United States Court of Appeals for the Fifth Circuit

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Fifth Circuit
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Lyle W. Cayce
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No. 24-60060

SHENZHEN YOUME INFORMATION TECHNOLOGY COMPANY, LIMITED; FRENDZ TRADING, INCORPORATED, *doing business as* VAPE-E-WAY,

Petitioners,

versus

FOOD & DRUG ADMINISTRATION,

Respondent.

Appeal from the Food & Drug Administration
Agency Nos. PM0000881.PD1,
PM0000885.PD1

Before WIENER, STEWART, and SOUTHWICK, *Circuit Judges*.

LESLIE H. SOUTHWICK, *Circuit Judge*:

Shenzhen Youme petitions for review of the Food and Drug Administration's denial of its application for approval of its electronic nicotine delivery system. It contends the denial was arbitrary and capricious. We DENY the petition for review.

FACTUAL AND ADMINISTRATIVE BACKGROUND

The Family Smoking Prevention and Tobacco Control Act of 2009 ("TCA") gives the Food and Drug Administration ("FDA") regulatory

authority over "cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco and to any other tobacco products that the Secretary by regulation deems to be subject to this subchapter." 21 U.S.C. § 387a(b). In 2016, FDA issued a rule that "deem[ed] all other products meeting the definition of 'tobacco product' under [21 U.S.C. §321 (rr)]" to be subject to FDA's authority. Deeming Tobacco Products to Be Subject to the Federal Food, Drug, and Cosmetic Act ("The Deeming Rule"), 81 Fed. Reg. 28974, 29056 (May 10, 2016) (codified at 21 C.F.R. pts. 1100, 1140, 1143); 21 C.F.R. § 1100.1. "Tobacco product" includes "any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product." 21 U.S.C. § 321(rr)(1) (2021).[1] Electronic nicotine delivery systems ("ENDS"), like the products that are the subject of this petition, are included in that definition since they are intended for use with nicotine.

Under the TCA, "new tobacco product[s]," or products not "marketed in the United States as of February 15, 2007," must obtain marketing authorization from FDA through one of three options: (1) a premarket tobacco product application ("PMTA"); (2) the substantial equivalence pathway; or (3) a substantial equivalence exemption report. 21 U.S.C. § 387j(a)(1)(A), (a)(2)(A)–(B), (a)(2)–(3); § 387e(j)(3)(A). Only the PMTA pathway is relevant here.

The PMTA pathway requires the applicant to show that the marketing of its tobacco product is "appropriate for the protection of the public health." § 387j(c)(2)(A). Whether a product is appropriate for the protection of the public health is "determined with respect to the risks and

[1] Congress later expanded the definition of "tobacco product" to include not only products containing nicotine derived from the tobacco plant, but also products "containing nicotine from any source." 21 U.S.C. § 321(rr)(1).

benefits to the population as a whole, including users and nonusers of the tobacco product." § 387j(c)(4). This determination considers both "(A) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and (B) the increased or decreased likelihood that those who do not use tobacco products will start using such products." § 387j(c)(4)(A)–(B).

ENDS products, as new tobacco products, may obtain marketing authorization through this PMTA pathway. FDA finalized guidance documents on PMTAs for ENDS products in June 2019. U.S. Food & Drug Admin., Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (Revised): Guidance for Industry ("PMTA Guidance") (Mar. 2023).[2] The "guidance is intended to assist persons submitting premarket tobacco product applications for [ENDS products]." *Id.* at 1. The Guidance does "not establish legally enforceable responsibilities" but serves to explain "the Agency's current thinking on a topic and should be viewed only as recommendations." *Id.* at 2. FDA bases its decisions not on the Guidance, but "on the obligations that arise from the [Food, Drug, and Cosmetic] Act and its implementing regulations." *Id.* at 1.

Once FDA deemed ENDS products subject to the TCA, manufacturers of such products were required to obtain FDA authorization before marketing its products. *Prohibition Juice Co. v. FDA*, 45 F.4th 8, 13–14 (D.C. Cir. 2022). Products already on the market without marketing approval were "deemed to be adulterated," making their continued sale illegal. 21 U.S.C. § 387b(6)(A). As a matter of enforcement discretion,

[2] https://tinyurl.com/48783rtz. The link is to an updated March 2023 version of the Guidance. Revisions since 2019 did not change the text relevant to the issues here.

however, FDA announced it would not immediately enforce the statutory requirement for authorization of products already on the market. The Deeming Rule, 81 Fed. Reg. at 28,977–78. FDA initially announced a two-to-three-year period of enforcement discretion for products already on the market while manufacturers prepared, and FDA reviewed, marketing applications. *Id.* at 28,978. In 2017, FDA extended that period until August 2022 for deemed ENDS products on the market as of August 2016. U.S. Food & Drug Admin., Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule: Guidance for Industry (Revised), 3 (2017). In 2019, however, a United States district court in Maryland vacated the guidance extending the submission deadline and ordered FDA to accelerate the PMTA submission deadline. *American Acad. of Pediatrics v. FDA*, 399 F. Supp. 3d 479, 487 (D. Md. 2019). The court permitted products with timely-filed PMTAs to remain on the market without enforcement action for a period of up to one year after the PMTA submission deadline. *Id.* The court directed FDA to require applications for PMTAs by September 9, 2020.

Petitioner Shenzhen Youme Information Technology Co., Ltd. ("Youme") is a Chinese manufacturer of ENDS products. ENDS use electricity supplied by a battery to a metallic heating element, or coil, to heat a solution containing nicotine, flavorings, and other ingredients ("e-liquid") into an aerosol that the user inhales. No ENDS products were commercially marketed in the United States as of February 15, 2007, so Youme must submit PMTAs to obtain marketing authorization from FDA for its ENDS products. In 2016, Youme launched its Suorin brand of ENDS products in the United States, including the open-system Suorin Air device that is the subject of this petition. The Suorin Air device is a refillable e-cigarette sold without any e-liquid. Instead, consumers purchase bottled e-liquid

separately and use it to fill the open-system device. These bottled e-liquids are available in a variety of nicotine strengths, ranging from zero nicotine to concentrations of up to 50 mg/mL (*i.e.,* five percent).

In August 2020, Youme submitted bundled PMTAs for its open-system Suorin Air device and the compatible empty replacement cartridge. Youme asserted its applications contained "robust studies and information" and that "[t]he information presented . . . shows a very detailed and well supported case for the population as a whole, and with respect to the risks and benefits of both users and nonusers, showing that e-cigarettes are" appropriate for the protection of the public health.

In July 2022, FDA completed its preliminary assessment of Youme's application materials, citing numerous deficiencies. In March 2023, FDA issued a deficiency letter to Youme that described deficiencies about which FDA sought additional information. FDA asked Youme to submit all responsive information by June 8, 2023, and stated it did not "intend to issue additional [d]eficiency letters" or "intend to provide an extension of time for response to deficiency letters." In May 2023, Youme requested an extension to submit additional responsive information that could not be adequately prepared within the 90-day response period. In early June 2023, while the extension request was still pending, Youme sent timely responses to some, but not all, of the deficiencies identified in FDA's deficiency letter.

In November 2023, FDA denied Youme's extension request because it did "not demonstrate that the extension of time is reasonable as the types of information needed to support the applications have been previously known and may have been provided with the PMTAs or as an amendment prior to the start of scientific review." FDA also stated it had "initiated scientific review based on content received by the date listed in [Youme's] Deficiency Letter."

In January 2024, FDA issued a denial order and its Technical Project Lead ("TPL") memorandum. The memorandum summarized FDA's findings, concluding that Youme did not demonstrate its products would be appropriate for the protection of the public health. FDA concluded that "the significant gaps in applicant data do not allow FDA to evaluate the risk-benefit profile of the new products" and "there remains a reasonable possibility that the risks of the new products outweigh its limited benefits to public health."

Youme petitioned this court for review.

JURISDICTION

Under the TCA, "any person adversely affected" by a regulation or a marketing denial "may file a petition for judicial review of such regulation or denial with the United States Court of Appeals for the District of Columbia or for the circuit in which such person resides or has their principal place of business." 21 U.S.C. § 387*l*(a)(1). FDA contends that because Youme is a Chinese corporation with no connection to this circuit, it was required to file its petition in the D.C. Circuit. We have previously held that venue in this circuit is proper if one of the petitioners has its principal place of business in this circuit. *R.J. Reynolds Vapor Co. v. FDA*, 65 F.4th 182, 188 (5th Cir. 2023), *aff'd*, 145 S. Ct. 1984 (2025). The Supreme Court recently affirmed that decision, holding that retailers who sell the product subject to a marketing denial are "adversely affected." *FDA v. R.J. Reynolds Vapor Co.*, 145 S. Ct. 1984, 1993 (2025).

Here, Petitioner Vape-E-Way has its principal place of business in Houston, Texas. Vape-E-Way has, and continues to, carry the products for which the marketing approval was sought and is adversely affected by the denial. Venue is proper in this circuit.

DISCUSSION

Youme contends FDA acted arbitrarily and capriciously by failing to weigh the public health risks and benefits of Youme's products and by limiting applicants to a single deficiency letter. We address each argument in that order, first explaining the relevant standards.

The Administrative Procedure Act directs courts to "hold unlawful and set aside agency action" that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). The agency must have "acted within a zone of reasonableness" meaning it "reasonably considered the relevant issues and reasonably explained the decision." *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021). Our scope of "review 'is narrow,' and [we] must exercise appropriate deference to agency decisionmaking and not substitute [our] own judgment for that of the agency." *FDA v. Wages & White Lion Invs., L.L.C.*, 145 S. Ct. 898, 917 (2025) (quoting *Motor Vehicle Mfrs. Ass'n. of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983)). We set aside agency action "that fails to account for 'relevant factors' or evinces 'a clear error of judgment.'" *BNSF Ry. Co. v. Fed. R.R. Admin.*, 62 F.4th 905, 910 (5th Cir. 2023) (quoting *University of Tex. M.D. Anderson Cancer Ctr. v. U.S. Dep't of Health & Hum. Servs.*, 985 F.3d 472, 475 (5th Cir. 2021)). The "agency's action must be upheld, if at all, on the basis articulated by the agency itself, not reasons developed *post hoc*." *Id.* at 910–11 (quotation marks omitted) (quoting *Texas v. United States*, 40 F.4th 205, 226 (5th Cir.2022)).

The TCA requires FDA to deny a marketing application if the application and evidence do not affirmatively demonstrate that marketing the product would be appropriate for the protection of the public health. 21 U.S.C. § 387j(c)(2)(A). FDA makes this determination "with respect to the risks and benefits to the population as a whole, including users and nonusers

of the tobacco product," considering both "the increased or decreased likelihood that existing users of tobacco products will stop using such products[,] and the increased or decreased likelihood that those who do not use tobacco products will start using such products." § 387j(c)(4)(A)–(B). The burden is on the applicant to make the appropriate showing by including all relevant information necessary to make that determination in its initial application. § 387j(b)(1)(A)–(G). Based on the application, FDA makes a "single predictive judgment whether a given tobacco product, on balance, will benefit the public as a whole." *Fontem US, LLC v. FDA*, 82 F.4th 1207, 1215 (D.C. Cir. 2023). When the application lacks evidence to support a showing that its product "will benefit the public as a whole," the application must be denied. *Id.*; § 387j(c)(2)(A).

I. FDA's Failure to Weigh

Youme contends that FDA failed to weigh the overall risks and benefits of its product, rendering its denial arbitrary and capricious. In particular, Youme asserts that FDA did not consider Youme's "extensive evidence of the potential public health benefits of its products." Instead, FDA found gaps in data caused by the imposition of new evidentiary requirements "after the fact" and then refused to allow Youme to satisfy those requirements.[3] They contend that, like in *Fontem*, FDA in this case failed to consider the evidence of potential benefits of the devices. *See Fontem*, 82 F.4th 1207. We examine that authority.

Fontem submitted applications for both flavored and unflavored products. *Id.* at 1211. The court approved the denial of the marketing

[3] Youme also contends that data submitted two weeks after the submission deadline satisfied the alleged new requirement, but that FDA acted arbitrarily and capriciously by refusing to weigh those benefits. We view this to be an argument that FDA's deadline is arbitrary and capricious, so we address this argument in Section II of the opinion.

application for the flavored products, finding FDA engaged in the proper weighing of benefits and risks by "focus[ing] on the question central to the public health inquiry — whether Fontem had shown the 'increased or decreased likelihood that existing users of tobacco products will stop using such products' outweighs the 'increased or decreased likelihood that those who do not use tobacco products will start using such products.'" *Id.* at 1217 (quoting § 387j(c)(4)(A)–(B)).

As to the petitioner's unflavored products, the court found that none of the deficiencies supported "FDA's finding that Fontem's unflavored products were not appropriate for the protection of public health." *Id.* at 1219. The court reasoned that "nowhere in the denial order did the FDA address potential benefits of Fontem's products" or "consider the possibility that existing users of combustible tobacco products such as cigarettes would reap health benefits by transitioning to Fontem's vaping products." *Id.* The court therefore found that FDA "failed to analyze the tradeoffs necessary to make a public health finding" and failed to "explain how the specific deficiencies relate to its overall conclusion that Fontem failed to demonstrate its unflavored products were appropriate for the protection of public health." *Id.* at 1217. "Instead, [FDA] identified highly granular deficiencies" such as "names, accreditation, and specifications of certain laboratories used by Fontem," "but failed to evaluate the potential effects of such deficiencies on the public health." *Id.* at 1220, 1222. FDA also failed to explain why the deficiencies "were so serious as to justify a finding that Fontem had not shown its products would be appropriate for the protection of the public health." *Id.* at 1220–21.

Relying on *Fontem*, Youme argues that it presented extensive evidence of the potential public health benefits, but FDA did not "give any indication that it attempted to properly weigh the applications' substantial evidence of public health benefits against the potential risks of Youme's products."

In this record, though, there is evidence that FDA expressly considered the potential benefits. A few examples: "ENDS carry the potential to positively impact population health when used as an alternative to combusted tobacco," "abuse liability of the new products is lower than that of a [combustible cigarette] when used with [certain nicotine concentrations]," and "[s]hould adults who currently use [combustible cigarettes] switch exclusively to use of the new products, they are likely to maintain similar or slightly lower nicotine dependence levels."

FDA evaluated that evidence, found it insufficient, and explained how the specific deficiencies related to its overall conclusion that Youme failed to show its products were appropriate for the protection of the public health. It explained that high nicotine content e-liquids are prevalent on the market and Youme failed to provide sufficient data to evaluate the risks associated with use of the new products with those high concentration liquids. FDA explained that abuse liability "indicates the degree to which users of the new products are likely to use and develop an addiction to the product and face the health risks posed by long term product use." FDA also explained that "high abuse liability may increase the likelihood that tobacco users and nonusers, including youth, who try the new product for the first time will continue using it." FDA asserts that Youme's evidence of potential public-health benefits depends on existing smokers transitioning away from combustible cigarettes. FDA found "only a moderate chance that some current [combustible-cigarette] users would switch completely to the new products."

Here, unlike in *Fontem,* FDA provided meaningful explanations of the importance of determining a product's abuse liability and the relevance of that information to the statutory public-health inquiry. FDA weighed the abuse-liability risk with the "evidence that Youme's products would help existing tobacco users quit or substantially reduce their use of combustible

cigarettes." FDA determined that "additional information on abuse liability, or on the likelihood that consumers would follow" product recommendations was necessary to prove the products were appropriate for the protection of the public health. The decision was reasonable and reasonably explained.

The same is true for Youme's argument that FDA changed its position, or imposed a new evidentiary requirement, when it stated that Youme's "own key study ... appears to show that subjective effects experienced from use of the new products *may reinforce* adults who smoke" with "only a moderate chance that some current [combustible-cigarette] users would switch completely to the new product." This is not a new requirement. The TCA requires FDA to consider "the increased or decreased likelihood that existing users of tobacco products will stop using such products." 21 U.S.C. § 387j(c)(4)(A). A product's potential to reinforce nicotine addiction in those who currently use combustible cigarettes is precisely the inquiry FDA is to make to determine whether a product is appropriate for the protection of the public health. FDA used slightly different language but the "distinction amounts to splitting hairs." *See Fontem*, 82 F.4th at 1216. The denial was reasonable and reasonably explained.

Youme also asserts that the gaps in information resulted from new evidentiary requirements FDA imposed "after the fact," with Youme having no opportunity to satisfy those requirements. Specifically, Youme contends FDA shifted its requirements from "testing of the device with a 'reasonable range of available e-liquids' to e-liquids that represent 'the highest and lowest nicotine concentrations' available on the market," thereby moving the regulatory goalposts. Youme contends this change is "exactly the sort of moving of the regulatory goalposts" found to be arbitrary

and capricious in *Wages & White Lion Invs., L.L.C. v. FDA*, 90 F.4th 357 (5th Cir. 2024) (en banc) *vacated*, 145 S. Ct. 898 (2025).

The Supreme Court has since vacated our holding in *Wages & White Lion*. *See Wages & White Lion*, 145 S. Ct. 898. The Court left open whether arguments relying on an agency's change in position applied to nonbinding agency guidance.[4] We assume, without deciding, they do. "Agencies are free to change their existing policies as long as they provide a reasoned explanation for the change." *Encino Motorcars, LLC v. Navarro*, 579 U.S. 211, 221 (2016). The first question is whether the "agency changed existing policy," *i.e.*, effected "a reversal of [its] former views as to the proper course" or "'disavow[ed] prior 'inconsistent' agency action as 'no longer good law.'" *Wages & White Lion*, 145 S. Ct. at 918 (first alteration in original) (first quoting *State Farm*, 463 U.S. at 41; and then quoting *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 517 (2009)). The second question is "[d]id the agency 'display awareness that it *is* changing position' and offer 'good reasons for the new policy.'" *Id.* (quoting *Fox Television Stations*, 556 U.S. at 515).

Youme argues that its testing of e-liquids "seemed to satisfy FDA's recommendation in its PMTA Guidance" that they test with a "reasonable range of available e-liquids." FDA concluded the "'test data lack[ed] sufficient information to demonstrate potential nicotine exposure to users' because 'FDA requires data from e-liquids with the highest and lowest nicotine concentrations, both with the highest VG concentration.'"

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[4] The Supreme Court "assume[d], without deciding, that the change-in-position doctrine applies to an agency's divergence from a position articulated in nonbinding guidance documents." *Wages & White Lion*, 145 S. Ct. at 918 n.5.

The PMTA Guidance recommended that "testing reflect the range of operating conditions . . . and use patterns . . . within which consumers are likely to use your product, and the types of products that consumers are likely to use in conjunction with your products." PMTA GUIDANCE at 30. Youme failed to test its products with such e-liquids. FDA did not change its policy but explained how Youme failed to follow the Guidance to test a "reasonable range" of e-liquids based on its particular product and how it is commonly used according to its own studies. FDA in essence found the range used was unreasonable. FDA's actions are consistent with its "case-by-case" approach and Section 387j(c)(3)'s instruction that the FDA include "a statement informing the applicant of the measures required to remove such application from deniable form." "FDA's denial order[] w[as] sufficiently consistent with its predecisional guidance and thus did not run afoul of the change-in-position doctrine." *See Wages & White Lion*, 145 S. Ct. at 919.

II. Deficiency Letter

Youme asserts that FDA's "one and done" approach to issuing deficiency letters was arbitrary and capricious because FDA (1) failed to give Youme an opportunity to address a newly raised issue, (2) continued the single-deficiency policy after the court-imposed deadline, (3) failed to consider post-deadline submissions, and (4) failed to treat like cases alike.

First, Youme argues FDA changed its policy to a single deficiency letter "so that the agency could make as many final determinations as possible by what it understood to be a court-directed deadline in September 2021." Youme argues that by the time FDA considered its response to the issues raised in the deficiency letter, FDA's stated rationale for limiting applicants to only a single deficiency letter no longer applied. FDA counters that nothing in the TCA requires FDA to issue any deficiency letters before

denying an application and instead Section 387j(c)(2)'s instruction that FDA "shall deny" an application that fails to demonstrate the product is appropriate for the protection of the public health.

Although the TCA does not require multiple deficiency letters, Youme argues FDA's prior practice of issuing multiple rounds of deficiency letters could be sufficient to create justifiable reliance on FDA's past practice of its iterative review process. "Agencies are free to change their existing policies as long as they provide a reasoned explanation for the change." *Encino Motorcars*, 579 U.S. at 221. The agency must, at a minimum, "'display awareness that it is changing position' and 'show that there are good reasons for the new policy.'" *Id.* (quoting *Fox Television Stations*, 556 U.S. at 515). An agency "cannot 'surprise' a party by penalizing it for 'good-faith reliance' on the agency's prior positions." *R.J. Reynolds Vapor Co.*, 65 F.4th at 189 (quoting *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156–57 (2012)). Continued reliance on longstanding and well-established practices are justifiable until the agency first publishes notice of its intent to change its policy. *See Calumet Shreveport Refin., L.L.C. v. EPA*, 86 F.4th 1121, 1135 (5th Cir. 2023), *vacated on other grounds*, 145 S. Ct. 1735 (2025). A legitimate reliance interest is a high bar, "requiring, for example, 'decades of industry reliance on [an agency's] prior policy.'" *Wages & White Lion*, 145 S. Ct. at 927 (alteration in original) (quoting *Encino Motorcars*, 579 U.S. at 222).

FDA received applications to market nearly 27 million deemed products, with more than 6.5 million before September 2020. *Combatting the Youth Vaping Epidemic by Enhancing Enforcement Against Illegal E-Cigarettes: Hearing before the S. Comm. on the Judiciary*, 118th Cong. 5 (2024) (statement of Brian A. King, Director, Ctr. for Tobacco Prods.) https://perma.cc/6LXP-3F2Y. In June 2021, FDA announced that it intended to issue only one deficiency letter and base its decision on the

applicant's response to that letter. U.S. Food and Drug Admin., Deemed Product Review: A Conversation with the Center for Tobacco Products Office of Science 24 (June 11, 2021), https://perma.cc/6PD3-FLXG. FDA explained its reason for the change in the review process: to more efficiently process the "very large number" of applications received around September 2020. *Id.* FDA "streamlined the process for all review programs and . . . generally limited the application review to one deficiency letter." *Id.*

FDA displayed an awareness that it was changing its process and provided reasons for the change. "An agency's control over its timetables is entitled to considerable deference." *Calumet Shreveport*, 86 F.4th at 1142. As for Youme's reliance interest, the change to the review and deficiency letter process occurred in June 2021. Although Youme submitted its application ten months prior, the notice of the change occurred nearly two years before FDA issued its single deficiency letter to Youme. Further, Section 387j requires that an applicant submit a complete application. 21 U.S.C. § 387j(b)(1). Youme has not explained how it would have submitted its application differently if it had known of the deficiency-process change at the time. Youme's reliance on FDA's prior iterative review process is not justifiable because Youme had an obligation to submit a completed application and had significant notice it would be issued only a single deficiency letter.

Youme also contends that FDA's sole deficiency was based on the lack of a labeling comprehension and human factors study whereby study participants are evaluated on their ability to understand and comply with the warning that the Suorin Air device is recommended for use with e-liquid concentrations up to a certain percent. They assert this deficiency was raised for the first time in the denial order, denying Youme the opportunity to address it. FDA counters that it cited the same abuse-liability concern

originally identified in the deficiency letter, but also explained in greater detail why Youme's response to the deficiency letter was inadequate to address the concern.

As mentioned already, FDA's deficiency letter cited concerns with the abuse liability of Youme's products when used with certain e-liquids. Youme responded to that deficiency by suggesting it would add instructions recommending use of the device only with e-liquids below the concerning concentrations. FDA's denial letter informed Youme that its response to the deficiency letter was inadequate to address the abuse-liability concern, in part because Youme failed to show that consumers would comprehend and comply with the new recommendation. This is not a new deficiency. The Technical Project Lead memorandum explained that the deficiency "relates to the abuse liability of the new products and the consumer comprehension of the new instructions the applicant added in response to" a deficiency noted in the deficiency letter. FDA then explained that Youme failed to test its product with e-liquids containing higher nicotine concentrations, and it was that failure to test that related directly to abuse-liability concerns. FDA explained further that "[i]f the applicant intends to demonstrate that consumers understand the risks associated with the use of nicotine concentrations greater than [a certain amount] and will not use such e-liquids with the new products, then data on consumer comprehension and the likelihood of compliance with the new instructions is needed to evaluate whether consumers will understand the appropriate e-liquid to use in the new products."

This is not a new deficiency, but an explanation of how Youme failed to address the abuse-liability concerns. Further, the PMTA Guidance recommends applicants "include studies demonstrating that users and nonusers understand the product's labeling and instruction for use, and use

the product according to its labeled instructions," so Youme was on notice these studies could be required. PMTA GUIDANCE at 43.

Youme also contends FDA failed to "treat like cases alike" by refusing to weigh evidence in Youme's post-deadline submission. "It is a bedrock principle of administrative law that an agency must 'treat like cases alike.'" *Univ. of Tex. M.D. Anderson*, 985 F.3d at 479 (quoting 32 CHARLES ALAN WRIGHT & CHARLES H. KOCH, FEDERAL PRACTICE AND PROCEDURE § 8248, at 431 (2006)). "This principle is an outgrowth of the old adage . . . that 'an agency changing its course must supply a reasoned analysis.'" *Id.* (quoting *State Farm*, 463 U.S. at 57).

Youme does not proffer any "like cases" for us to consider. Youme instead argues that "by FDA's own admission in an internal memorandum created *after* Youme submitted its response to the deficiency letter, the agency has periodically considered and weighed evidence from such late amendments," so FDA's failure to review its post-deadline submission shows that it did not treat like cases alike. To support the assertion, Youme quotes one part of a sentence that states "there have been instances since August 2020 where [the Center for Tobacco Products' Office of Science] has reviewed late amendments." The complete sentence, however, provides that "[a]lthough there have been instances since August 2020 where [the Center for Tobacco Products' Office of Science] has reviewed late amendments, [it] aims to improve consistency and predictability in the PMTA program."

FDA's internal memorandum mentions it will consider "all solicited and unsolicited amendments received prior to the start of substantive scientific review," but that "amendments received after this time will not be considered" absent two exceptions. The two exceptions are "safety information or real-world safety data" and "amendments received for

applications that were likely to receive a marketing granted order prior to receipt of the amendment." FDA explained that it intended to review late amendments of this kind "to ensure products made available to the public are appropriate for the protection of the public health." Youme does not contend it satisfies either exception. FDA's refusal to weigh Youme's post-deadline submission was not arbitrary and capricious.

Finally, Youme cites cases involving an iterative review process, but those cases precede FDA's policy change. Further, the examples Petitioners cite in which FDA issued multiple deficiency letters are not similarly situated, as one product is a smokeless tobacco product and the other was through the substantial-equivalence pathway, not the PMTA pathway that Youme's product must satisfy. Youme discusses an ENDS product in its reply brief, but the argument is forfeited because Youme did not present it in its opening brief. *United States v. Fernandez*, 48 F.4th 405, 412 (5th Cir. 2022).

The denial of the application was reasonable and reasonably explained. The petition for review is DENIED.