IN THE SUPREME COURT OF THE UNITED STATES

No. 21A176

BREEZE SMOKE, LLC, APPLICANT,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION

ON APPLICATION FOR AN EMERGENCY STAY OF AGENCY ORDER PENDING THE DISPOSITION BY THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT OF A PETITION FOR REVIEW AND ANY FURTHER PROCEEDINGS IN THIS COURT

MEMORANDUM FOR THE RESPONDENT IN OPPOSITION

The Solicitor General, on behalf of the United States Food and Drug Administration (FDA), respectfully files this memorandum in opposition to the application for a stay of the agency's order pending the disposition of applicant's petition for review in the United States Court of Appeals for the Sixth Circuit.

INTRODUCTION

This case concerns applicant's desire to continue to sell dessert-flavored and fruit-flavored "e-cigarettes" while it challenges FDA's denial of its application for premarket authorization to permit the sale of those products. It is

uncontested that applicant's flavored e-cigarettes are tobacco products that, by statute, are unlawful to market without FDA authorization. It is also uncontested that it was unlawful to market such products for several years before applicant began selling them without FDA authorization in May 2019. And it is uncontested that in the past few years there has been "exponential growth" in children's use of e-cigarettes, with an estimated "3.6 million youth [e-cigarette] users in 2020," the majority of whom use "flavored" products like applicant's. Appl. App. 26a.

Under the Family Smoking Prevention and Tobacco Control Act (TCA), Pub. L. No. 111-31, Div. A, 123 Stat. 1776 (2009), all "new tobacco products," such as applicant's e-cigarettes, are unlawful to market absent FDA authorization. Congress directed FDA to deny an application for such authorization unless the agency finds that the applicant has shown that marketing the product would be appropriate for the protection of the public health. Congress specified that FDA must evaluate both the likelihood that existing tobacco users would stop such use and the likelihood that those who do not use tobacco products will start. Under that standard, FDA weighs, among other things, the risk that a new product poses to youth who may begin to use it against the product's potential benefit in helping adults limit or cease traditional cigarette use. FDA has made substantial progress acting on marketing applications it has received for millions of new tobacco products,

and has to date denied authorization to "more than 946,000 flavored [e-cigarette] products because [the] applications lacked sufficient evidence" of a public-health benefit given the "alarming levels" at which children use those products. FDA, FDA Makes Significant Progress in Science-Based Public Health Application Review, Taking Action on Over 90% of More Than 6.5 Million 'Deemed' New Tobacco Products Submitted (Sept. 9, 2021) (September 2021 Announcement).[1] FDA continues to consider the possibility that, despite the dangers to youth of tobacco products flavored like candy or fruit, a manufacturer could demonstrate that its flavored e-cigarette product satisfies the criteria Congress set out in the TCA. See ibid. But FDA has denied marketing authorization to applicant and others that have not made the requisite public-health showing under the statute.

Applicant failed to persuade the court of appeals that a stay of FDA's order denying its application would be appropriate, and now seeks extraordinary relief from this Court while the Sixth Circuit considers applicant's petition for review on an expedited basis. Applicant's cursory attempt to show that this Court would grant a writ of certiorari to review a decision by the court of appeals upholding FDA's order is unavailing, which should alone preclude a stay here. Moreover, as the court of appeals concluded,

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[1] https://www.fda.gov/news-events/press-announcements/fda-makes-significant-progress-science-based-public-health-application-review-taking-action-over-90.

applicant cannot establish a likelihood of success on the merits of its claim that FDA wrongfully concluded that applicant failed to show that authorizing its flavored e-cigarettes would be appropriate for the protection of the public health under the TCA's criteria. FDA's decision was supported by "well-developed evidence showing that flavored [e-cigarette] products' special appeal to youths harms the public health to a degree not outweighed by the (far-less-supported) effects of adult cigarette smokers switch[ing] to e-cigarettes." Appl. App. 9a. And applicant's dissatisfaction with several aspects of FDA's decision-making provides no basis to overturn the agency's conclusion.

Additionally, a stay of FDA's order denying marketing authorization would not permit applicant to lawfully market and sell products like its "Strawberry Cream" e-cigarettes. FDA's order denying marketing authorization did not render applicant's products unlawful to sell; they were already unlawful under the statute. And staying (or even rescinding) that order would not make it lawful to sell them, as they would still lack the statutorily required authorization by FDA. That would be true for any e-cigarette manufacturer, but applicant's claim to some form of reliance interest in continuing to sell unauthorized e-cigarettes is particularly weak. Applicant began selling those products only in 2019, and thus does not appear to be within the ambit of FDA's 2016 announcement that it intended to temporarily

defer enforcement against e-cigarette products already on the market when such products became subject to the premarket authorization requirement. At minimum, FDA's actions should have made it clear to applicant since the day it started selling e-cigarettes that its products were presumptively unlawful -- a fact undermining any claim that equity supports a stay purportedly facilitating applicant's continued sale of unauthorized tobacco products during proceedings in the court of appeals.

Finally, applicant's concerns about an imminent FDA enforcement action are misplaced. While there is no legal barrier to such an action, FDA has not departed -- and does not intend to depart here -- from its usual practice of sending a warning letter, affording a chance for a response, and considering that response before it initiates an enforcement proceeding. Consistent with that practice, FDA has informed this Office that it will not initiate an enforcement action related to premarket-authorization requirements for new tobacco products against applicant in fewer than 30 days after sending any such warning letter. Thus, while simply denying a stay would be the most appropriate course, this Court in the alternative could deny applicant's current request without prejudice to renewal should FDA send a warning letter before the commencement of an enforcement action, which would provide sufficient time to consider applicant's arguments in a concrete context.

STATEMENT

1. The TCA established a comprehensive scheme for the regulation of tobacco products. The Act was predicated on Congress's finding that the use of tobacco products by youth "is a pediatric disease of considerable proportions." TCA § 2(1), 123 Stat. 1777. The TCA applies to products such as cigarettes and smokeless tobacco, as well as to other products made or derived from tobacco that FDA by regulation deems to be subject to the Act. 21 U.S.C. 387a(b); 21 U.S.C. 321(rr); see pp. 7-8, infra (discussing FDA's decision deeming e-cigarettes subject to the TCA).

The TCA provision at issue here makes it unlawful for a manufacturer to introduce in interstate commerce any "new tobacco product" unless the manufacturer obtains premarket authorization from FDA. 21 U.S.C. 387j(a)(1) and (2). The statute defines a "new tobacco product" as a tobacco product that was not commercially marketed in the United States as of February 15, 2007, or that was modified after that date. 21 U.S.C. 387j(a)(1).

The TCA provides that FDA "shall deny" a manufacturer's application to market a new tobacco product "if, upon the basis of the information submitted to [FDA] as part of the application and any other information before [FDA] with respect to such tobacco product," the agency "finds that * * * 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." 21 U.S.C. 387j(c)(2)(A). The TCA specifies that, in making that public-health determination, FDA must evaluate "the risks and benefits to the population as a whole, including users and nonusers of the tobacco product," taking into account both 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." 21 U.S.C. 387j(c)(4). Because "[v]irtually all new users of tobacco products are under the minimum legal age to purchase such products," TCA § 2(4), 123 Stat. 1777, FDA weighs (among other things) the risk that a new tobacco product will be attractive to youth against the product's potential for helping adults who smoke combustible cigarettes to switch to a less dangerous alternative.

2. Electronic nicotine delivery systems -- which are colloquially known as e-cigarettes -- deliver nicotine, which is "among the most addictive substances used by humans," "by vaporizing a liquid that includes other chemicals and flavorings." Nicopure Labs, LLC v. FDA, 944 F.3d 267, 270 (D.C. Cir. 2019). "The device heats the liquid until it generates an aerosol -- or 'vapor' -- that can be inhaled." Ibid.

In 2016, FDA exercised its statutory authority to deem e-cigarettes (among other tobacco products) to be subject to the TCA's requirements. 81 Fed. Reg. 28,974 (May 10, 2016). Because

e-cigarettes meet the TCA's definition of a "new tobacco product," the TCA made it unlawful to market e-cigarettes without FDA authorization after the 2016 rule's effective date. As a policy matter, however, FDA decided against immediate enforcement of that statutory prohibition, but only for products on the market as of that effective date. Id. at 28,977-28,978; see id. at 29,011 n.13 (stating "any new tobacco product that was not on the market on the effective date of the rule (i.e., 90 days after the publication date) is not covered by th[e] compliance policy and will be subject to enforcement if marketed without authorization after the effective date"). Through enforcement policies that FDA has revised over time, the agency has sought to strike a balance between the well-documented, serious risks that e-cigarettes pose for youth, on the one hand, and the potential for some such products to help addicted adult smokers seeking to quit or significantly reduce smoking combustible cigarettes, on the other. But FDA has "repeatedly emphasized that the availability of non-combustible options should not come at the expense of addicting a generation of children to nicotine through these same delivery vehicles." FDA, Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised) 38 (Apr. 2020) (2020 Guidance) (describing the evolution of FDA's enforcement

policies).[2] Moreover, FDA has "consistently informed industry that its compliance policies will be responsive to changed circumstances," id. at 35, and that "manufacturers cannot have settled expectations to market unlawful products, especially in the face of evolving public health concerns," id. at 36.

Initially, FDA announced that, for e-cigarettes already on the market as of the 2016 rule's effective date, the agency generally would not take enforcement action based on a product's lack of premarket authorization for a two-to-three-year period, while manufacturers prepared, and FDA reviewed, applications for authorization to market their products. 81 Fed. Reg. at 28,978. In 2017 guidance, FDA extended that intended non-enforcement period until 2022. See 2020 Guidance 5. Prior to that announcement, nationally representative data suggested that youth use of e-cigarettes had declined beginning in 2016. Ibid.

By late 2017, however, FDA noticed an alarming increase in the use of e-cigarettes by middle school and high school students. 2020 Guidance 6. In 2018, FDA took additional steps to target e-cigarette marketing to youth and prevent children's access to such products. Id. at 6-7. In addition, FDA requested that certain manufacturers submit plans to help restrict minors' access to e-cigarettes. Id. at 7. In response to that 2018 request,

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[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-priorities-electronic-nicotine-delivery-system-ends-and-other-deemed-products-market.

manufacturers proposed safeguards such as age-verification technology for online sales, enhanced monitoring of retailer compliance with age-verification and sales restrictions, contractual penalties for retailers that failed to comply with such requirements, and limits on the quantity of e-cigarettes that a customer could purchase within a particular period of time. Ibid.

Despite these measures, in 2019, youth e-cigarette use hit the highest levels ever recorded. 2020 Guidance 8. FDA thus revised its enforcement policy. Although FDA continued to enforce youth-sales restrictions, FDA concluded that "age verification alone is not sufficient to address this issue, given the most recent data that youth use of [e-cigarette] products continues to increase." Id. at 44; see also id. at 21. "The reality," FDA explained, "is that youth have continued access to [e-cigarette] products in the face of legal prohibitions and even after voluntary actions by some manufacturers." Id. at 21. Indeed, FDA observed that many youth obtain e-cigarette products from friends or sources in their social networks. Id. at 45. FDA determined that sales restrictions alone would "not be sufficient to address youth use of these products." Id. at 44.

Instead of focusing solely on how an e-cigarette product is sold, FDA's 2020 compliance policy concerning products on the market prior to August 2016 prioritized enforcement against

products that were, in 2020, especially popular with youth: certain types of flavored e-cigarettes (other than tobacco-flavored or menthol-flavored products). 2020 Guidance 10; see also Appl. App. 20a n.ii (defining "flavored" e-cigarettes as excluding tobacco and menthol flavors). FDA emphasized the "extraordinary popularity" of such flavored e-cigarette products with youth, id. at 13, noting for example that 93% of e-cigarette users aged 12-17 reported that their first e-cigarette use was with a flavored product and that 71% of youth users indicated they used e-cigarettes "because they come in flavors I like," id. at 14 (citation omitted). And while FDA focused its concern at that point on particular types of "cartridge-based" products, it made clear that it would "make enforcement decisions on a case-by-case basis" and that FDA "retains discretion to pursue enforcement action at any time against any deemed new tobacco product marketed without premarket authorization." Id. at 11.

Although the 2020 enforcement policy led to the removal of many flavored products from the market and contributed to a decline in youth use, such use remained at levels comparable to those that originally led FDA to declare a youth vaping epidemic in 2018. Appl. App. 21a-22a. FDA explained in its decision in this case that the resulting level of usage illustrated that the removal of some flavored products prompted youth to migrate to others that offered the desired flavor options, "underscoring the fundamental

role of flavor in driving appeal." Id. at 25a. Data from the 2020 National Youth Tobacco Survey confirmed that flavor drives underage use: 84.7% of high school e-cigarette users and 73.9% of middle school users reported using a flavored product. Id. at 23a. And the role of flavor for youth was consistent across different device types. Id. at 24a-25a.

3. a. Shortly before September 9, 2020, FDA received a large volume of applications to market e-cigarette products. That influx resulted in part from a court-ordered deadline imposed in an action brought against FDA by public-health organizations. See Am. Acad. of Pediatrics v. FDA, 399 F. Supp. 3d 479 (D. Md. 2019), aff'd in part, appeal dismissed in part sub nom. In re Cigar Ass'n of Am., 812 Fed. Appx. 128 (4th Cir. 2020) (per curiam). The court observed in that case that, "however laudable the FDA's intended regulatory response is, the record before me shows a purposeful avoidance by the industry of complying with the premarket requirements despite entreaties from the FDA that it can do so, and it establishes a shockingly low rate of filings." Id. at 485. The court therefore directed FDA to require that "for new tobacco products on the market as of the August 8, 2016 effective date of the Deeming Rule * * * applications for marketing orders must be filed within 10 months" -- a date later extended to September 9, 2020, as a result of the pandemic -- and provided that such products for which timely applications had been submitted could

remain on the market without being subject to FDA enforcement action for one year pending FDA review, although the agency retained enforcement discretion. Id. at 487; 18-cv-883 D. Ct. Doc. 182 (D. Md. Apr. 22, 2020).

FDA has acted on many of those e-cigarette applications. To date, the applications that FDA has granted have been for tobacco-flavored e-cigarette products. See FDA, Technical Project Lead (TPL) Review of PMTAs (submission of R.J. Reynolds Vapor Company) (Oct. 12, 2021).[3] In authorizing the marketing of those products, FDA determined that youth interest in tobacco flavors is generally low. Id. at 17. For example, a 2020 nationwide survey found that the prevalence of use of tobacco-flavored e-cigarette products was 2.9% among 10th and 12th grade e-cigarette users, as compared with 59.3% for fruit flavors. Ibid. Furthermore, FDA explained that adults had the "highest purchase intent" for tobacco-flavored products. Ibid.; see id. at 4. FDA thus concluded that the applicant seeking authorization for a tobacco-flavored e-cigarette had demonstrated that current adult smokers are particularly interested in the proposed new products to assist in intended switching from combustible cigarettes, and that those products have the potential to benefit that group as compared to continued exclusive use of combustible cigarettes. Id. at 4. After conducting a full scientific review, FDA found that permitting the

[3] https://www.fda.gov/media/153017/download.

marketing of those tobacco-flavored products would be appropriate for the protection of the public health. Ibid.

b. FDA has denied, or is still considering, applications to market some e-cigarette products with flavors such as fruit and candy. In issuing the order here, in which FDA denied authorization to market flavored e-cigarettes that applicant first began to sell in 2019, FDA explained that the serious risk that such flavored products pose to youth is well documented by nationally representative studies. Appl. App. 23a-24a, 40a. Thus, FDA explained, an application to market flavored products must show that such a significant risk to youth is outweighed by likely benefits to existing users of tobacco products "substantial enough such that the net impact to public health would be positive." Id. at 27a. "[A]s the known risks [of a product] increase, so too does the burden of demonstrating a substantial enough benefit" to establish that the marketing of the product is appropriate for the protection of the public health, as the TCA requires. Ibid.

In reviewing applicant's application, FDA therefore considered whether applicant provided robust and reliable evidence showing that its flavored products at issue would provide a significant benefit to existing users of tobacco products by facilitating smokers completely switching away from or significantly reducing their smoking of combustible cigarettes. Appl. App. 28a-29a. The agency also looked for evidence that the

benefit to existing users would be greater than the benefit provided by comparable tobacco-flavored products, which present a less significant risk to youth. Ibid. FDA indicated that such evidence "could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of [applicant's] flavored [e-cigarette] products over an appropriate comparator tobacco-flavored" e-cigarette, but FDA also stated its willingness to "consider other evidence" that "reliably and robustly evaluated the impact of the new flavored vs. tobacco-flavored products on adult smokers' switching or cigarette reduction over time." Id. at 32a. Some manufacturers submitted evidence of a type that could potentially support such a finding for their flavored products; those applications require further evaluation and remain under agency review. See, e.g., Turning Point Brands, Inc. v. U.S. Food and Drug Admin., 21-3855 C.A. Doc. 19 (6th Cir. Oct. 8, 2021) (noting FDA's agreement to reconsider applications when it overlooked such evidence). FDA concluded, however, that applicant did not submit such evidence, explaining that the "survey data" applicant provided "is not sufficient to show a benefit to adult smokers of using these flavored [e-cigarettes] because it does not evaluate product switching or cigarette reduction resulting from use of these products over time or evaluate these outcomes based on flavor type to enable comparisons between tobacco and other flavors." Appl. App. 32a.

FDA thus denied the application on September 16, 2021. Id. at 12a-14a.

4. Two weeks later, on October 4, 2021, applicant filed a petition for review in the Sixth Circuit. The court of appeals agreed to expedite the case, setting a briefing schedule to conclude by December 24, 2021. See C.A. Doc. 9-2 (Oct. 15, 2021). The court denied applicant's request for an administrative stay, C.A. Doc. 21-2 (Oct. 27, 2021), and on November 12, 2021, it issued a published order denying applicant's motion for a stay, Appl. App. 1a-10a. A majority of the panel explained that applicant "has not made a strong showing that it would likely succeed on its claim that the FDA's review of its application was arbitrary or capricious." Id. at 3a. Nor did applicant "ma[ke] a strong showing that the FDA's denial of its application contradicted the FDA's nonbinding 2019 guidance," which "contemplated more rigorous scientific data than [applicant's] application contained." Ibid.

The court of appeals observed that "flavored e-cigarettes disproportionately appeal to children," and that "[t]he FDA, under a statutory obligation to approve only those products that are 'appropriate for the protection of the public health,' must determine whether applicants can show that their flavored [e-cigarette] product will benefit public health enough to outweigh this public-health detriment to children," particularly given the existence of tobacco-flavored e-cigarettes already on the market

that may help adult smokers shift away from combustible tobacco products. Appl. App. 5a. The court explained that although "FDA suggested that randomized control trials would present the strongest evidence of appropriateness for the public health," it also "acknowledged that applicants theoretically could 'rely on, and bridge to,' data concerning general [e-cigarette] category literature." Id. at 6a (quoting id. at 28a). When the court reviewed the evidence applicant submitted, however, it determined that applicant had offered only "mixed findings on flavored [e-cigarette] products," and concluded that "as the FDA noted in its denial of [appliant's] application, the 'clear and consistent patterns of real-world use' showing youth initiation of flavored [e-cigarette] products rendered" such evidence "insufficient." Id. at 6a-7a. The court also observed that applicant's "survey presents methodological issues" that "suggest[] biased respondents," given that it was "submitted via Google Form" and "contained responses from customers solicited . . . by request in the retail stores." Id. at 7a (citation and internal quotation marks omitted).

The court of appeals also explained that applicant and the Fifth Circuit were wrong to conclude that FDA had "orchestrated a 'surprise switcheroo'" in terms of the evidence required. Appl. App. 7a (quoting Wages & White Lion Invs., L.L.C. v. FDA, 16 F.4th 1130, 1138 (5th Cir. 2021)). The agency, the court observed, had

only indicated that "it might accept evidence other than long-term studies, if that evidence had sufficient scientific underpinnings to meet the TCA's statutory mandate of demonstrating that flavored [e-cigarette] devices are appropriate for the protection of public health." Ibid. FDA found applicant's "evidence lacking against this standard," and the court declined to embrace applicant's claim "that the FDA's willingness to consider some forms of evidence * * * required the FDA to accept that evidence as meeting a statutory requirement even where the FDA found the evidence unsatisfactory." Id. at 8a (emphasis added).

Although the court of appeals stated that "FDA likely should have more thoroughly considered [applicant's] marketing plan," it nonetheless found that "the FDA likely properly concluded that [applicant] failed to show that its products adequately protected the public health" and that applicant failed to meet its "burden of showing a strong likelihood of success on the merits." Appl. App. 8a-9a. The court of appeals observed that "FDA reasonably concluded that [applicant's] application did not meet the TCA's requirements that new tobacco products be appropriate for the protection of the public health," noting that the agency "cited well-developed evidence showing that flavored [e-cigarette] products' special appeal to youths harms the public health to a degree not outweighed by the (far-less-supported) effects of adult cigarette smokers switch[ing] to e-cigarettes." Id. at 9a. Given

applicant's failure to show "a strong likelihood of success on the merits," the court did not consider "the other stay factors" or "FDA's argument that, were [the court] to grant a stay, [applicant] would still lack the necessary authorization to market its products." Id. at 10a.

Judge Kethledge dissented, stating he would follow the Fifth Circuit and grant a stay. Appl. App. 11a.

ARGUMENT

Applicant asks (Appl. 1) this Court to grant "an immediate stay" of FDA's order denying applicant's request for authorization to lawfully market its flavored e-cigarettes. When an individual Justice is asked to stay an order while a case is pending in the court of appeals, the Justice must "try to predict whether four Justices would vote to grant certiorari should the Court of Appeals affirm the * * * order without modification; try to predict whether the Court would then set the order aside; and balance the so-called 'stay equities.'" San Diegans for the Mt. Soledad Nat'l War Mem'l v. Paulson, 548 U.S. 1301, 1302-1303 (2006) (Kennedy, J., in chambers) (citation omitted). A stay on a matter currently pending before a court of appeals is an extraordinary remedy that is "rarely granted." Heckler v. Lopez, 463 U.S. 1328, 1330 (1983) (Rehnquist, J., in chambers) (quoting Atiyeh v. Capps, 449 U.S. 1312, 1313 (1981) (Rehnquist, J., in chambers)). Applicant has not carried its burden of showing a stay is justified here.

1. Applicant only briefly attempts (Appl. 32-33) to make the required showing that a grant of certiorari would be likely if the court of appeals ultimately sustains FDA's marketing denial order. Applicant does not attempt to identify any particular question on which it believes certiorari would be warranted. To the extent applicant suggests that this Court's review would be warranted to correct any error the court of appeals might make following review on the merits, that is incorrect. See Sup. Ct. R. 10. And applicant's apparent reliance (Appl. 32) on its prediction that a conflict will develop among the circuits in their ultimate merits decisions regarding FDA's approach to flavored e-cigarettes is misplaced; such prognostications are at minimum premature, given that the courts of appeals are just beginning to consider denials of applications and this case is only one of two in which a court has given even a preliminary explanation of its views regarding challenges to the denial of authorization to market e-cigarettes. Even assuming some courts ultimately vacate FDA orders and other courts sustain them, applicant gives no reason to think that any divergence would focus on a single and concrete legal issue that would warrant this Court's attention.

That is particularly so given that many of the challenges that applicant and other manufacturers have made to FDA's decisions regarding e-cigarettes would at most require a remand to the agency for further consideration or explanation. See, e.g., Fla. Power

& Light Co. v. Lorion, 470 U.S. 729, 744 (1985); Appl. 29 (contending that FDA failed to consider evidence); White Lion, 16 F.4th at 1139 (addressing another manufacturer's claim that "FDA insufficiently addressed alternatives" to a denial order). Even if different circuits were to reach different conclusions as to such challenges, thus requiring further agency proceedings in some cases, there is no reason to foresee the development of the sort of intractable division among the circuits as to the ultimate disposition of premarket-authorization applications and petitions for review filed by similarly situated manufacturers that might warrant certiorari. The unlikelihood that this Court would grant certiorari means that a stay is unwarranted irrespective of applicant's arguments that it will be irreparably harmed in the absence of a stay. See Stephen M. Shapiro et al., Supreme Court Practice § 17.13(b), at 17-38, 17-40 (11th ed. 2019) (citing cases).

2. Apart from applicant's failure to establish a likelihood of a future grant of certiorari, the application for a stay should be denied because applicant cannot establish a likelihood of success on the merits of its claim that FDA erred in declining to authorize it to market dessert-flavored and fruit-flavored e-cigarettes of the sort that have been found to attract children. As the court of appeals explained, "FDA reasonably concluded that [applicant's] application did not meet the TCA's requirements that

new tobacco products be appropriate for the protection of the public health," in light of the "well-developed evidence" of risks to youth that outweigh any public health benefits to adult smokers. Appl. App. 9a. Applicant cannot show that FDA's decision on that score "contradicted" the agency's earlier guidance or "that [applicant] would likely succeed on its claim that the FDA's review of its application was arbitrary or capricious." Id. at 3a; see id. at 3a-10a.

a. As the court of appeals explained, FDA reasonably concluded, based on solid data, that applicant failed to make the requisite showing regarding the public-health benefits of its dessert-flavored and fruit-flavored e-cigarettes. In applying the TCA's public-health standard to applicant's application to market flavored e-cigarettes, FDA explained that evidence of the role of flavored products in youth initiation is well-established and that the resulting nicotine addiction has lifelong consequences. FDA noted, for example, that in 2020, approximately 19.6% of U.S. high school students and 4.7% of middle school students -- approximately 3.6 million students -- were current users of e-cigarettes, making e-cigarettes "the most widely used tobacco product among youth by far." Appl. App. 23a.

Of the 3 million high school students who reported current e-cigarette use, the vast majority (84.7%) used flavored products. Appl. App. 23a; see id. at 5a. Studies also consistently

demonstrate that the overwhelming number of children and young adults who use e-cigarettes were initiated into use by flavored products. For example, in a 2016-2017 study, 93.2% of youth and 83.7% of young adults reported that their first e-cigarette had been a flavored product. Id. at 23a-24a; see id. at 5a. Of youth currently using e-cigarettes, "71% reported using [e-cigarettes] 'because they come in flavors I like.'" Id. at 24a.

FDA explained that the appeal of flavored products to children and adolescents is of exceptional importance because that age group is particularly vulnerable to nicotine addiction, which often persists into adulthood. See Appl. App. 25a (observing that "[y]outh and young adult brains are more vulnerable to nicotine's effects than the adult brain due to ongoing neural development"). If young people can avoid tobacco use in that critical period, the chances of addiction drop dramatically. See id. at 23a (noting that almost 90% of adult daily smokers started smoking by age 18).

As FDA explained in denying applicant's application, "as the known risks increase, so too does the burden of demonstrating a substantial enough benefit." Appl. App. 27a. Thus, because the risk that flavored e-cigarettes pose for youth initiation and use is clearly documented, "an applicant would have to show that the significant risk to youth could be overcome by likely benefits substantial enough such that the net impact to public health would be positive." Ibid. FDA also explained that, because "tobacco-

flavored" e-cigarettes "may offer the same type of public health benefit as flavored" e-cigarettes -- "i.e., increased switching and/or significant reduction in smoking" -- "but do not pose the same degree of risk of youth uptake," it was appropriate to consider whether "the flavored products have an added benefit relative to that of tobacco-flavored [e-cigarettes] in facilitating smokers completely switching away from or significantly reducing their smoking." Id. at 20a.

As the court of appeals noted, such data "bring[] into focus the problem facing the FDA: e-cigarettes offer potential health benefits, to the extent that they convince combustible-tobacco users to get their nicotine from e-cigarettes instead," but "flavored e-cigarettes disproportionately appeal to children." Appl. App. 5a. After "[c]onsidering all of [applicant's] evidence," id. at 7a, the court concluded that "FDA likely properly concluded that [applicant] failed to show that its products adequately protected the public health," id. at 9a.

b. Applicant ignores the great body of evidence on which FDA relied in concluding that its dessert-flavored and fruit-flavored tobacco products pose a risk to youth, which FDA concluded was not outweighed by any public-health benefits they may offer. Instead, applicant contends (Appl. 24-28) that FDA pulled a "surprise switcheroo on regulated entities" by requiring "product-specific, long-term studies" after the agency, according to

applicant, disclaimed any need for such studies. Appl. 24 (quoting White Lion, 16 F.4th at 1138). The court of appeals correctly rejected that assertion, which fails in two ways: (1) FDA never categorically exempted manufacturers from the possible need to provide any particular type of evidence, or categorically assured them that certain other types of evidence would suffice; and (2) FDA did not deny applicant's application for lack of any particular type of evidence.

First, the court of appeals explained that applicant and the Fifth Circuit were wrong that the agency pulled a "switcheroo" regarding the evidence required to secure marketing authorization. Appl. App. 7a. Rather than making a categorical promise that an applicant would not need a long-term study to support its application, "FDA said that * * * it might accept evidence other than long-term studies, if that evidence had sufficient scientific underpinnings to meet the TCA's statutory mandate of demonstrating that flavored [e-cigarette] devices are appropriate for the protection of public health." Id. at 7a-8a (noting, e.g., that the 2019 Guidance stated that "[i]f there is an established body of evidence regarding the health impact * * * of your product or a similar product that can be adequately bridged to your product, * * * these data may be sufficient to support a[n application]"

(second set of brackets in original)).[4] And "against th[at] standard," FDA reasonably concluded that applicant's evidence -- consisting of "'quite mixed'" findings about the role of flavors in promoting switching among adult smokers -- was "lacking." Appl. App. 8a (quoting id. at 29a). Simply because FDA indicated its "willingness to consider some forms of evidence," such as bridging studies connecting an applicant's product to preexisting data, it was not "required * * * to accept that evidence as meeting a statutory requirement even where" the evidence was "unsatisfactory." Id. at 8a.

[4] The Fifth Circuit suggested that FDA's proposed and final rules regarding marketing applications reinforced an expectation that manufacturers across-the-board would not need to provide long-term studies. See White Lion, 16 F.4th at 1138. But those documents make clear, as the court of appeals here correctly observed, that FDA merely announced the possibility that evidence other than such studies could suffice, and its willingness to consider alternative forms of evidence. See 86 Fed. Reg. 55,300, 55,387 (Oct. 5, 2021) ("As discussed in this section, FDA does not expect that long-term clinical studies will need to be conducted for each [application]; instead, it expects that it should be able to rely on other valid scientific evidence to evaluate some [applications].") (emphases added); see also 84 Fed. Reg. 50,566, 50,619 (Sept. 25, 2019) ("FDA recognizes that * * * long-term data is not available for all categories of products and does not expect that long-term clinical studies (i.e., those lasting approximately 6 months or longer) will need to be conducted for each PMTA") (emphasis added). Indeed, contrary to applicant's suggestion that the "entire industry" misunderstood FDA's guidance, Appl. 27, some manufacturers have submitted applications, still under review, containing the types of evidence applicant claims FDA represented would be unnecessary. See Turning Point, supra (No. 21-3855).

Second, applicant is wrong in asserting that the agency mechanically considered only whether its application included certain types of long-term studies. See Appl. 24-25. In reproducing the agency's "box-checking" form, id. at 13-16 (citing C.A. App. 345), applicant fails to replicate the portion of that form containing a final section for evaluation of whether there was "[o]ther evidence in the [application] related to potential benefit to adults," C.A. App. 346. As reflected in that box, FDA considered the other evidence applicant provided: "[a] non-product specific cross sectional survey," in which applicant reported "customer[s] had to navigate [applicant's] website to participate." See ibid. FDA criticized "unclear" aspects of that survey and explained that it "does not provide the necessary information to evaluate the magnitude of the potential benefit to adult users that is needed to complete [the agency's] assessment." Ibid.; see id. at 350-351 (similar).

Other portions of the record also make clear that FDA examined the evidence applicant provided. In denying applicant's application, FDA specifically explained that it "would consider other evidence" besides a "randomized controlled trial and/or longitudinal cohort study," but that the "survey data" applicant included in its application "is not sufficient to show a benefit to adult smokers of using these flavored [e-cigarettes]." Appl. App. 12a; see id. at 12a-13a (noting that applicant's data did not

"evaluate product switching or cigarette reduction resulting from use of these products over time or evaluate these outcomes based on flavor type to enable comparisons between tobacco and other flavors"); see also id. at 31a (explaining that the agency looked for randomized controlled trials, longitudinal cohort studies, "and/or other evidence regarding the impact of the new products on switching or cigarette reduction that could potentially demonstrate the added benefit to adult users of their flavored [e-cigarette] over an appropriate comparator tobacco flavored [e-cigarette]") (emphasis added); id. at 32a (noting that as an "[a]lternative[]" to a "longitudinal cohort study," "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"). FDA thus considered the "survey data" in applicant's application, but concluded that "this evidence is not sufficiently strong to support the benefit to adult smokers of using these flavored [e-cigarette products]." Id. at 31a; see id. at 12a-13a, 32a; C.A. App. 346, 351.[5] That applicant's evidence was inadequate

[5] Applicant contends that FDA applied a "fatal flaw" approach to evaluate its application, considering only whether an applicant provided a randomized controlled trial or a longitudinal cohort study. See Appl. 13-18, 24-25. While FDA earlier considered such an approach, see C.A. App. 310-311, it rescinded it in an August 17 memorandum before acting on applicant's application, see id. at 323 n.ix (making clear FDA would "also consider evidence from another study design, provided that it could reliably and robustly assess behavior change (product switching or

to show the necessary public-health benefit to offset the dangers of dessert-flavored and fruit-flavored tobacco products to children does not mean that the agency failed to consider that evidence or performed a "bait-and-switch" regarding the types of data it would evaluate when reviewing marketing applications. Appl. 25.

c. Although applicant does not dispute the extent of underage use of e-cigarettes generally or the extent to which flavored products drive their popularity, it claims that it has a marketing plan targeting only adults and containing other measures to prevent youth use of its products. Appl. 29. Applicant argues that FDA acted arbitrarily and capriciously by not evaluating its specific measures to prevent youth use of its products, asserting that FDA "entirely fail[ed] to consider an important aspect of the problem" before it. Ibid. (citation and internal quotation marks omitted).

FDA stated in denying applicant's application that "[i]t is theoretically possible that significant mitigation efforts could adequately reduce youth access and appeal such that the risk for youth initiation would be reduced." Appl. App. 28a n.xix. But

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cigarette reduction) over time, comparing users of flavored products with those of tobacco-flavored products"). FDA subsequently rescinded the August 17 memorandum, C.A. App. 343, and FDA has informed this Office that it did not reinstate the "fatal flaw" approach, as reflected in FDA's analysis in denying applicant's application here.

the agency's 2020 Guidance had already explained that despite significant efforts by FDA and measures taken by manufacturers in this regard, youth e-cigarette use nonetheless hit the highest levels ever recorded in 2019. 2020 Guidance 6-8. FDA detailed its own enforcement measures, such as warning letters sent in response to e-cigarette advertising resembling kid-friendly products and thousands of complaints or warnings issued to retailers regarding minors' access to e-cigarettes. Ibid. And it described manufacturer efforts to limit youth access to such products, such as age-verification technology for online sales, enhanced monitoring of retailer compliance with age-verification requirements, and contractual penalties for retailers that failed to comply with sales restrictions. Id. at 7. But even against the backdrop of such measures designed to limit youth use of e-cigarettes, FDA observed that "the reality is that youth have continued access to [e-cigarette] products in the face of legal prohibitions and even after voluntary actions by some manufacturers." Id. at 44; see id. at 21. FDA observed that many youth obtain their e-cigarette products from friends or sources in their social networks. Id. at 45. And FDA determined that youth-access restrictions alone would "not be sufficient to address youth use of these products." Id. at 44.

Given the magnitude of the problems "regarding youth use" of flavored e-cigarettes, FDA explained in denying applicant's

application that no known "advertising and promotion restrictions" have been identified that would adequately "decrease appeal to youth to a degree significant enough to address and counter-balance" such "substantial concerns." Appl. App. 28a n.xix. Under these circumstances, and in light of FDA's independent determination that applicant had not submitted sufficient evidence that its flavored e-cigarettes would have public-health benefits by causing smokers to cease using or lessen dependence on combustible-tobacco products, FDA reasonably determined that consideration of the specific marketing measures proposed in applicant's application would not alter its conclusion regarding applicant's flavored e-cigarettes. See ibid. And applicant does not assert that its proposals were novel or materially better than the types of measures that FDA had previously indicated were inadequate to prevent youth use.[6]

In any event, even assuming that FDA erred in failing to reiterate its earlier explanations in response to applicant's proposed marketing plan, that would not establish that applicant would be likely to succeed on the merits. The TCA makes FDA's

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[6] Other manufacturers have proposed materially different marketing restrictions, and FDA continues to actively consider applications that -- unlike applicant's -- claim to have novel and effective device-specific age verification technology. See, e.g., Jennifer Maloney, Juul Pitches Locked E-Cigarette in Bid to Stay on U.S. Market, Wall Street Journal, Feb. 24, 2020, https://www.wsj.com/articles/juul-pitches-locked-e-cigarette-in-bid-to-stay-on-u-s-market-11582576496.

marketing orders subject to review "in accordance with chapter 7 of title 5," 21 U.S.C. 387*l*(b), thus incorporating the Administrative Procedure Act's rule of harmless error, see 5 U.S.C. 706 (instructing that "due account shall be taken of the rule of prejudicial error" in conducting arbitrary-and-capricious review). Applicant points to measures such as forgoing cartoons in its advertising and distributing "stickers, pamphlets, and educational signs" to help "educate retail stores and Authorized Distributors regarding safety measures" such as "checking the photo ID of everyone under the age of 27 who attempts to purchase [applicant's] products." Appl. App. 41a; see C.A. App. 164-167 (containing applicant's proposed marketing plan). Applicant does not claim that those measures materially differ from those that FDA indicated in 2020 were insufficient to prevent an increase in children's e-cigarette use. See 2020 Guidance 6-8, 44-45. Given that FDA has already considered and found wanting previously proposed advertising and promotion restrictions intended to "decrease appeal to youth," as well as "access restrictions," and deemed them inadequate to "counter-balance" the very serious youth vaping problem, Appl. App. 28a n.xix, it is unlikely that applicant will be able to demonstrate that any harm flowed from any failure-to-consider error. See Shinseki v. Sanders, 556 U.S. 396, 409–411 (2009) (explaining that the "burden of showing that an error is harmful normally falls upon the party attacking the agency's

determination"). Indeed, despite its conclusion that "FDA likely should have more thoroughly considered [applicant's] marketing plan," the court of appeals explained that any inadequacy in FDA's approach to applicant's marketing plan "has not 'permeated the entire [adjudication] process,'" and found that applicant could not demonstrate a likelihood of success. Appl. App. 8a-9a (quoting Public Citizen v. Federal Motor Carrier Safety Admin., 374 F.3d 1209, 1217 (D.C. Cir. 2004)) (brackets in original).

3. Given the court of appeals' conclusion that applicant failed to establish a likelihood of success on the merits, the court did not address applicant's argument regarding irreparable harm or the government's argument regarding the disconnect between applicant's asserted harms and the requested relief. See Appl. App. 10a. But that disconnect independently weighs against a stay.

Applicant's inability to market its products lawfully flows from the Tobacco Control Act itself. A stay of the FDA denial order would neither make applicant's products lawful to market nor bar FDA from taking action against unlawfully marketed products. That is because Congress itself barred the marketing of new tobacco products unless and until they receive FDA authorization. 21 U.S.C. 387j(a)(1) and (2). And Congress provided that FDA "shall deny" an application for authorization to market a new tobacco product if FDA finds that "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." 21 U.S.C. 387j(c)(2)(A). Thus, absent an affirmative public-health finding by the agency, the TCA makes the marketing of a new tobacco product unlawful.

In that respect, the statutory provisions that govern new tobacco products parallel the statutory provisions that govern the marketing of new drugs. Under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 et seq., it is unlawful for a manufacturer to market any new drug without FDA approval. 21 U.S.C. 331(d), 355(a). A court could set aside the denial of a new drug application if, for example, FDA failed to consider relevant evidence critical to an evaluation. But by setting aside a denial, a court would not thereby authorize the marketing of a drug that FDA has not found to be safe and effective. Instead, it would remand to the agency to undertake further review in light of the court's decision.

That is equally the case for new tobacco products. If the court of appeals were ultimately to conclude that FDA failed to adequately consider relevant evidence or otherwise erred, and that such an error was not harmless, it could remand to FDA for further consideration consistent with the court's decision. But such arguments provide no support for the emergency relief sought here. Unless or until FDA finds that applicant's products meet the statutory requirements for lawful marketing, applicant has no entitlement to market its flavored e-cigarettes.

Contrary to applicant's suggestion (Appl. 34-38), FDA's denial order did not render applicant's marketing of its products unlawful. Applicant had no right to market its products lawfully before FDA denied its application. For that reason, a stay of FDA's order denying applicant's request for marketing authorization would not permit those products' lawful marketing. The Fifth Circuit's conclusion that it could issue an order permitting an applicant to continue marketing its products rested on an unsound analogy to "[t]he immigration context." White Lion, 16 F.4th at 1143-1144. Unlike an administrative order that provides authority to remove a noncitizen from the United States -- which courts can, of course, stay, thereby "giving the [noncitizen] interim relief," ibid. -- the marketing denial order at issue here is not the "'source of the Government's authority to'" enforce the statute, and so "'the temporary setting aside'" of that order does not affect FDA's authority to enforce the TCA's provisions against applicant, ibid. (quoting Nken v. Holder, 556 U.S. 418, 429 (2009)).

Nor does the fact that applicant has profited from the unlawful marketing of those products in the past establish a right to continued profits during the pendency of these proceedings. Applicant's claim of irreparable injury rests entirely on the fact that it chose to sell its products between its market entry in 2019 and the date on which FDA made the public-health determination

at issue here. Well before that period, however, FDA had already made clear that any reliance on the sale of e-cigarettes was ill-founded. From the moment it began selling the e-cigarettes at issue here in 2019, applicant should have been aware that doing so without authorization was unlawful by virtue of the statute itself and that securing FDA authorization was the only way to lawfully market its products. Moreover, as discussed above, even assuming that applicant could ultimately persuade the court of appeals after merits briefing that FDA failed to fully consider some significant aspect of its application, applicant would be entitled only to a remand, not to an injunction requiring FDA to allow applicant's products to be marketed without authorization. Such an injunction would be contrary to Congress's decision to prohibit the marketing of new tobacco products without FDA authorization.

Applicant's position is particularly untenable because applicant began selling its flavored e-cigarettes three years after FDA had deemed such products subject to the TCA's authorization requirement. See Appl. App. 40a (asserting that applicant began selling products in May 2019); 81 Fed. Reg. at 28,974 (May 10, 2016 rule deeming e-cigarettes subject to the TCA's requirements effective Aug. 8, 2016). Applicant thus cannot contend that when it decided to start selling its flavored e-cigarettes in 2019, it could have legitimately relied on an assumption that those products would fall outside the TCA's

requirements. Nor could applicant have relied on FDA's announcement in 2016 that it intended to exercise its discretion to temporarily forbear from enforcement actions against manufacturers whose products were already on the market to afford them a chance to "prepare applications for marketing authorization." 81 Fed. Reg. at 28,977-28,978 (creating compliance period and nonenforcement policy for "manufacturers of all newly deemed, new tobacco products"); see id. at 29,011 n.13 (stating that "any new tobacco product that was not on the market on the effective date of the rule (i.e., 90 days after the publication date) is not covered by th[e] compliance policy and will be subject to enforcement if marketed without authorization after the effective date").[7] Indeed, FDA has continued to limit its compliance policy to products that were on the market prior to the 2016 effective date of the deeming rule. See, e.g., 2020 Guidance 2 n.2, 4, 5. That applicant has previously earned tens of millions of dollars (Appl. App. 41a-42a), and entered into business relationships with distributors and retailers (Appl. 34), based on the sale of products that FDA had already made clear were unlawful when applicant placed them on the market provides no

[7] Applicant does not assert that it should fall within FDA's exercise of enforcement discretion because it acquired its product line from a manufacturer that had marketed them before the deeming rule. In the absence of such a showing, any product offered by a new manufacturer falls outside the plain terms of FDA's temporary non-enforcement policy.

equitable basis for facilitating applicant's continued sale of those products in violation of the TCA.

Insofar as applicant argues that equity favors relief here because certain other manufacturers are continuing to sell flavored e-cigarettes during FDA's consideration of their marketing applications or the pendency of stays entered by two other courts of appeals, applicant errs. See Appl. 35-38; see also id. at 4 (citing Fifth and Seventh Circuit stays). The Seventh Circuit did not explain its reasoning, and as the court of appeals here observed in denying applicant's stay request, the Fifth Circuit's ruling reflects a misunderstanding of FDA's reasoning and prior statements. See Appl. App. 7a-8a. In any event, no principle of equity supports the idea that either regulatory or judicial action across a large universe of regulated entities must proceed in temporal lockstep. FDA is in the midst of acting on marketing applications for thousands of flavored e-cigarette products, many of which remain pending before the agency; given differences in processing time and the course of litigation in different courts, it is to be expected that some manufacturers will feel the effects of an unsuccessful marketing application before others. Permitting such differences to drive the entry of extraordinary equitable relief risks allowing the effects of erroneously entered relief to spread nationwide.

4. Finally, even if applicant could establish a likelihood of a certiorari grant and reversal, a likelihood of success on the merits, and a demonstration that equitable factors support a stay, this Court should nonetheless deny the current request given the absence of an imminent FDA enforcement action. As reflected in the marketing denial order at issue here, there is no legal barrier to FDA's initiation of an enforcement action against applicant. See Appl. App. 13a ("Failure to comply with the [Food, Drug and Cosmetic] Act may result in FDA regulatory action without further notice."). But FDA has not altered its usual practice of sending a warning letter affording the recipient 15 business days to respond and then considering that response before bringing any such action -- and it has publicly committed to following that process should it decide to enforce the TCA in circumstances like those presented here. See September 2021 Announcement (noting that products "with a Marketing Denial Order * * * are among [FDA's] highest enforcement priorities," but that "the agency intends to follow its usual enforcement practices" if such products remain on the market and "will issue a warning letter before initiating enforcement action (such as civil money penalties, seizure, or injunction) and afford the recipient an opportunity to respond"). Consistent with that practice and in line with its representations in several other instances, FDA has informed this Office that it will not initiate an enforcement action related to

premarket-authorization requirements for new tobacco products against applicant in fewer than 30 days after sending any such warning letter. See, e.g., Turning Point Brands, Inc. v. U.S. Food and Drug Admin., 21-3855 C.A. Doc. 19, Ex. A at 1-2 (6th Cir. Oct. 8, 2021).

In the absence of any immediate threat of the type of enforcement action applicant points to (Appl. 35-36) as justifying this Court's entry of extraordinary relief, this Court should at a minimum deny a stay at this time, without prejudice to applicant's renewal of its request should it receive a warning letter indicating that FDA could begin an action after giving applicant an opportunity to respond and considering that response.

CONCLUSION

The application for a stay of the agency's order should be denied.

Respectfully submitted.

ELIZABETH B. PRELOGAR
Solicitor General
Counsel of Record

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