United States Court of Appeals for the Fifth Circuit

United States Court of Appeals
Fifth Circuit
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Lyle W. Cayce
Clerk

No. 21-60766

WAGES AND WHITE LION INVESTMENTS, L.L.C., *doing business as* TRITON DISTRIBUTION,

Petitioner,

versus

FOOD AND DRUG ADMINISTRATION,

Respondent,

CONSOLIDATED WITH

No. 21-60800

WAGES AND WHITE LION INVESTMENTS, L.L.C., *doing business as* TRITON DISTRIBUTION; VAPETASIA, L.L.C.,

Petitioners,

versus

FOOD AND DRUG ADMINISTRATION,

Respondent.

Petitions for Review of an Order of the
Food and Drug Administration

Before JONES, HAYNES, and COSTA, *Circuit Judges*.

HAYNES, *Circuit Judge*:

Petitioners Wages and White Lion Investments, LLC, d/b/a Triton Distribution ("Triton") and Vapetasia, LLC ("Vapetasia") sought to market flavored nicotine-containing e-liquids for use in open-system e-cigarette devices. To do so, Petitioners needed to submit premarket tobacco product applications as required by 21 U.S.C. § 387j—which the Food and Drug Administration ("FDA") deemed applicable to e-cigarette tobacco products in 2016. FDA denied the requested marketing authorizations, finding that Petitioners failed to offer reliable and robust evidence (such as randomized controlled trials or longitudinal studies) to overcome the risks of youth addiction and show a benefit to adult smokers.

Petitioners seek review of those marketing denial orders ("MDOs"), and prior to the consolidation of the two cases, Triton requested a stay pending that review. Without (of course) the benefit of full merits briefing, a prior panel of this court granted the stay, determining (as any court granting a stay application must determine) that there was "a strong likelihood of success on the merits." *Wages & White Lion Invs., L.L.C. v. FDA*, 16 F.4th 1130, 1136, 1144 (5th Cir. 2021). But having now had the opportunity to review the merits briefing followed by oral argument, we DENY the petitions for review.

I. Statutory & Regulatory Landscape

To fully appreciate the events that gave rise to the petitions before us, we begin with a careful review of the statutory and regulatory background. Nearly a century ago, Congress passed the Food, Drug, and Cosmetics Act ("FDCA"), Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified at 21 U.S.C.

§ 301, *et seq.*), which established broad regulatory authority—such as a premarket "new drug" authorization requirement—to protect the public against the dangers of "adulterated and misbranded food, drugs, devices, and cosmetics." 52 Stat. at 1040, 1052; *see generally id.* at 1040–59.

The FDCA developed substantially over the next fifty-eight years, but tobacco remained unregulated through the Act and its accompanying regulations. That is, until 1996, when FDA determined that it could regulate tobacco given its existing authority to regulate drugs and devices. Nicotine in Cigarettes and Smokeless Tobacco Is a Drug, 61 Fed. Reg. 44,619 (Aug. 28, 1996). "Like the products that FDA traditionally regulates," tobacco products are "placed within the human body; like many of these products, they deliver a pharmacologically active substance to the bloodstream; and like these products, they have potentially dangerous effects. Indeed, no products cause more death and disease . . . ." *Id.* at 44,628. On that basis, FDA determined that it had jurisdiction to regulate tobacco products. *Id.*

The Supreme Court disagreed. In a landmark decision, the Court held that "Congress . . . precluded the FDA's jurisdiction to regulate tobacco products." *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000). The Court's reasoning centered on Congress's failure to amend the FDCA to give FDA that authority, Congress's enactment of several tobacco statutes, and FDA's prior assertion that it lacked jurisdiction. *Id.* at 155–57. Following *Brown & Williamson Tobacco Corp.*, if Congress wanted FDA to regulate tobacco, it would have to grant the agency that authority expressly.

So Congress did precisely that. In 2009, it passed the Family Smoking Prevention and Tobacco Control Act ("TCA"), Pub. L. No. 111-31, 123 Stat. 1776 (2009) (codified at 21 U.S.C. § 387, *et seq.*), which amended the FDCA to include the regulation of tobacco. Section 2 of the Act laid out myriad congressional findings, which pointed to the dangerous effects of tobacco on

both adults and children. *See, e.g.*, TCA § 2(34), 123 Stat. at 1779 ("Because the only known safe alternative to smoking is cessation, interventions should target all smokers to help them quit completely."); *id.* § 2(1), 123 Stat. at 1777 ("The use of tobacco products by the Nation's children is a pediatric disease of considerable proportions that results in new generations of tobacco-dependent children and adults."). "Obviously," given the extensive congressional record, "the TCA's purpose sounds in (1) protecting public health and (2) preventing young people from accessing (and becoming addicted to) tobacco products." *Big Time Vapes, Inc. v. FDA*, 963 F.3d 436, 444 (5th Cir. 2020), *cert. denied*, 141 S. Ct. 2746 (2021) (mem.).

Congress also found that FDA had the relevant "scientific expertise to . . . evaluate scientific studies supporting claims about the safety of products[] and to evaluate the impact of labels, labeling, and advertising on consumer behavior in order to reduce the risk of harm and promote understanding of the impact of the product on health." TCA § 2(44), 123 Stat. at 1780. To that end, Congress gave FDA broad authority to regulate tobacco products, requiring that most "new tobacco product" receive authorization from the FDA prior to marketing. 21 U.S.C. § 387j(a)(2)(A).

The TCA defines "new tobacco product" (in relevant part) as "any tobacco product . . . that was not commercially marketed in the United States as of February 15, 2007." *Id.* § 387j(a)(1)(A). The Act lists specific categories of tobacco products subject to regulation—"all cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco"—but it also provides that the Act will apply "to any other tobacco products that the Secretary by regulation deems to be subject to this subchapter." *Id.* § 387a(b).[1] In 2016, FDA used that authority to deem e-cigarettes and their

[1] We recently rejected the argument that this provision constitutes an unlawful delegation of congressional power. *Big Time Vapes*, 963 F.3d at 447. In reaching that

component parts (including e-liquids) as tobacco products subject to the requirements of the TCA. Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, 81 Fed. Reg. 28,974 (May 10, 2016) ("Deeming Rule").[2]

Relevant here, the Deeming Rule subjected e-cigarette manufacturers to the TCA's prior authorization requirement—manufacturers of "new tobacco product[s]" must submit premarket tobacco product applications ("PMTAs"). *See* 21 U.S.C. § 387j(a)(2). FDA reviews the PMTAs and is statutorily required to decline them if "there is a lack of a showing that permitting such tobacco product to be marketed would be appropriate for the protection of the public health." *Id.* § 387j(c)(2)(A). In determining whether a product is appropriate for the protection of the public health (referred to as the "APPH" standard), FDA must consider "the risks and benefits to the

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decision, this court extensively examined the TCA's purpose and relevant background. *Id.* at 444.

[2] As Petitioners showcased at oral argument, e-cigarettes can come in various forms. FDA provided a helpful explanation in its briefing:

> Some devices have "pods" or "cartridges" that hold nicotine-containing liquid known as "e-liquid." Some pods or cartridges (known as closed systems) come pre-filled with e-liquid and are replaced after the e-liquid is used up, while others (known as open systems) can be refilled by the user. Tank or "mod" (short for "modifiable") devices can also be refilled by users and are also usually customizable. Disposable e-cigarettes come prefilled with the e-liquid, and the entire device is designed to be discarded after the e-liquid runs out.

Collectively, these devices are referred to as electronic nicotine delivery systems ("ENDS"), but the term "ENDS" is sometimes used interchangeably with e-cigarettes. We mimic one of our sister courts in simply using the term "e-cigarettes" for ease of reference. *See Nicopure Labs, LLC v. FDA*, 944 F.3d 267, 273 n.1 (D.C. Cir. 2019) ("We use the term 'e-cigarettes' to refer to the full range of products that the Industry calls 'vapor products' and the FDA calls Electronic Nicotine Delivery Systems, or ENDS. They go by many other names as well . . . .").

population as a whole." *Id.* § 387j(c)(4). This includes considering "the increased or decreased likelihood that existing users of tobacco products will stop using such products," *id.* § 387j(c)(4)(A), as well as "the increased or decreased likelihood that those who do not use tobacco products will start using such products," *id.* § 387j(c)(4)(B).

The Deeming Rule was set to go into effect on August 8, 2016, but FDA delayed enforcement of the regulation as to existing e-cigarette manufacturers. 81 Fed. Reg. at 28,977. Instead, manufacturers would have a two- to three-year period to come into compliance. *Id.* at 28,977–78. In 2017, the FDA pushed that deadline to 2022.[3] But shortly after extending the deadline, the American Academy of Pediatrics sued the FDA for granting the extension. *See Am. Acad. of Pediatrics v. FDA*, 399 F. Supp. 3d 479 (D. Md. 2019). A federal court vacated FDA's 2017 guidance and required FDA to set a new deadline at ten months after the issuance of its order. *Id.* at 480–81, 487. The deadline shifted once again due to the COVID-19 pandemic, making the final deadline September 9, 2020.

II. The Petitions

Waiting to file until the deadline date, on September 9, 2020, Petitioners submitted PMTAs in an effort to manufacture and sell various flavored e-cigarette products.[4] Specifically, they sought approval for products that came in flavors like sour grape, pink lemonade, crème brulee,

[3] FDA, Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised): Guidance for Industry 5 (2020) ("2020 Guidance"), https://www.fda.gov/media/133880/download.

[4] Triton and Vapetasia submitted nearly identical PMTAs because Triton operates as a contract manufacturer for Vapetasia and the two worked together extensively (as they continue to do in this litigation). Triton prepared Vapetasia's PMTAs, and the two jointly filed Vapetasia's petition for review.

peachy strawberry, milk & cookies, and pound cake and with names such as "Jimmy The Juice Man Strawberry Astronaut" and "Suicide Bunny Bunny Season."

On September 14 and 16, 2021, FDA issued marketing denial orders to Petitioners. FDA listed the following as the "key basis" for Triton's MDO (with emphasis on the language Petitioners take issue with):

> All of your PMTAs lack sufficient evidence demonstrating that your flavored ends will provide a benefit to adult users that would be adequate to outweigh the risks to youth. In light of the known risks to youth of marketing flavored ends, robust and reliable evidence is needed regarding the magnitude of the potential benefit to adult smokers. *This evidence could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of your flavored ends products over an appropriate comparator tobacco-flavored ends.* Alternatively, FDA would consider other evidence but only if it reliably and robustly evaluated the impact of the new flavored vs. Tobacco-flavored products on adult smokers' switching or cigarette reduction over time. We did not find such evidence in your PMTA[s]. Without this information, FDA concludes that your application is insufficient to demonstrate that these products would provide an added benefit that is adequate to outweigh the risks to youth and, therefore, cannot find that permitting the marketing of your new tobacco products would be appropriate for the protection of the public health.

Vapetasia received a very similar basis for denial, but for Vapetasia, FDA added:

> Although your PMTAs contained a cross-sectional survey "Vapetasia PMTA Survey and Testimonial", this evidence is not sufficient to show a benefit to adult smokers of using these flavored ENDS because it does not evaluate the specific products in the application(s) or evaluate product switching or

> cigarette reduction resulting from use of these products over time.

Along with each MDO, FDA provided a Technical Project Lead report that described their reasoning in much greater detail.

Petitioners timely sought review of the MDOs in this court. They argue, primarily, that FDA lacks the authority to impose a comparative efficacy requirement and that FDA acted arbitrarily and capriciously by "requiring" scientific studies. Triton moved for a stay. After the stay was granted, the two cases were consolidated for appeal.

III. Jurisdiction & Standard of Review

We have jurisdiction under 21 U.S.C. § 387*l*(a)(1)(B), which authorizes federal court review of the denial of premarket tobacco product applications in a U.S. Court of Appeals "for the circuit in which" the individual or entity that received such a denial "resides or has their principal place of business." Triton's principal place of business is Richardson, Texas, giving us jurisdiction over its petition and the petition it jointly filed with Vapetasia.

The FDA's denial of Petitioners' premarket authorizations is reviewed under the standards set by the Administrative Procedure Act ("APA"). *See* 21 U.S.C. § 387*l*(b). The APA allows a reviewing court to set aside an agency determination if that determination was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). "The scope of review under the 'arbitrary and capricious' standard is narrow[,] and a court is not to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983).

IV. Discussion

Petitioners advance two primary arguments: (1) FDA acted arbitrarily and capriciously by pulling a "surprise switcheroo" on Petitioners and failing to consider important aspects of the PMTAs; and (2) FDA lacks statutory authority to impose a comparative efficacy requirement.[5] We are unpersuaded by either argument.

A. FDA Authority

We begin with the simpler matter. Petitioners argue that FDA "lacks authority . . . to impose a requirement that Triton demonstrate its flavored ENDS products are more effective at promoting smoking cessation than its tobacco flavored ENDS products." Petitioners are blatantly wrong—the TCA authorizes FDA to consider comparative cessation evidence, if not expressly then impliedly.

Beginning with the express authority. 21 U.S.C. § 387j is the relevant provision: subsection (b) sets out the requirements for a premarket tobacco application, and subsection (c) outlines the actions FDA may take with regards to the application. *Id.* § 387j(b), (c). Under subsection (b), applicants are *required* to include in their applications "full reports . . . concerning investigations which have been made to show the health risks of such tobacco product *and whether such tobacco product presents less risk than other tobacco products*." *Id.* § 387j(b)(1)(A) (emphasis added). Under subsection (c), FDA is then *required* to consider "the information

[5] Upon success on the first argument (that FDA acted arbitrarily and capriciously) but failure on the second (that FDA lacks statutory authority), Petitioners request that the court grant them an eighteen-month-long injunction against the agency so that they could conduct randomized controlled trials and longitudinal studies. FDA rejects this request as incongruent with the APA, arguing that remand is the only appropriate remedy. Because we deny the petitions for review, we need not address the propriety of the requested relief.

submitted to the Secretary as part of the application," which necessarily includes the comparative efficacy reports that applicants must provide. *Id.* § 387j(c)(2).

Petitioners ask us to ignore these provisions, arguing that the word "risk" in § 387j(b)(1)(A) "refers to physiological *health* risks, not some broader concept of risk that encompasses initiation and cessation behaviors." This argument is unpersuasive. Initiation and cessation behaviors *are* physiological health risks. In fact, as Petitioners themselves note, cessation is one of the reasons Congress enacted the TCA in the first place. TCA § 3(9), 123 Stat. at 1782; *see also* TCA § 2(34), 123 Stat. at 1779 ("Because the only known safe alternative to smoking is cessation, interventions should target all smokers to help them quit completely.").

Moreover, subsection (c) provides further express authority for FDA to consider comparative efficacy. The statute provides that to determine compliance with the APPH standard, FDA must 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). The phrase "increased or decreased likelihood" necessarily implies a comparative analysis. Nothing can "increase" or "decrease" in a vacuum.[6] Petitioners surely understood as much because, as FDA points out, Petitioners actually included evidence of comparative cessation in their PMTAs.

But even if Petitioners are right that FDA lacks the express authority to consider such evidence, FDA certainly has implied authority to do so. In addition to the provisions cited above, FDA may consider "any other

[6] If someone smoked 10 cigarettes today, you could not say that she "increased" or "decreased" her smoking ritual without having evidence of her prior smoking habits—that is, evidence that would allow you to *compare* her smoking today to her smoking yesterday and before.

information before the Secretary with respect to [the] tobacco product," 21 U.S.C. § 387j(c)(2), may commission an investigation to determine whether a product meets the APPH standard, *id.* § 387j(c)(5)(A), and may consider other "valid scientific evidence," *id.* § 387j(c)(5)(B). Therefore, FDA's consideration of the lack of cessation as a risk and comparing that risk between new tobacco products and old tobacco products "fall[s] squarely within the ambit of the FDA's expertise and merit[s] deference." *Cf. Schering Corp. v. FDA*, 51 F.3d 390, 399 (3d Cir. 1995).

B. Arbitrary and Capricious

We now turn to the core issue upon which our motions panel relied to grant a stay. Petitioners argue that they relied on FDA's statements that scientific studies were not necessary, but that FDA seemed to consider the lack of studies the only relevant factor in its decision, ignoring all the reasons it should have authorized their products. The motions panel largely agreed. It determined that FDA pulled a "surprise switcheroo" and either inadequately considered or failed to consider altogether several relevant aspects of Petitioners' applications, including: "(1) Triton's marketing plan; (2) Triton's reliance interests; (3) less disruptive alternatives; (4) device-type preferences; and (5) evidence on the potential benefits of flavored e-cigarettes." *Wages & White Lion*, 16 F.4th at 1136.

Notably, after our court entered that decision, the Sixth Circuit denied a stay application of a similar MDO. *Breeze Smoke, LLC v. FDA*, 18 F.4th 499, 506 (6th Cir. 2021) ("Considering all of Breeze Smoke's evidence, we disagree with Breeze Smoke, and with our colleagues on the Fifth Circuit, who say that the FDA orchestrated a 'surprise switcheroo.'").[7]

[7] Other circuits have granted stays but provide little in the way of explanation that addresses the considerations herein. *See Gripum LLC v. FDA*, No. 21-2840 (7th Cir. Nov. 4, 2021) (order granting stay pending review); *Bidi Vapor LLC v. FDA*, No. 21-13340 (11th

Examining largely the same factors our court pointed out, our sister court determined that FDA appropriately considered this evidence and reached a contrary conclusion. *Id.* at 506–08.

Before diving into these specific issues, we should note that our job here is quite limited. We are not tasked with determining whether we *agree* with FDA's decision (that is, whether we would have granted authorization if the PMTAs were submitted to us in the first instance). Instead, we review the MDOs for whether they were arbitrary and capricious. There are only narrow circumstances under which we would consider an agency action arbitrary and capricious:

> if the agency has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise.

Motor Vehicle Mfrs., 463 U.S. at 43.

Moreover, where the parties disagree on the science, we owe the FDA deference. After all, Congress deemed only the FDA as the scientific expert here—not the federal courts. *See* TCA § 2(44), 123 Stat. at 1780 ("The Food and Drug Administration is a regulatory agency with the scientific expertise to . . . evaluate scientific studies supporting claims about the safety of products[] . . . ."). With those general caveats in place, we now address the relevant specifics.

Cir. Feb. 1, 2022) (same); *Johnny Copper, L.L.C. v. FDA*, No. 21-13438 (11th Cir. Feb. 1, 2022) (same); *Vapor Unlimited LLC v. FDA*, No. 21-13454 (11th Cir. Feb. 1, 2022) (same).

(1) Evidence on Potential Benefits

Petitioners argue that FDA dismissed their evidence regarding benefits to adults because the evidence did not consist of the specific studies FDA recommended. We are unpersuaded by Petitioners. As FDA aptly summarized in its briefing before this court: "FDA denied petitioners' applications *not* because they failed to include a randomized controlled trial or longitudinal cohort study but because they failed to include *any* evidence robust enough to carry petitioners' burden under the statute." The key piece of evidence that Petitioners focus on in their briefing is a cross-sectional survey conducted by Vapetasia. Petitioners emphasize that according to this study, 82.99% of survey respondents indicated that e-cigarettes helped them quit smoking combustible tobacco. But that survey suffered from several methodological flaws: (1) only 294 people were surveyed; (2) the survey respondents are all Vapetasia customers; and (3) it's not clear how these individuals were selected to take the survey.[8] In other words, there were strong reasons to doubt the survey's results. The FDA therefore did not act arbitrarily in concluding that Vapetasia's survey "is not sufficient to show a benefit to adult smokers."[9]

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[8] As the Sixth Circuit explained given a similar customer survey:

> On this record, Breeze Smoke's survey presents methodological issues. The FDA's 2019 guidance suggested that applicants include studies "with robust rationale, acute toxicological endpoints or other clinical endpoints that may relate to long-term health impacts." Breeze Smoke's study, submitted via Google Form, contained responses from customers "solicited . . . by request in the retail stores."

Breeze Smoke, 18 F.4th at 506 (citations omitted).

[9] The motions panel discussed a study cited by Triton (and conducted by the Consumer Advocates for Smoke-Free Alternatives Association) as key evidence that the FDA ought to have considered. The panel noted:

(2) Device-Type Preferences

Petitioners argue that FDA failed to consider device-type preferences amongst youth. E-cigarettes can come in various forms: "closed systems," which are e-cigarettes designed to have cartridges inserted into the device; "open systems," which are e-cigarettes with built-in tanks that are filled by the user; and disposables, which are e-cigarettes where the entire device is thrown out when the e-liquid runs out (as opposed to just the empty cartridge being thrown out in a closed-system device).[10] In 2019, FDA witnessed the highest level ever recorded of youth e-cigarette use. *See* Enforcement Priorities for Electronic Nicotine Delivery Systems and Other Deemed Products on the Market Without Premarket Authorization, 85 Fed. Reg. 720, 722 (Jan. 7, 2020) ("Data from the 2019 NYTS also show that 2019 was the

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> Triton urged the FDA to consider a 2015 survey of 20,000 e-cigarette users showing that nearly a third of the respondents "started out using tobacco or menthol flavors" and then began using other flavored e-cigarettes. Similarly, Triton asserted that flavored e-cigarettes "could serve an important role in transitioning existing adult users away from more harmful, combustible cigarette products." But in the Order, the FDA ignored the first point altogether and gave the second short shrift.

Wages & White Lion, 16 F.4th at 1140 (citations omitted).

Petitioners do not actively discuss this study in their briefing, only referring to it a couple of times in passing. Regardless, the Technical Project Lead reports explain that FDA "reviewed the application for any acceptably strong evidence." It found none. At most, Petitioners fault FDA for not *mentioning* the study in the MDO (unlike how it handled the Vapetasia study). But unlike the Vapetasia study, Triton did *not* conduct or commission this survey, and in any event, FDA not mentioning the study is not the same as "entirely fail[ing] to consider an important aspect of the problem." *State Farm*, 436 U.S. at 43.

[10] The motions panel inadvertently confused closed-system devices with disposable devices. *See Wages & White Lion*, 16 F.4th at 1130. To clarify, the distinction is whether the device as a whole is thrown out (disposable) as opposed to a component part being thrown out (closed system).

second consecutive year in which current (past 30-day) e-cigarette use among youth reached unprecedented levels.").

FDA's 2020 Guidance explained that, based on 2019 data, youth were particularly attracted to closed-system devices. 2020 Guidance at 19. ("[D]ata from the 2019 NYTS indicate that youth overwhelmingly prefer cartridge-based ENDS products. These products are easy to conceal, can be used discreetly, may have a high nicotine content, and are manufactured on a large scale." (footnote omitted)). Given this data, FDA began to ramp up its enforcement efforts against closed-system devices. Former FDA Commissioner Scott Gottlieb even made a speech after he no longer served as Commissioner in which Gottlieb called for a complete ban on closed-system devices and noted that open-system devices are not as popular with youth. Nicholas Florko, *Former FDA Commissioner Calls for A Full Ban on Pod-Based E-Cigarettes*, STAT (Nov. 12, 2019), https://www.statnews.com/2019/11/12/gottlieb-ban-pod-based-e-cigarettes/.

Petitioners rely heavily on the Gottlieb statement and FDA's enforcement efforts against closed-system devices. They argue that FDA acted arbitrarily and capriciously because it failed to consider that their e-cigarettes are open-system devices. But in reality, Petitioners fault FDA for refusing to turn a blind eye to all the evidence that has emerged since 2019. Particularly, after FDA increased enforcement actions against closed-system devices, the youth-smoking epidemic did *not* end; instead, youth smokers migrated to *other* device types with flavored e-liquids: "[W]hen FDA changed its enforcement policy to prioritize pod-based flavored ENDS, which were most appealing to youth at the time, we subsequently observed a substantial rise in use of disposable flavored ENDS—a ten-fold increase (from 2.4% to 26.5%) among high school current e-cigarette users." *See*

Triton TPL Report at 8; Vapetasia TPL Report at 8.[11] To the extent Petitioners rely on the Gottlieb statement and the 2020 Guidance, their reliance is misplaced. Both were based on data from 2019—that is, data from *before* the FDA's subsequent enforcement actions and the observed youth migration.[12] As well, Gottlieb was no longer the FDA Commissioner, so his comments have no greater weight than anyone else's thoughts. In contrast to the evidence on device-type preference, FDA concluded that "across these different device types, the role of flavor is consistent." In other words, FDA *did* consider Petitioners' device type, and it concluded (reasonably) that what truly impacts youth smokers is flavor preference, not device preference.

(3) Reliance Interests

Petitioners argue, and the motions panel concluded, that FDA "pulled a surprise switcheroo" in "requir[ing] the very studies it originally expected it didn't need." *Wages & White Lion*, 16 F.4th at 1138 (internal quotation marks, brackets, and citation omitted). But the FDA does not now—and has not ever—*required* studies of smoking cessation. Contrary to the motion panel's determination that FDA made a "radical" change, *id.* at 1138–39, FDA has always suggested and continues to suggest that such studies *might* be useful, in particular where, as here, the evidence presented in an application is otherwise weak. *See Nicopure Labs, LLC v. FDA*, 944 F.3d 267, 282 (D.C. Cir. 2019) ("The FDA has *expressed willingness* to accept

[11] The notion in the dissenting opinion that Petitioners only received the TPLs via FOIA was not an argument raised adequately by Petitioners in their briefing.

[12] While Petitioners cite two studies that purport to include data from 2020 and 2021, these studies do not show (or at least, Petitioners fail to explain how they show) what the percentage breakdown across devices is, what effect the FDA enforcement actions had on this usage, or how these statistics map on to statistics regarding flavor. The evidence provided on device-type preferences is, therefore, unpersuasive.

scientific literature reviews instead of commissioned studies in support of e-cigarette applications *in appropriate circumstances*." (emphasis added)).

One needs to look no further than the FDA's own conditional language over the last several years to reach that conclusion. The record is replete. *See, e.g.*, Premarket Tobacco Product Applications and Recordkeeping Requirements (Final Rule), 86 Fed. Reg. 55,300, 55,387 (Oct. 5, 2021) ("FDA does not expect that long-term clinical studies will need to be conducted for each PMTA; instead, it expects that it *should be able* to rely on other *valid* scientific evidence to evaluate some PMTAs." (emphasis added)); Premarket Tobacco Product Applications and Recordkeeping Requirements (Proposed Rule), 84 Fed. Reg. 50,566, 50,619 (Sept. 25, 2019) ("FDA will determine . . . whether the available evidence, *when taken as a whole*, is adequate to support a determination that permitting the new tobacco product to be marketed would be APPH." (emphasis added)); FDA, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (ENDS): Guidance for Industry 13 (2019), https://www.fda.gov/media/127853/download ("[I]nstead of conducting clinical studies that span months or years to evaluate potential clinical impact, applicants *could* demonstrate possible long-term health impact by including existing longer duration studies in the public literature with the appropriate bridging information . . . ." (emphasis added)); *id.* at 46 ("[T]hese data *may* be sufficient to support a PMTA . . . ." (emphasis added)); 81 Fed. Reg. at 28,997 ("[I]n *some cases*, it *may be* possible for an applicant to obtain a PMTA marketing authorization order without conducting any new nonclinical or clinical studies where there is an established body of evidence regarding the public health impact of the product." (emphasis added)).

The evidence cited by the dissenting opinion to the contrary ignores the FDA's continuous use of conditional language. For example, quoting the

TPLs, the dissenting opinion frames FDA as stating that longitudinal "studies are 'most likely' to provide reliable and robust evidence to satisfy the APPH standard." But the dissenting opinion ignores the next line in the TPL: "other types of evidence could be adequate[] and will be evaluated on a case-by-case basis." Similarly, per the dissenting opinion, "FDA announced that it would authorize the flavored ENDS products *only if* the PMTAs included previously purely optional studies." Dissenting Op. at 3–4. For this argument, the dissenting opinion relies on an FDA press release, while ignoring the line in that press release that says, "the agency does not foreclose the possibility that other types of evidence could be adequate if sufficiently robust and reliable." *See* FDA, Press Release, FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health (Aug. 26, 2021), https://bit.ly/2YsYmzd. Finally, the dissenting opinion's reliance on a subsequently retracted internal FDA memo does not alter any of the conditional language that FDA continued to provide.

Having reviewed this record, we agree with the Sixth Circuit's conclusion regarding the lack of any scientific study "requirement." *See Breeze Smoke*, 18 F.4th at 506–07. *Breeze Smoke* was decided after *Wages & White Lion*, and following the *Breeze Smoke* decision, Petitioners presented an application for a stay (i.e., a stay of the FDA's denial) to Justice Kavanaugh, who referred the application to the Court. *See Breeze Smoke, LLC v. FDA*, 142 S. Ct. 638 (2021) (mem.). The application was denied, without any recorded dissent from the Supreme Court. *Id.* Having had the benefit of these subsequent developments as well as full briefing and oral argument, we take a different view from the stay panel.[13]

[13] It should go without saying, but the dissenting opinion wrongly implies that four judges of this court have "found" the merits lacking. Dissenting Op. at 1. Our precedent

The fact that Petitioners presented other scientific evidence does not make that scientific evidence valid, and it is entirely consistent with FDA's prior statements to reject that evidence. Moreover, Petitioners' attempts to distinguish *Breeze Smoke* are unavailing. Petitioners make two arguments: (1) "the Sixth Circuit's motions panel considered only one excerpt from FDA's 2019 Guidance, and not the representations made by FDA at the two public meetings with applicants or the Final PMTA Rule"; and (2) "*Breeze Smoke* . . . dealt exclusively with disposable ENDS products, not bottled e-liquids." As to the first argument, as noted above, all the representations made by the FDA consistently said that other evidence *might* be accepted. As to the second argument, the device-type distinction is unpersuasive for the reasons set out earlier, and that distinction has no impact on the FDA's prior statements regarding scientific studies. Therefore, we (like our sister court) conclude that FDA has not pulled an impermissible "surprise switcheroo." *See Breeze Smoke*, 18 F.4th at 506–07.[14]

(4) Marketing Plan

Finally, Petitioners argue that FDA did not appropriately consider their marketing scheme. Instead, FDA stated that "for the sake of efficiency, the evaluation of the marketing plans in applications will not occur at this stage of review, and we have not evaluated any marketing plans submitted

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makes clear that a stay panel's determination regarding the likelihood of success on the merits is *not* itself a determination on the merits. That determination is for this panel to make alone.

[14] For these same reasons, we disagree with the dissenting opinion's attempt to distinguish *Breeze Smoke* and specifically disagree with the dissenting opinion's accusation that the Sixth Circuit "fail[ed] to acknowledge the abundant administrative record concerning FDA's public engagement with ENDS product suppliers, FDA's Sept. 2019 proposed rule, and the Final Rule, all of which are inconsistent with its perfunctory denial orders." Dissenting Op. at 5 n.4. The Sixth Circuit considered each extensively. *See Breeze Smoke*, 18 F.4th at 505–08.

with these applications." The motions panel rebuked this statement, noting that "'efficiency' is no substitute for 'reasoned decisionmaking.'" *Wages & White Lion*, 16 F.4th at 1137 (quoting *Michigan v. EPA*, 576 U.S. 743, 750 (2015)). After careful consideration, we have determined that the FDA did not act arbitrarily and capriciously in not reviewing the marketing plans, and if they did, such error was harmless.

As an initial matter, FDA did not consider the marketing plan because although "[i]t is theoretically possible that significant mitigation efforts could adequately reduce youth access and appeal," FDA had not once evaluated a marketing plan that actually did so. This was not a novel observation on the FDA's part. In fact, part of the reason Congress passed the TCA is *because* marketing restrictions simply were not working: "Because past efforts to restrict advertising and marketing of tobacco products have failed adequately to curb tobacco use by adolescents, comprehensive restrictions on the sale, promotion, and distribution of such products are needed." TCA § 2(6), 123 Stat. at 1777.

Moreover, Petitioners should have known that marketing plans on their own are not particularly useful.[15] FDA explained as much in its 2020 Guidance, in which it noted that youth usage continued to rise *despite* FDA's 2018 efforts to curb predatory marketing, such as its issuance of "warning letters to manufacturers, distributors, and retailers for selling e-liquids with labeling and/or advertising that resemble kid-friendly food products, such as juice boxes, candy, or cookies." 2020 Guidance at 6–9. This finding by FDA

[15] To be clear, in saying this we do not "blame" Petitioners for not knowing that their marketing plans would not be useful. *See* Dissenting Op. at 8. Instead, the record shows that it would have been unreasonable for Petitioners to believe that marketing plans in and of themselves would suffice for FDA to grant their PMTAs. An unreasonable belief on the part of an applicant is not the same as arbitrary and capricious action on the part of an agency.

directly refutes the dissenting opinion's claim that, until the MDOs, "[e]very single statement by the agency . . . reasonably led petitioners to believe that if they devised marketing arrangements that would prevent underage persons from purchasing their flavored e-liquids . . . they would have surmounted a significant requirement for marketing approval." Dissenting Op. at 8. The record not only undermines this statement, it contravenes it entirely—FDA stating that marketing plans would "help FDA determine" whether the new tobacco product meets the APPH standard is *not* the same as FDA stating that *if* marketing plans exist *then* market authorization was a step away.[16]

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[16] The dissenting opinion does not address the substance of FDA's finding that youth usage continued despite FDA's 2018 efforts to curb predatory marketing, focusing instead on the *source* in which FDA issued that finding: the 2020 Guidance. Dissenting Op. at 7-8. Instead, it provides four reasons the 2020 Guidance should not be considered. We address each in turn.

First, the dissenting opinion takes issue with the 2020 Guidance not "amending" the earlier Guidance. But both the 2020 Guidance and the earlier 2019 Guidance (which the dissenting opinion calls the "definitive" and "final" guidance) contained *nonbinding recommendations*. Lest anyone get confused, each document had a header that said, in bold print, "Contains Nonbinding Recommendations." Nothing in the record suggests that it is necessary or even common for FDA to amend a document no one was ever bound by.

Second, the dissenting opinion notes that "there is no evidence at all that these petitioners marketed or sold to youth." Dissenting Op. at 7. But there is no statutory requirement that for FDA to deny authorization, it must (or even should) have evidence that a particular applicant marketed or sold to youth.

Third, the dissenting opinion states that the 2020 Guidance is not referenced in the MDOs. This statement is technically true, but misleading. After all, the MDOs also didn't mention the 2019 Guidance. Nor is that the purpose of an MDO. An MDO is merely a short letter stating FDA's conclusion. Its reasoning is described more fully in the TPLs, which, of course, discuss the 2020 Guidance at length.

Fourth, the dissent's final concern—"the high level of youth vaping that spawned the 2020 Guidance had been underway since 2018, yet FDA did not adjust its PMTA Guidance materials significantly during this period"—asks FDA to do the impossible and analyze something that did not yet exist. Although vaping was a large issue amongst youth in 2018, the primary study FDA relied on for that data was not released until *November* 2018. FDA then quickly implemented new enforcement priorities. It then studied the

Instead, based on its expertise, FDA determined that traditional marketing schemes do not work and that absent a "novel or materially different" scheme, youth appeal would continue. Of course, one could argue that without having actually reviewed the marketing plans, FDA could not have known that Petitioners' plans would not have been unique. But at oral argument, FDA clarified that what it did review included a summary of the marketing plans.[17] We, therefore, do not believe that the agency acted arbitrarily and capriciously—Petitioners' plans were not unique; FDA did not need to go any further.

Quoting the stay panel, the dissenting opinion objects to this line of reasoning, analogizing FDA's actions to a judge that "stopped reading briefs because she previously found them unhelpful" and arguing that FDA only did so because it was inundated with a backlog of PMTAs. Dissenting Op. at 7. With this framing in mind, it's no wonder that the dissenting opinion calls the FDA's conduct "obviously illogical and unreasonable." Dissenting Op. at 7. But that framing does not appropriately capture what happened here.

We offer a different analogy. Consider a district court, inundated with a backlog of motions. Of course the court will not consider a summary judgment motion on the merits if it concludes that it must grant a motion to dismiss for lack of jurisdiction because it doesn't matter how good of a merits argument a plaintiff has, such an argument cannot cure a jurisdictional defect.

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effect of its new enforcement priorities in 2019 and developed updated guidance based on that data in 2020. Asking FDA to have provided data earlier would be asking FDA to release guidance with potentially no actual data. *That* would be an arbitrary and capricious agency action.

[17] Parties clarify factual matters before appellate courts all the time—it's one of the benefits of oral argument. Clarifying what happened factually is not, by any stretch of the imagination, "judicial post hoc reasoning about a post hoc justification." *See* Dissenting Op. at 8.

We recognize that, for efficiency, a district court need not review every single motion before it when a motion will have no effect on the outcome of the litigation, and we understand that not addressing every issue is not the same as a failure of reasoned decision making.

We cannot hold a federal agency, operated by a co-equal branch of government, to a higher standard than we hold the federal courts. FDA, per its expertise, understood that whatever the specific details of Petitioners' marketing plans were, those details could not cure the other defects in Petitioners PMTAs. It did not need to assess the details of the marketing plan, and its failure to do so is not a failure of reasoned decision making.

In any event, nothing in Petitioners' briefing to this court indicates that their marketing plan was in fact unique. Instead, "Triton and Vapetasia's PMTA marketing plans called for their products to be only sold in age-gated vape and specialty tobacco shops and through age-gated online sales." But FDA had already explained that such attempts do *not* work:

> FDA has been focusing enforcement efforts on age verification as a strategy to address youth use of tobacco products, and FDA continues to enforce age restrictions. However, FDA believes that age verification alone is not sufficient to address this issue, given the most recent data that youth use of ENDS products continues to increase. FDA determined that focusing on how the product was sold would not be sufficient to address youth use of these products given the many sources of products available for youth access. The reality is that youth have continued access to ENDS products in the face of legal prohibitions and even after voluntary actions by some manufacturers.

2020 Guidance at 44.

The burden falls on Petitioners to show that they would have received authorization had FDA considered these plans. *See, e.g.*, *Shinseki v. Sanders*,

556 U.S. 396, 409 (2009); *Am. Airlines, Inc. v. Dep't of Transp.*, 202 F.3d 788, 797 (5th Cir. 2000). They have not done so. Given that the TCA incorporates the APA's harmless error rule—*see* 21 U.S.C. § 387*l*(b); 5 U.S.C. § 706—Petitioners' failure to show harm necessitates the denial of relief.

* * *

Congress passed the TCA in an active effort to protect public health. In serving that purpose, we cannot say that FDA acted arbitrarily and capriciously by disagreeing with Petitioners as to the significance of the evidence they presented. Of course, nothing prevents Petitioners from reapplying with further evidence (and then seeking judicial review after further agency action). But as to the present state, we conclude that the petitions are DENIED.

EDITH H. JONES, *Circuit Judge*, dissenting:

Six judges of this court have reviewed the FDA's "reasons" for removing from the market and destroying the business for these petitioners' electronic nicotine delivery system ("ENDS") products. Four of us have found the agency's decisions seriously inadequate, but at least the debate with my colleagues is founded on known standards. Not so FDA's actions. In a mockery of "reasoned" administrative decision-making, FDA (1) changed the rules for private entities in the middle of their marketing application process, (2) failed to notify the public of the changes in time for compliance, and then (3) rubber-stamped the denial of their marketing applications *because of* the hitherto unknown requirements. *See DHS v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1909 (2020). Kafka would have understood the FDA all too well. The agency's decisions are arbitrary and capricious. I dissent.

I. BACKGROUND

Petitioners' flavored nicotine-flavored liquids are among a host of "tobacco products" (although they contain no tobacco) that have fallen within the regulatory purview of the FDA since 2016. *See* 81 Fed. Reg. 28974 (May 10, 2016) ("the deeming rule").[1] To continue selling their flavored liquids, Petitioners had to submit a premarket tobacco product application ("PMTA") to the FDA by September 9, 2020. *See* 21 U.S.C. § 387j; *Vapor Tech. Ass'n v. FDA*, 97 F.3d 496, 498-501 (6th Cir. 2020). If the FDA issues a marketing denial order ("MDO") in response to a PMTA, sales of the products become unlawful. Given that ENDS product companies' very

[1] Petitioners' products are used in "open system" e-cigarettes, which are distinct from "closed system" cartridge-type and disposable e-cigarettes. According to FDA's studies, disposable or cartridge-based products are overwhelmingly more attractive to youthful users because they are discreet, easy to operate and conceal.

existence depended on securing marketing approval, petitioners had significant incentives to get the applications right. Recognizing this, the FDA put an extensive amount of information out to the public about what was relevant to a successful application, and what was not.

Toward that end, in October 2018 the FDA held a two-day public meeting to "improve public understanding . . . on the process for the submission and review of [PMTAs]." Tobacco Product Application Review – A Public Meeting (October 22, 2018), https://bit.ly/3FhPxJi. In relaying the types of studies that could support a PMTA, an FDA representative stated: "*No specific studies are required for a PMTA*; it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies given *other data sources* can support the PMTA." Premarket Tobacco Product Application Content Overview: Iilun Murphy – OS/Division of Individual Health Science (October 23, 2018) (emphasis added).

In June 2019, the FDA issued final guidance on PMTAs for ENDS products, the purpose of which was to "assist persons submitting [PMTAs] for [ENDS]" products and to "enable ENDS manufacturers to consider and strengthen their applications." FDA, Guidance for Industry, Premarket Tobacco Applications for Electronic Nicotine Delivery Systems (June 2019); Triton-FDA2-004408, 004411. The FDA's guidance made four salient points. First, "in general, *FDA does not expect that applicants will need to conduct long-term studies to support an application*." Triton FDA2-004423 (emphasis added). Second, although randomized clinical studies "could address cessation behavior of users of tobacco products, FDA believes this would *also be true for observational studies (perception, actual use, or both) examining cessation behaviors*." Triton-FDA2-004448 (emphasis added). Third, FDA intended to review each PMTA and weigh all the benefits and

risks from the product. Fourth, FDA would specifically pay attention to marketing restrictions that could restrict distribution to underage users.

In September 2019, FDA's proposed rule governing PMTAs reinforced all of these points. In particular, the agency stated once again that long-term studies were *not* expected. In addition, the FDA re-emphasized that marketing plans *were* critical:

> *"[t]he applicant's marketing plans* will help FDA determine whether permitting the marketing of the new tobacco product would be [appropriate for the protection of the public health] because they *will provide input that is critical* to FDA's determination of the likelihood of changes in tobacco product use behavior, especially when considered in conjunction with other information contained in the application. *FDA will review the marketing plan* to evaluate potential youth access to, and youth exposure to the labeling, advertising, marketing, or promotion of, a new tobacco product."

84 Fed. Reg. 50566, 50581 (Sept. 25, 2019) (emphasis added).

Petitioners assumed that these guidelines governed their applications, and accordingly prepared applications that emphasized their restrictive marketing but did not include long-term studies on smoking cessation behavior. The PMTAs were timely filed on September 9, 2020.

1. The New Rules.

Ten months later, when FDA was inundated by literally millions of PMTAs, the agency circulated an internal memorandum providing a new "standard of evidence" for some PMTAs for flavored ENDS products. *See* Triton-FDA2-005144-005155 (July 9, 2021). This memo was not publicly released, though its intent was to facilitate "final action on as many applications as possible by September 10, 2021." *See* Triton-FDA2-005144. Given the "large number of applications that remain[ed] to be reviewed by September 9, 2021," the memo explained that in lieu of reviewing applications on an individualized basis, the FDA would "conduct a Fatal

Flaw review . . . a simple review in which the reviewer examines the submission to identify whether or not it contains *the necessary type of studies*[].” Triton-FDA2-005145 (emphasis added). The “fatal flaw” would be the absence of studies—that is to say, long-term studies that the agency previously stated were neither necessary nor expected. Triton-FDA2-005144 - 45. Put bluntly, the memo ensured that even if an applicant followed FDA’s pre-deadline public statements and proposed rule, the FDA would nonetheless deny a PMTA because it failed to satisfy the internal non-public requirement for “the necessary type of studies” crafted in July 2021. FDA asserts that the Fatal Flaw memo was rescinded, but its approach appears to have been followed in a check-box “scientific review” form that indicated only whether a PMTA included a randomized controlled trial or longitudinal cohort study. Triton FDA1-000247-000260.

Similarly, FDA changed its mind about reviewing marketing plans and decided not to do so “for the sake of efficiency.” Significant sections of that internal memo, though also claimed by FDA to be rescinded,[2] are copied word-for-word in the TPLs for petitioners’ products.

2. The Late Notice.

The FDA revealed its new *modus operandi* concerning long-term studies on August 26, 2021 in a press release when it denied 55,000 ENDS products PMTAs in one day. Thus, nearly a year after the PMTA deadline, FDA announced that it would authorize the flavored ENDS products only if the PMTAs included previously purely optional studies, *i.e.*, long-term studies showing that the applicant’s flavored ENDS products effectively promoted cessation from cigarette smoking in a manner that outweighs the potential risk to youth. FDA, Press Release, FDA Denies Marketing

[2] PMTA Review: Evidence to Demonstrate Benefit of Flavored ENDS to Adult Smokers. FDA, Aug. 25, 2021.

Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health (Aug. 26, 2021), https://bit.ly/2YsYmzd.

Petitioners' PMTAs were not among the first batch of denials. *Id.* In an attempt to adjust to the new requirement, petitioners submitted a letter to the FDA on September 1, 2021, stating that they intended to conduct additional behavioral studies on adult smoking cessation and long-term studies of their products to supplement their PMTAs.

3. Rubber-stamped denials.

Their prompt reaction was in vain. On September 14, FDA issued MDOs denying them the right to sell their flavored liquids in the United States. The MDOs refused to consider, much less evaluate the petitioners' marketing plans "for the sake of efficiency."[3] TRITON-FDA 1–000279. Petitioners were denied any attempt to comply with the new rule, FDA informed them, because the September 1, 2021 letter was "received near the completion of scientific review." Triton-FDA1-000123. The MDOs perfunctorily concluded that their evidence failed to demonstrate "robustly" and "reliably" the magnitude of their flavored products' potential benefit to adult smokers. Such evidence, however, "could have been provided using a randomized controlled trial and/or longitudinal study that demonstrated the benefit of your flavored ends products over an appropriate tobacco-flavored ends." Triton-FDA1-000124.

[3] This MDO also states that "none of the ENDS PMTAs that FDA has evaluated have proposed advertising and promotion restrictions that would decrease appeal to youth to a degree significant enough to address and counter-balance the substantial concerns, and supporting evidence, discussed above regarding youth use." Because FDA had not seen a successful marketing plan on past applications, it generalized, all future applications must lack worthwhile marketing plans. So much for individualized consideration of marketing plans.

The TPLs furnished to petitioners as alleged backup for the MDOs is more egregiously out of step with all of FDA's pre-deadline policies, as it states that, "[b]ased on existing scientific evidence and our experiences in conducting premarket review employing the APPH standard *over the last several years,* FDA has determined….most likely product specific evidence from a randomized controlled trial (RCT) or longitudinal controlled study" will be adequate. Triton-FDA1-000271. Later, the TPL recounts, contrary to the agency's previous representations, that the types of studies it earlier promoted must also be conducted "over time."

4. The Post Mortem Rule

FDA published its final PMTA Rule on October 4, 2021, a rule consistent with its prior pre-August 2021 policies but inconsistent with the process described in petitioners' MDOs. FDA, Premarket Tobacco Product Applications and Recordkeeping Requirements, Final Rule, 86 Fed. Reg. 55300. The Final Rule, yet again, states that the FDA does "not expect that applicants will need to conduct long-term clinical studies to support an application." 86 Fed. Reg. 55300, 55387. Contrary to the fatal flaw approach, the final rule states that the "FDA declines to create a series of criteria that either all products or a specific subset of products must meet in order for marketing of such products to be considered as part of this rule." *Id.* at 55386. Instead, FDA assured that it would "consider[] many factors," *id*. at 55314, would not rely on "one static set of requirements" *id*. at 55385, does not assign weight to different types of evidence, *id*. at 55335, and carefully "balances" risks and benefits, *id*. at 55384.

Concerning marketing plans, the FDA's Final Rule repeatedly contradicts the MDOs' flat refusal to consider them, as it explains that "FDA has rationally concluded that the required descriptions of marketing plans will directly inform its assessment of who may be exposed to the

[marketing processes] and, as a result, its consideration of the potential impact on youth initiation and use. *Id.* at 55324.[4]

II. Discussion

As noted, the majority and I agree that according to the Administrative Procedure Act, we must decide whether the FDA's decisions are "arbitrary and capricious…or not in accordance with law." 5 U.S.C. § 706(2)(A). The Supreme Court has succinctly explained that "[t]he APA's arbitrary and capricious standard requires that agency action be reasonable and reasonably explained." *FCC v. Prometheus Radio Project,* 141 S. Ct. 1150, 1158 (2021); *see also Motor Vehicle Mfs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 50, 103 S. Ct. 2856, 2870 (1983). We know our rules; I disagree that FDA followed those rules.

Although courts may not substitute our policy view for that of the agency, we must ensure the agency turns square corners[5] in dealing with the public to whom it is subservient. Consequently, agency action may not be justified to a court based on *post hoc* rationalization; the agency must "defend

[4] Several other courts have ruled on motions to stay FDAs MDOs concerning other ENDS products. Two courts granted stays, like the motions panel here, and one denied a stay. *See Gripum LLC v. FDA*, No. 21-2840, ECF No. 18 (7th Cir. Nov. 4, 2021); *Bidi Vapor LLC v. FDA, et al.*, No. 21-13340, Per Curiam Order (11th Cir. Feb 1, 2022); *Breeze Smoke, LLC v. United States Food & Drug Admin.*, 18 F.4th 499 (6th Cir. 2021) (denying motion to stay similar MDOs). In particular, I would distinguish the Sixth Circuit's ruling, touted by the panel, because it fails to acknowledge the abundant administrative record concerning FDA's public engagement with ENDS product suppliers, FDA's Sept. 2019 proposed rule, and the Final Rule, all of which are inconsistent with its perfunctory denial orders.

[5] Square corners is a turn of phrase used by Justice Robert Jackson. *See Fed. Crop Ins. Corp. v. Merrill*, 332 U.S. 380, 387–88, 68 S. Ct. 1, 5 (1947) (J. Jackson dissenting) (observing that regulatory law is a two-way street and that agencies when dealing with the regulated, just as much as citizens subject to their regulations, must turn square corners).

its actions based on the reasons it gave when it acted." *DHS v. Regents of the Univ. of Cal.,* 140 S. Ct. 1891, 1909 (2020). Nor may an agency wholly fail to consider "relevant factors" and "important aspect[s] of the problem." *Michigan v. EPA,* 576 U.S. 743, 752, 135 S. Ct. 2699, 2707 (2015). Nor may an agency thwart legitimate reliance interests by pulling a "surprise switcheroo" by changing its requirements too late for the petitioners to respond. *See Env't Integrity Project v. EPA*, 425 F.3d 992, 996 (D.C. Cir. 2005) (Sentelle, J.); *accord Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1810 (2019) (citing the "surprise switcheroo" doctrine).

The majority's analysis of these MDOs looks almost exclusively at the bottom-line result of FDA's decisions and finds nothing to criticize. But the facts recited above speak for themselves. FDA refused to review petitioners' marketing restrictions, which it had repeatedly stated were key to discouraging youthful use of the products and were thus critical components of the PMTAs. FDA repeatedly counselled applicants that long term studies were likely unnecessary and it said nothing about comparative efficacy studies—until the PMTA deadline was long gone; and then it refused petitioners the opportunity to conduct such studies. Finally, FDA's defense against petitioners on the merits of their applications is loaded with *post hoc* rationalizations. Any of these errors is a "fatal flaw." Taken together, they are mortal wounds.

The MDOs should be vacated, and the case remanded to FDA with instructions to allow these petitioners to develop and offer further evidence in support of the PMTAs.

A. Marketing Plans

The majority holds that the FDA's decision to ignore and not review the petitioners' plans was not arbitrary and capricious. To do this, the majority must themselves ignore the MDOs' only stated reason for ignoring

the plans: "for the sake of efficiency." The majority does not deny that "'efficiency' is no substitute for 'reasoned decisionmaking.'" *Wages & White Lion Invs., L.L.C. v. FDA*, 16 F.4th 1130, 1137 (5th Cir. 2021) (quoting *Michigan v. EPA,* 576 U.S. 743, 750, 135 S. Ct. at 2706). Instead, the majority relies on FDA's *post hoc* justifications for ignoring the marketing plans.

First, the majority accepts FDA's assertion that it had not in the past evaluated a marketing plan that discouraged youth from using ENDS products. This is not a "reason" for refusing to even look at these petitioners' MDOs. As the stay panel noted, this excuse is akin to a judge's saying, "she stopped reading briefs because she previously found them unhelpful." *Wages & White Lion,* 16 F.4th at 1137. It is obviously illogical and unreasonable to infer from the general to the particular, especially when FDA acknowledged its duty to consider each PMTA individually and holistically. Nor is the mere invocation of agency "expertise" a non-arbitrary substitute for an explanation how such expertise was brought to bear on the particular PMTA. "The requirement of explanation presumes the expertise and experience of the agency and still demands an adequate explanation in the particular matter." *CS Wind Viet. Co., Ltd. v. United States,* 832 F.3d 1367, 1377 (Fed. Cir. 2016)*(*citations omitted*).* The agency's failure to meaningfully consider an aspect of the petitioners' PMTAs that it had previously deemed essential is quintessentially arbitrary and capricious. *Univ. of Texas M.D. Anderson Cancer Ctr. v HHS,* 985 F.3d 472, 475 (5th Cir. 2021).

Second, the majority makes much of an FDA 2020 Guidance that decried increasing adolescent use of tobacco products starting in 2018 even after the agency cracked down on vape companies that marketed and sold ENDS products in packaging that looked like juice boxes and candy cartons. The 2020 Guidance, however, has nothing to do with this case because (a) it

discussed enforcement priorities, and it did not purport in any way to amend the definitive PMTA Guidance documents that emphasized the importance of marketing plans; (b) there is no evidence at all that these petitioners marketed or sold to youth directly or indirectly, knowingly or objectionably; (c) the 2020 Guidance was not referenced at all in the MDOs and is therefore an inadmissible *post hoc* explanation; and (d) the high level of youth vaping that spawned the 2020 Guidance had been underway since 2018, yet FDA did not adjust its PMTA Guidance materials significantly during this period.[6] Moreover, recourse to the 2020 Guidance as a basis for FDA's having disregarded the marketing plans is flatly contradicted by the Final PMTA Rule, which continued to stress the importance of such plans as a "critical factor" in FDA's approval decisions.

Third, the majority admits that since FDA never reviewed the marketing plans, "one could argue" it had no basis to find them neither "novel or materially different" from others. But wait—the majority relies on FDA's statement—in oral argument to *this court*—that its review actually included a summary of the marketing plan. This is judicial post hoc reasoning about a post hoc justification.

Fourth, and most objectionably, the majority blames *petitioners* for not knowing that "marketing plans on their own are not particularly useful."

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[6] The 2020 Guidance also focuses almost exclusively on the continuing attractiveness to youth of closed-system ENDS products, and very little if at all on bottled e-liquids for use in open systems. These petitioners produce bottled e-liquids. To the extent FDA means to say that youth will migrate to any flavored ENDS products if other avenues are closed off, it provided no evidence of that migration toward petitioners' products during the periods in question. In fact, the 2020 Guidance stated that it "should have minimal impact on those vape shops that primarily sell non-cartridge ENDS products and ensure that purchasers are of the requisite age and are not purchasing for resale[.]" Triton FDA-2-000321-000322.

That statement stands the requirement of reasoned *agency* decisionmaking on its head. Every single statement by the agency, until it issued its MDOs to these petitioners, reasonably led petitioners to believe that if they devised marketing arrangements that would prevent underage persons from purchasing their flavored e-liquids for open systems, they would have surmounted a significant requirement for marketing approval.

Finally, to assert that the agency's deliberate lapse amounted to "harmless error" is simply incorrect. Prejudice in the administrative law context does not involve a "complex system of 'burden shifting' rules or a particularly onerous requirement." *Shinseki v. Sanders,* 556 U.S. 396, 410, 129 S. Ct. 1696, 1706 (2009). An "APA deficiency is not prejudicial only when it is one that clearly had no bearing on the procedure used or the substance of decision reached." *United States v. Johnson,* 632 F.3d 912, 930 (5th Cir. 2011). Taken in conjunction with the agency's violation of other administrative norms through its failures of notice and ignoring petitioners' reliance interests, the majority has no basis for claiming harmless error.

For all these reasons, the agency cannot run away from individually reviewing petitioners' marketing plans when, for two years, it assured the public that properly tailored marketing of flavored ENDS products could protect youth from exposure and abuse while the products also helped those who need to stop smoking. It is the epitome of agency hubris to pull the rug out from entities whose very existence depends on the agency's careful balancing of all factors relevant to this public health issue.

B. Notice and Reliance Interests

The majority puts down petitioners' claimed "reliance interests" and denies that FDA pulled a "surprise switcheroo" by rejecting their PMTAs for lack of "randomized controlled trials" or "longitudinal cohort studies" showing the benefits of their products in enabling smoking cessation. The

majority reads FDA's pronouncements to have consistently conditioned its criteria for APPH studies or evidence and *never* to have *required* comparative efficacy studies of smoking cessation.

This is surprising, because petitioners were only advised in the TPLs underlying their MDOs[7]—when it was too late—that such studies are "most likely" to provide reliable and robust evidence to satisfy the APPH standard.[8] And only then were they advised that studies "over time" should have been included. From October 2018 through the September 2020 PMTA deadline, and until August 2021, the FDA continually repeated that such studies were neither necessary nor expected.[9] Instead, FDA stated that other forms of evidence, including observational and consumer-perception studies, as well as scientific literature reviews, could be acceptable. In August 2021, contrary to those pronouncements, FDA announced that it had denied 55,000 PMTAs precisely because they lacked "the evidence of benefits to adult smokers for such products [that] would likely be in the form of a randomized controlled trial or longitudinal cohort study…."

If this meandering administrative course is not an "administrative switcheroo," it is hard to know what is. For one thing, from FDA's denials

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[7] Petitioners did not receive TPLs automatically; they obtained them only through FOIA requests.

[8] Whether a product is "appropriate for the protection of the public health" is "determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product" and takes into account the likelihood that existing users of tobacco products will stop using such products; and the likelihood that those who do not use tobacco products will start using such products. 21 U.S.C. § 387j(c)(4).

[9] As has been explained, FDA also steadfastly represented the critical importance of marketing plans that would prevent underage youth from obtaining petitioners' products—until it backtracked on that requirement in the TPLs.

of 55,000 PMTAs one might reasonably infer that other manufacturers besides these petitioners were fooled by FDA's previous instructions. And that legitimate reliance interests were built into the previous FDA announcements is attested by an affidavit of petitioners' executive in charge of filing their PMTAs. Moreover, petitioners' business was generating $15 to 20 million annual revenues. Petitioners invested a half million dollars to complete their PMTAs and filed 9 gigabytes of information, including hundreds of files, with FDA in seeking marketing approval. They had every reason to file PMTAs most conscientiously and comprehensively because the existence of the company depended on agency approval of their products.

In light of all the circumstances, there are two ways to look at the MDOs in this case. Under one scenario, FDA changed its policies: from individualized consideration of PMTAs and flexibility as to the type of scientific evidence it would hold acceptable,[10] to perfunctory disapproval of PMTAs lacking longitudinal studies.[11] The majority nowhere acknowledges that during the entire pre-deadline process, FDA kept stating that it did not "expect" long-term studies to be necessary.

Viewed as a policy change, FDA acted arbitrarily and capriciously by failing to inform petitioners and by failing to consider their legitimate reliance interests. After all, "[t]hose regulated by an administrative agency are entitled to know the rules by which the game will be played." *Alaska Prof'l*

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[10] *See Nicopure Labs, LLC v. FDA,* 944 F.3d 267, 282 (D.C. Cir. 2019)("[t]he FDA has expressed willingness to accept scientific literature reviews instead of commissioned studies in support of e-cigarette applications in appropriate circumstances").

[11] The Triton MDO indicates that to be acceptable, the petitioner's "other evidence" had to "evaluat[e] the impact of the new flavored vs. tobacco-flavored products on adult smokers' switching or cigarette reduction *over time*." (emphasis added). Triton-FDA1-000115. This looks like a requirement of a commissioned, longitudinal study of some kind.

Hunters Ass'n. v. FAA, 177 F.3d 1030, 1035 (D.C. Cir. 1999) (abrogated on other grounds by *Perez v. Mortg. Bankers Ass'n*, 575 U.S. 92, 135 S. Ct. 1199 (2015)). Agencies must provide fair warning of conduct the agency "prohibits or requires" and cannot "unfair[ly] surprise" a party by penalizing it for "good-faith reliance" on the agency's prior positions. *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156-57, 132 S. Ct. 2156, 2167-68 (2012). The fair notice requirement applies as much to agencies' other public pronouncements as to its regulations. *See Gen. Elec. Co. v. EPA,* 53 F.3d 1324, 1329 (D.C. Cir. 1995) ("in many cases the agency's pre-enforcement efforts to bring about compliance will provide adequate notice," such as notifying regulated entities of process requirements). Serious reliance interests, moreover, must be taken into account when an agency changes longstanding policies. *See DHS v. Regents of the Univ. of Cal.*, 140 S. Ct. 1891, 1913 (2020). FDA's disregard for the principles of fair notice and consideration of reliance interests is exacerbated here by its refusal to allow petitioners to supplement their applications according to the new requirements.

This is not to say that FDA could not have formally changed its APPH requirement from the earlier Guidance documents and declared that *only* long-term, specific product studies would be acceptable, but it did not do that. *See Regents, id.* at 1914 ("[m]aking that difficult decision was the agency's job, but the agency failed to do it").

The second scenario posits that FDA's carefully crafted Guidance language authorized maximum agency discretion to approve or disapprove PMTAs as circumstances evolved. The "circumstances" entailed the increasing underage use of ENDS products, which resulted in the 2020

Guidance on which the majority rests much of its analysis.[12] Relying on snippets of Guidance language, FDA does not admit that it changed its evaluation policy, and the majority agrees. But this scenario is of no use in defending the MDOs. To begin, it is counterfactual. The MDOs rested on rejecting the types of evidence the agency had previously found likely sufficient, while requiring product-specific studies conducted "over time" that it had previously found unnecessary. But laying that aside, the Supreme Court holds that "[w]hen an agency changes its existing position, it…must at least display awareness that it is changing position and show that there are good reasons for the new policy." *Encino Motorcars, LLC v. Navarro,* 579 U.S. 211, 136 S. Ct. 2117, 2125-26 (2016) (quotation omitted). It follows that "unexplained inconsistency in agency policy is a reason for holding an [action] to be an arbitrary and capricious change from agency practice." *Id.* at 2126 (quotation omitted). FDA's migration from stating that "in general, FDA does not expect that applicants will need to conduct long-term studies to support an application" to denying petitioners' MDOs because they lacked long-term studies of comparative efficacy is "unexplained" and "inconsistent" and therefore arbitrary and capricious.

FDA, in sum, sealed the petitioners' doom by changing its evaluation rules without giving them notice and by ignoring individualized consideration of their plan for marketing restrictions to prevent underage youth access. Even with the noblest of motives in mind, a federal agency does not have license to run companies out of business without adhering to fixed rules of fair procedure. I respectfully dissent.

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[12] To repeat, however, the 2020 Guidance made no mention of and did not consider the elements necessary for petitioners to file successful PMTAs, nor did it alter agency policy regarding PMTAs; and it presumed "minimal impact" on shops selling products like those of petitioners.