 52 F.4th 533, 537, 541 (3d Cir. 2022)	Study lacking a comparison between flavored e-liquids with unflavored e-liquids; survey that failed to discuss switching or reduction; mixed literature review.
Avail Vapor, LLC *v. FDA*, 55 F.4th 409, 417, 420 (4th Cir. 2022)	Online study for 2 weeks; focus group of 39 participants; national attitude survey; study of 18 participants; mixed literature review.
Breeze Smoke, LLC v. FDA, 18 F.4th 499, 506 (6th Cir. 2021)	Online survey of existing retail-store customers; mixed literature review.
Gripum, LLC v. FDA, 47 F.4th 553, 557 (7th Cir. 2022)	Consumer surveys; insufficient literature review (no "bridge").
Lotus Vaping Techs., LLC v. FDA, 73 F.4th 657, 666, 672–73 (9th Cir. 2023)	Survey of existing customers; survey of thousands of participants; insufficient literature review (no "bridge").

found that 76% of high-school and middle-school students preferred flavors for the open systems. ER31, 348.

The FDA thus did not act arbitrarily and capriciously by regarding the scientific evidence as inadequate to approve the petitioners' applications.

6. Even if the FDA should have reviewed the marketing plans, the error would have been harmless.

Electric Clouds and Cloud 9 also argue that the FDA erred by failing to review their marketing plans. But even if an error had taken place, it would have been harmless because the FDA would have regarded the marketing plans as deficient for reasons already stated.

The Tobacco Control Act incorporates the harmlessness standard from the Administrative Procedure Act. *See* 21 U.S.C. § 387*l*(b) (instructing courts to apply 5 U.S.C. § 706); *see also All Indian Pueblo Council v. United States*, 975 F.2d 1437, 1443 (10th Cir. 1992) (considering harmlessness in the review of agency decisions). Under this standard, the petitioners must show that the FDA's alleged error was harmful. *See St. Anthony Hosp. v. U.S. Dep't of Health & Hum. Servs.*, 309 F.3d 680, 691 (10th Cir. 2002).

Generally, we cannot affirm an agency's decision on grounds that the agency didn't supply. *SEC v. Chenery Corp.*, 332 U.S. 194, 196 (1947). But an exception exists if the error clearly didn't affect the outcome. *See Allen v. Barnhart*, 357 F.3d 1140, 1145 (10th Cir. 2004) (explaining that we apply the harmless-error standard when "no reasonable administrative

factfinder, following the correct analysis, could have resolved the factual matter in any other way").

This exception applies here. The FDA had warned before that similar marketing plans had proven ineffective. So the petitioners' marketing plans couldn't have overcome the other deficiencies in the applications.

These marketing plans focused on restrictions designed to prevent children from getting the e-liquids. Cloud 9's plan consisted of a single paragraph, promising only warnings and a 21+ age-verification system.[13] ER365. Electric Clouds submitted a more detailed plan, which proposed requirements for identifying customers at retail stores, age verification for online sales, child-resistant packaging, and prohibitions on marketing or packaging that targeted minors.

But the FDA had already rejected these types of restrictions. For example, in the 2020 Guidance, the FDA had addressed similar measures, which included

- technology to verify the customer's age when making online purchases,

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[13] In its opening brief, Cloud 9 cited a more detailed marketing plan. But this marketing plan was not part of the administrative record or included with Cloud 9's application. And Cloud 9 concedes that the more detailed marketing plan isn't material to the issue. Petitioners' Reply Br. at 24 n.6, 24–25. So we need not consider the more detailed marketing plan cited in Cloud 9's opening brief. *See* note 11, above (stating that we consider evidence only if it was in the administrative record).

- enhanced monitoring to ensure that retailers complied with the age requirements,
- contractual penalties for retailers that sell tobacco to minors, and
- restrictions on the amount of e-liquids that customers can buy within a given time-period.

The FDA concluded that these measures hadn't stopped children from using e-cigarettes: "The reality is that youth have continued access to these products in the face of legal prohibitions *and even after voluntary actions by some manufacturers*." ER66 (emphasis added). The FDA thus warned manufacturers that marketing plans wouldn't suffice if they focused only on "how the product was sold." *Id.*

Electric Clouds and Cloud 9 don't assert that their proposed marketing restrictions differ from the marketing restrictions that the FDA had already found ineffective. Because Electric Clouds and Cloud 9 had already failed to present adequate scientific evidence, their marketing plans couldn't have salvaged their applications.

In similar circumstances, six federal appellate courts have found similar errors harmless for marketing plans like those submitted by Electric Clouds and Cloud 9. *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 16, 24–25 (D.C. Cir. 2022); *Magellan Tech., Inc. v. FDA*, 70 F.4th 662, 630–31 (2d Cir. 2023); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 543–44 (3d Cir. 2022); *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 417, 425–27 (4th Cir.

2022); *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 508 (6th Cir. 2021); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 666, 674–75 (9th Cir. 2023).

For example, the Ninth Circuit considered a marketing plan that

- relied on age verification and
- required that the product be "strictly marketed and sold to adults in adult-only retailers and through age-verified online websites."

Lotus Vaping Techs., 73 F.4th at 674 (quoting the manufacturer's marketing plan). But the Ninth Circuit concluded that any error would have been harmless because

- those measures "track those that the FDA found were ineffective to counterbalance the risk of youth use" and
- the manufacturer had not "otherwise argue[d] that any of marketing tactics were novel."

Id. at 675.

The Fourth Circuit similarly addressed harmlessness when the marketing plans "focused solely on age verification and avoiding marketing that would make its products attractive to youth." *Avail Vapor, LLC v. FDA*, 55 F.4th 409, 426 (4th Cir. 2022). The court regarded these measures as "insufficient," but suggested that the manufacturer could have supported its application with "novel access restrictions beyond those that the FDA previously determined were not working." *Id.*

The Third Circuit agreed that "marketing plans would not change the result" when the manufacturers had "not explained how the [proposed] approaches . . . differ from ones previously found insufficient or how [the proposed] marketing plans would have cured other noted deficiencies in its applications." *Liquid Labs, LCC v. FDA*, 52 F.4th 533, 544 (3d Cir. 2022).

We are persuaded by the reasoning of the Third, Fourth, and Ninth Circuits. Electric Clouds and Cloud 9 presented marketing plans focused on age verification; these plans involved only the kinds of measures that the FDA had already rejected.

Two circuits have concluded that similar errors weren't harmless, basing these conclusions on two different reasons. The Fifth Circuit has rejected harmlessness based on its interpretation of *Calcutt v. FDIC*, 598 U.S. 623 (2023). *Wages & White Lion Invs., LLC v. FDA*, 90 F.4th 357, slip op. at 3, 49–52 (5th Cir. 2024) (en banc). The Eleventh Circuit has rejected harmlessness because the marketing plans included novel marketing restrictions that the FDA hadn't previously discussed. *Bidi Vapor v. FDA*, 47 F.4th 1191, 1205 (11th Cir. 2022). Neither of these rationales apply here.

Calcutt does not bar consideration of harmlessness. To the contrary, *Calcutt* prohibits courts from basing harmlessness on a rationale that the agency didn't invoke. *Calcutt*, 598 U.S. at 624, 628. This prohibition doesn't apply here because we're basing harmlessness on the FDA's

existing approach to marketing restrictions, not a reason that we've detected on our own. And *Calcutt* acknowledged that the court may not need to remand when the agency's prior actions make the outcome clear. *Id.* at 629–30.

The Eleventh Circuit rejected harmlessness because there the manufacturers had used marketing plans unlike those that the FDA had addressed. *Bidi Vapor*, 47 F.4th at 1205 (discussing proposed "Trace/Verify technology" and an authentication system for preventing counterfeit products); *see also Avail Vapor, LLC v. FDA*, 55 F.4th 409, 417–18, 427 (4th Cir. 2022) (distinguishing the novel measures in *Bidi Vapor* from "garden variety restrictions" like age-verification services); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th at 675 (distinguishing age verification and restrictions on retailers from the novel measures addressed in *Bidi Vapor*).

Electric Clouds and Cloud 9 don't contend that their marketing plans contained any novel measures, but argue that the FDA

- ignored the importance of device types and
- could have required extra measures to overcome deficiencies in the proposed plans.

These arguments are unconvincing for two reasons.

First, Electric Cloud and Cloud 9 say that because they manufacture e-liquids for open-system devices, the FDA shouldn't have assumed that

age restrictions would be ineffective. But the FDA warned manufacturers that flavored e-liquids had become increasingly popular among children regardless of device type. *See* pp. 25–27, above. Given that warning, other circuits have rejected arguments about prejudice based on the FDA's failure to review similar marketing plans for open-system e-liquids. *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 26 (D.C. Cir. 2022); *Liquid Labs, LLC v. FDA*, 52 F.4th 533, 545 (3d Cir. 2022); *Lotus Vaping Techs., LLC v. FDA*, 73 F.4th 657, 671 n.14 (9th Cir. 2023). That reasoning is persuasive here.

Second, Electric Clouds and Cloud 9 agree that the FDA should have considered the possibility of imposing measures to reduce the risk to children. But the manufacturers bore the burden to show that their e-liquids weren't too risky for children. *See* 21 U.S.C. § 387j(c)(2)(A) (stating that the FDA "shall deny" applications that fail to make the required showing). Electric Clouds and Cloud 9 failed to carry that burden.

We thus agree with other circuits that found no prejudice when the FDA had failed to review similar marketing plans:

Circuit Case Affirming FDA Denial	**Manufacturers' Proposed Marketing Plans**
Prohibition Juice Co. v. FDA, 45 F.4th 8, 15–16 (D.C. Cir. 2022)	Age-verification measures on websites; marketing and packaging not directed and minors.
Magellan Tech., Inc. v. FDA, 70 F.4th 662, 631 (2d Cir. 2023)	Age-verification measures.
Liquid Labs, LLC v. FDA, 52 F.4th 533, 544 (3d Cir. 2022)	Age-verification measures; mystery-shopper program; marketing not directed at minors.
Avail Vapor, LLC *v. FDA*, 55 F.4th 409, 417–18 (4th Cir. 2022)	Non-descriptive names; age verification in stores; program to bind distributors.
Lotus Vaping Techs., *LLC v. FDA*, 73 F.4th 657, 666 (9th Cir. 2023)	Age verification in stores; age-verification measures on websites; individual purchase limits for online sales; age-gated industry trade shows; program to bind retailers.

7. Conclusion

The FDA didn't mislead Electric Clouds or Cloud 9 about what to put in their applications, and the FDA could reasonably regard the literature reviews and customer surveys as inadequate.

Along with the literature reviews and customer surveys, Electric Clouds and Cloud 9 submitted marketing plans. Though the FDA didn't review these marketing plans, any possible error would have been harmless. These plans relied on youth-prevention measures that the FDA had previously rejected as ineffective.

We thus deny the petitions for judicial review of the denial of the applications to market flavored e-liquids.