No. 10-5032

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

SOTTERA, INC., DOING BUSINESS AS NJOY,

Appellee,

v.

FOOD AND DRUG ADMINISTRATION, *et al.,*

Appellants.

On Appeal from the United States District Court
for the District of Columbia

Brief of *Amici Curiae* American Academy of Pediatrics, American Cancer Society, American Cancer Society Cancer Action Network, American Legacy Foundation, American Lung Association, American Medical Association, Campaign for Tobacco-Free Kids, and Public Citizen Supporting Appellants' Petition for Rehearing and Rehearing En Banc

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CERTIFICATE OF PARTIES, RULINGS, AND RELATED CASES

All parties, intervenors and *amici* appearing in this case are listed in the Appellants' Petition for Rehearing and Rehearing En Banc, as are all rulings and related cases.

IDENTITY AND INTEREST OF THE *AMICI*, AND THE SOURCE OF AUTHORITY TO FILE THIS BRIEF

Concurrently with the filing of this brief, the *amici* have sought the invitation of the Court to file an amicus brief in support of Appellants' petition for rehearing en banc, pursuant to Circuit Rule 35(f). The *amici* are all national organizations committed to preserving the public health and have each been at the forefront of efforts to regulate the use of cigarette and other tobacco and nicotine-delivery products in the United States in order to reduce the morbidity and mortality caused by tobacco use. The *amici* have a strong interest in the question of whether FDA may regulate the electronic nicotine-delivery products at issue in this case. A brief description of each of the amici follows.

a. The **American Academy of Pediatrics** ("AAP") was founded in 1930 and is a national, not-for-profit organization dedicated to furthering the interests of children's health and the pediatric specialty. Since its inception, the membership of AAP has grown from the original group of 60 physicians specializing in children's health to 60,000 primary care physicians, pediatric medical subspecialists, and pediatric surgical specialists. Over the past 79 years,

AAP has become a powerful voice for children's health through education, research, advocacy, and expert advice and has demonstrated a continuing commitment to working with hospitals and clinics, as well as with state and federal governments to protect the well-being of America's children. AAP has engaged in broad and continuous efforts to prevent harm to the health of children and adolescents caused by the use of tobacco products and exposure to second-hand tobacco smoke.

b. The **American Cancer Society** ("ACS") has more than three million volunteers nationwide, including 50,000 physicians. The organization works to eliminate cancer as a major health problem by preventing cancer, saving lives and diminishing suffering from cancer, through research, advocacy and service. Since its founding in 1913, ACS has conducted groundbreaking research to identify the use of tobacco products as a major cause of cancer and has worked to educate the public about its deadly effects. The **American Cancer Society Cancer Action Network** (ACS CAN) is the advocacy affiliate of ACS, helping to educate government officials on cancer as a public policy issue. ACS CAN has almost half a million grassroots advocates, and supports effective tobacco control legislation and regulations across the country.

c. The **American Legacy Foundation** ("Legacy") is dedicated to building a world where young people reject tobacco and anyone can quit. The

foundation was established in March 1999 as a result of the Master Settlement Agreement reached between the attorneys general in 46 states and five U.S. territories and the tobacco industry. Legacy develops programs that address the health effects of tobacco use through grants, technical assistance and training, youth activism, strategic partnerships, counter-marketing and grass roots marketing campaigns, research, public relations and outreach to populations disproportionately affected by the toll of tobacco.

e. The **American Lung Association** ("ALA") is the nation's oldest voluntary health organization, with volunteers in all 50 states, and the District of Columbia. ALA has nearly 400,000 volunteers. The American Lung Association is the leading organization working to save lives by improving lung health and preventing lung disease through education, advocacy and research.

f. The **American Medical Association** ("AMA"), an Illinois non-profit corporation founded in 1847, is the largest professional association of physicians, residents, and medical students in the United States. Additionally, through state and specialty medical societies and other physician groups, seated in the AMA's House of Delegates, substantially all United States physicians, residents, and medical students are represented in the AMA's policy making process. Its objects are to promote the science and art of medicine and the betterment of public health. The AMA has long had an interest in the regulation of tobacco products and the

tobacco industry. As an institution, it has developed expertise in the pharmacology of nicotine, the toxic effects of cigarette smoke, and the societal implications of tobacco usage. For many years, the AMA has been one of the leading anti-smoking organizations in the United States.

g. The **Campaign for Tobacco-Free Kids** ("Tobacco-Free Kids") works to raise awareness that cigarette smoking is a public health hazard by advocating public policies to limit the marketing and sales of tobacco to children, and altering the environment in which tobacco use and policy decisions are made. Tobacco-Free Kids has over 100 member organizations, including health, civic, corporate, youth, and religious groups dedicated to reducing children's use of tobacco products.

h. **Public Citizen** is a consumer advocacy organization founded in 1971, with more than 200,000 members and subscribers nationwide. Public Citizen is active before Congress, regulatory agencies, and the courts in matters relating to public health in general and regulation by the Food and Drug Administration (FDA) in particular. Concerned about the severe health risk posed by tobacco products, Public Citizen has long advocated for increased regulation of these products and of the promotional efforts of the tobacco industry.

The *amici* are all non-profit institutions. No publicly-held corporation has an ownership stake of greater than 10% in any of the *amici*. No counsel or party to

this case has made a monetary contribution intended to fund the preparation or submission of this brief, nor has any counsel or party to this case authored this brief in whole or in part.

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GLOSSARY

CDC	Centers for Disease Control and Prevention
CDER	FDA's Center for Drug Evaluation and Research
FDA	Appellant U.S. Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetics Act, Pub. L. No. 75-717, 52 Stat. 1040
HHS	U.S. Department of Health and Human Services
NDA	New Drug Application
NRT	Nicotine Replacement Therapy
Tobacco Act	Family Smoking Prevention and Tobacco Control Act, Pub. L. No. 111-31, 123 Stat. 1776.

INTRODUCTION AND SUMMARY OF ARGUMENT

Amici agree with the Food and Drug Administration and other Appellants (FDA) that Appellee's "electronic cigarettes" meet the Federal Food, Drug, and Cosmetic Act's (FFDCA's) definitions of "drugs," and are therefore subject to regulation by FDA as drugs, notwithstanding the Supreme Court's decision in *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120 (2000). The panel majority, however, disagreed, affirming the District Court decision that enjoined FDA from regulating these products.

The panel majority's decision involves a question of exceptional importance because the decision threatens to strip FDA of authority to regulate a range of nicotine products. Most directly, under the panel majority's decision, FDA will have no authority to regulate e-cigarettes as drugs unless a manufacturer makes a therapeutic claim and will not have authority to regulate these products under the Family Smoking Prevention and Tobacco Control Act of 2009 (the Tobacco Act) until it issues a regulation pursuant to section 901(b), leaving these products on the market in the interim and in an uncertain status even after the FDA issues a regulation. Moreover, the panel majority's decision has implications far beyond e-cigarettes, because it would for the first time exclude from drug regulation nicotine products derived from tobacco, including, but not limited to, nicotine replacement therapy (NRT), so long as the product does not make explicit therapeutic claims.

This result is a dramatic departure from how nicotine and NRTs have been regulated for many decades, as the FDA explains in its petition.

We agree with Judge Garland that products that contain nicotine but do not otherwise contain tobacco, including NRTs, are not the type of products that the Court held in *Brown & Williamson* are excluded from the definition of devices and drugs within the FFDCA. As Judge Garland points out, the Supreme Court's discussion of tobacco products, the context of the case and the Supreme Court's reasoning all support the conclusion that *Brown & Williamson* applies only to products containing tobacco and not to e-cigarettes, which contain only nicotine derived from tobacco. Concurrence 1-6. Significantly, in contrast to traditional tobacco products, we do not know if e-cigarettes are unsafe and, therefore, regulating e-cigarettes as drug-delivery systems under the FFDCA would allow a determination of safety and may not lead to a ban. Instead, regulation as a drug would require the manufacturers to demonstrate that these products are safe and effective, as other manufacturers of nicotine products currently on the market have successfully done.

The majority's approach would tie the agency's hands in regulating nicotine-based products that otherwise do not contain tobacco as well as NRT products for which no therapeutic claims are made. In contrast, Judge Garland states that there is "ambiguity" in the relevant statutory provisions, which would appear to allow

the agency to regulate such products after issuing an authoritative agency interpretation of the Tobacco Act explaining that FDA retains authority under the FFDCA to regulate nicotine products, including NRTs for which no therapeutic claims are made. Concurrence 9-10. Thus, while the majority's opinion would lead to devastating consequences with respect to the regulation of NRTs, under Judge Garland's approach the agency would have authority to regulate NRTs as drugs.[1]

As explained in Section I, the effort to reduce the mortality and morbidity associated with tobacco use is one of the great public health challenges of our time, and safe and effective nicotine substitute products are needed to help meet that challenge. And, as explained in Section II, the panel majority's decision, if allowed to stand, would have serious adverse impacts on the public health, for three reasons.

First, the regulation of NRT products as drugs provides a critical incentive for companies working to develop the next generation of tobacco cessation products to ensure that their products are safe and effective. Congress explicitly

[1] NJOY deliberately bypassed its administrative remedies as "futile" and should not be able to use the absence of a formal agency decision as a basis for withholding deference. If additional formality is required, the matter should be remanded to FDA and NJOY should be directed to exhaust its administrative remedies which would provide an opportunity to provide an authoritative decision on whether the Tobacco Act limits FDA's prior jurisdiction to regulate NRTs as drugs.

recognized in the Tobacco Act the need for the development of such products. A decision permitting certain nicotine products to side-step safety and effectiveness evaluation by simply avoiding therapeutic claims may encourage other manufacturers of nicotine products to follow suit, avoiding FDA review and resulting in fewer safe and effective products being developed.

Second, under the panel majority's decision, electronic cigarettes and similar products would not need to be deemed safe or effective by FDA before marketing. And, in the absence of a regulation to address their content, these products would be available without any objective evaluation or control over the level or potency of the nicotine in the products, or the quantity or quality of other ingredients. Because there has been and is no control over the level of nicotine, the manner of delivering nicotine, or the purity of the nicotine in electronic cigarettes and these products have not been subject to the kind of objective, rigorous scientific study FDA requires, the evidence is inadequate to conclude that electronic cigarettes are either safe or effective – and there is data suggesting that these products could present real dangers to the public health. Thus, their unregulated presence on the market must be viewed as a threat to the public health.

Moreover, the injunction, if upheld, will also encourage other companies to end-run the regulatory process, leading to the marketing of other potentially unsafe and/or ineffective products used and advertised as tobacco alternatives. The

presence on the market of these unapproved nicotine alternatives may cause many tobacco users to use unapproved products instead of approved ones that have been screened for safety and effectiveness.

Third, the panel majority's decision could result in *increases* in tobacco use, especially among children, by introducing non-smokers to smoking behaviors and nicotine through use of unregulated products like electronic cigarettes. The problem is exacerbated by the fact that these products are not currently subject to the advertising restrictions to which cigarettes and other conventional tobacco products are subject and therefore can be manufactured and marketed in ways that appeal to children – *e.g.,* by using flavors that appeal to children and that Congress banned in cigarettes precisely because of that appeal. *See* Tobacco Act, 21 U.S.C. 387g(a)(1)(A).

In short, the panel majority's decision will make it substantially more difficult to address the problem of tobacco use in America and will have serious adverse consequences for the public health.

ARGUMENT

I. Effective Regulation of NRTs Is Essential to Reducing Tobacco Use, Which Is One of the Great Public Health Challenges of Our Time.

Tobacco use accounts for 435,000 deaths each year in America and is widely regarded as the chief preventable cause of illness and death worldwide.[2] About 21 percent of U.S. adults − approximately 45 million Americans − smoke cigarettes,[3] and millions of additional adults use smokeless tobacco.[4] A 2004 Surgeon General Report, supported by more than 16,000 reports and studies, concluded that "[s]moking harms nearly every organ of the body" and causes cancer, cardiovascular disease, respiratory disease, reproductive harms, and many other health problems,[5] a conclusion that was confirmed and expanded upon by the recently issued 2010 Report of the Surgeon General.[6]

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[2] U.S. Department of Health and Human Services, Public Health Service, "Treating Tobacco Use and Dependence: Clinical Practice Guideline" (2008 Update) (hereafter, "Treating Tobacco Use"), at 11 (citing, *inter alia*, data from the Centers for Disease Control and Prevention (CDC)).

[3] *Id.* (citing, *inter alia*, CDC, "Cigarette smoking among adults – United States 2006" (2007)).

[4] *Id.* at 163 (citing CDC data that the use of smokeless tobacco was reported among 4 percent of U.S. adult men in 2005).

[5] "The Health Consequences of Smoking: A Report of the Surgeon General," May 27, 2004, at 8. Meanwhile, health risks from smokeless tobacco include abrasion of teeth, gingival recession, periodontal bone loss, leukoplakia, and oral and pancreatic cancer. Treating Tobacco Use at 163.

[6] "How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General," US Department of Health and Human Services, December 9, 2010.

While millions of Americans are addicted to tobacco and nicotine, more than 70 percent of American adult smokers, approximately 30 million persons, want to quit.[7] There is therefore a clear demand and need for products and services proven to aid smoking and tobacco use cessation. Several such products have been deemed safe and effective by FDA and are on the market today, including NRTs, which deliver a carefully calibrated amount of nicotine into the body without the damaging effects of smoking or other tobacco use.[8] These products, and others still in development, are an important component of the fight against tobacco use: existing FDA-approved NRTs have been shown to increase by 50-70% the likelihood of success of a tobacco quit attempt.[9]

II. The Panel Majority's Decision Will Hinder Efforts to Reduce the Mortality and Morbidity Associated with Tobacco Use and Harm the Public Health.

If upheld, the panel majority's decision enjoining FDA regulation of electronic cigarettes and permitting the marketing of these products without an agency determination of safety and effectiveness would have serious public health consequences.

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[7] Treating Tobacco Use, at 15 (citing CDC, "Cigarette smoking among adults – United States 2006" (2007)).

[8] These products include nicotine gum, the transdermal patch, nicotine inhaler, nicotine lozenges, and nicotine nasal spray.

[9] L. Stead, et al., *Nicotine replacement therapy for smoking cessation*, Cochrane Database of Systematic Review, Issue 4 (January 23, 2008).

a. The panel majority's decision will undermine the incentive to develop new, better alternative nicotine products.

Although existing FDA-approved NRTs have been shown to increase the likelihood of success of a tobacco quit attempt, quit rates remain low: only 44% of U.S. adult smokers even attempt to quit each year (although 70% want to do so), and each year only a small percentage are successful − in 2005, for example, a mere 4-7 percent.[10] There are many reasons for these low quit rates, but the numbers nonetheless highlight the potential need for more effective NRTs on the market.

In the recently-enacted Tobacco Act, Congress underscored the importance of developing new safe and effective products to help tobacco users quit, providing in section 918(a) of that legislation that a sponsor of a new smoking cessation device, including an NRT, may petition FDA for fast-track consideration of its application.[11] The Tobacco Act further provides in section 918(b) that the Secretary of Health and Human Services (HHS) shall report to Congress on:

> [H]ow best to regulate, promote and encourage the development of innovative products and treatments . . . to better achieve, in a manner that best protects and promotes the public health -
>
> (A) total abstinence from tobacco use;
>
> (B) reductions in consumption of tobacco; and

[10] Treating Tobacco Use at 15 (citing, *inter alia*, data from the CDC).
[11] Tobacco Act, 123 Stat. at 1825.

> (C) reductions in the harm associated with continued tobacco use.[12]

To meet this need, the incentive for companies to undertake the critically important process of securing an FDA safety and effectiveness determination must be maintained. The panel majority's decision, however, would weaken the incentive for nicotine product makers to undertake the rigorous testing needed to secure FDA approval. Some companies interested in developing nicotine products for FDA approval to assist tobacco users to quit may, as a result of this decision, opt to sell their products without therapeutic claims, avoiding the need to conduct the safety and efficacy tests required prior to the approval of any new drug. And other companies that currently abide by FDA requirements may be inclined to avoid investing in the development of more effective nicotine replacement products altogether if they perceive that they will be competing with less expensive, unregulated products.

b. The panel majority's decision will allow the marketing of potentially dangerous and addictive nicotine products.

As noted above, FDA has approved as drugs nicotine replacement products that meet its regulatory standards, including products containing nicotine derived from tobacco, such as nicotine patches and nicotine gum. FDA approved these products as safe and effective after rigorous agency review. The approval of these

[12] *Id*. at 1825-26.

NRTs shows that there is no reason to assume that FDA review of electronic cigarettes will necessarily lead to a ban on the product. Strict review, however, is compelled not only by the great public need for such products, discussed above, but also by the risks associated with the use of nicotine itself, an "addictive drug"[13] that is "dangerous or even fatal" when administered in large doses.[14] A declaration in this case from Dr. Janet Woodcock, Director of FDA's Center for Drug Evaluation and Research (CDER), details the many health risks related to nicotine use, including the cardiovascular effects.[15]

There can be no question, therefore, that all nicotine products deserve close scrutiny from FDA to protect the public health. As with all new drugs, the standards governing FDA approval of NRTs are rightly strict ones. A New Drug Application (NDA) for an NRT must include detailed safety data, as well as manufacturing controls to ensure that each individual product contains an identified, specific and accurately calibrated amount of nicotine. Finally, product labels for FDA-approved NRTs must contain precautions for patients that have cardiovascular disease: specifically, patients with coronary artery disease, serious

[13] Tobacco Act, 123 Stat. at 1777 (Finding 3).
[14] JA 546 (Declaration of Janet Woodcock. M.D. ("Woodcock Decl"), at ¶ 4).
[15] JA 546, 549 (Woodcock Decl. at ¶ ¶ 4, 14).

cardiac arrhythmias, or other vasospastic disease are advised to consult their physicians before nicotine replacement therapy is prescribed.[16]

If the panel majority's decision in this case stands, however, products like electronic cigarettes, despite having undergone no FDA review, will be available to recreational users, including youth, and consumers looking for help in quitting tobacco. As a result, a non-tobacco user or a smoker who turns to electronic cigarettes because they have been touted as "a great alternative to help . . . stop smoking cigarettes" or "healthier than real cigarettes" will have no way of knowing whether the product contains harmful contaminants, whether the product contains a dangerous level of nicotine or, alternatively, a wholly ineffective level of nicotine, or whether the person should forgo using the product because he or she suffers from another medical condition – much less whether the product will actually help the smoker quit.

While the long-term health consequences of electronic cigarettes are unknown, due to the minimal review they have undergone, FDA's limited testing of a small sample of electronic cigarettes in July 2009 has already revealed numerous potential safety problems with electronic cigarettes, including:

- the wide variability in the amount of nicotine emitted with each puff, from 26.8 to 43.2 mcg nicotine/mL;

[16] JA 547, 549 (Woodcock Decl. at ¶¶ 7, 14).

- the presence of diethylene glycol – a solvent that is toxic to humans and has resulted in "significant fatalities" when used in pharmaceuticals – in one of the tested electronic cigarette cartridges;

- the presence of tobacco-specific nitrosamines, which are human carcinogens, in half the samples tested; and

- the presence of tobacco-specific impurities suspected of being harmful to humans – anabasine, myosmine, and B-nicotine – in a majority of the samples tested.[17]

These are precisely the kinds of safety issues that FDA review of nicotine products has historically been designed to identify and address, and that e-cigarette manufacturers ought to be required to resolve before they are allowed to market their products for use by the tens of millions of Americans looking for recreational drug use or alternatives to tobacco. These test concerns are symptomatic of potential dangers. Some manufacturers have offered for sale vials of nicotine to consumers to add to their e-cigarettes, thus enabling consumers to add uncontrolled levels of nicotine.

Moreover, the presence of unregulated nicotine products on the market will exacerbate the problem of tobacco use by competing with and discouraging the use of FDA-approved smoking cessation products. Current smokers may opt for unregulated nicotine products instead of products proven effective for smoking

[17] JA 547-548 (Woodcock Decl. at ¶¶ 9-12). FDA has also received reports of short-term side effects caused by electronic cigarettes, including racing pulse, dizziness, slurred speech, mouth ulcers, heartburn, coughing, diarrhea, and sore throat. JA 549 (Woodcock Decl. at ¶ 14).

cessation.[18] Further, the confusion caused by the presence on the market of unregulated nicotine products viewed by the public as unsafe or ineffective may lead consumers to forgo all smoking cessation products, even those FDA has actually found to be safe and effective. Misperceptions about the safety or effectiveness of smoking cessation products generally – already a problem for NRTs[19] – will be reinforced by the presence on the market of nicotine products that have yet to be proven safe and effective and may well be dangerous and ineffective.

c. The panel majority's decision may lead to greater nicotine use and greater tobacco use among children.

Unregulated nicotine products like electronic cigarettes not only may fail to help address the problems of tobacco use; they may also exacerbate that very problem − for example, by introducing non-tobacco users, especially children, to smoking behaviors and nicotine products for the first time.

As noted above, youth tobacco use is a particularly significant public health issue – one that Congress most recently tackled in the Tobacco Act, which contains numerous findings regarding the impact and prevalence of tobacco advertising

[18] JA 549 (Woodcock Decl. at ¶ 15).

[19] *See* FDA Citizen Petition filed by the Association for the Treatment of Tobacco Use and Dependence (ATTUD) and the Society for Research on Nicotine and Tobacco, February 12, 2010, FDA Docket No. FDA- 2010-P-0089, at 18 and n.59. *See also id.* at 18 n.62 (noting survey in which 66 percent of smokers or ex-smokers agreed somewhat with the statement that "stop-smoking products with nicotine are just as harmful as cigarettes.").

aimed at young persons[20] and has as a goal the restriction of such advertising. Under the panel majority's decision, however, electronic cigarettes would not be subject to any regulatory restrictions covering "drugs," nor are they currently subject to any regulation applicable to tobacco products, such as warning labels, advertising restrictions or restrictions on sales to minors.

Consequently, electronic cigarettes do not carry any mandated health warnings, and may be – and are − sold in flavors such as strawberry, chocolate, and mint that appeal to children and teenagers, and in places like shopping malls frequented by young people.[21] Thus, the lack of regulation over these products enables them to be manufactured, sold and marketed in a manner that, rather than helping people quit smoking, could actually *introduce* non-smokers – in particular children – to smoking behaviors and nicotine and, potentially, lead them eventually toward tobacco use. As noted by Dr. Woodcock, "FDA is concerned that this novel nicotine product, to the extent it remains an unapproved and unregulated product, will attract new constituencies to nicotine use . . . ."[22]

CONCLUSION

For the foregoing reasons, this Court should grant the petition for rehearing and rehearing *en banc*.

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[20] *See, e.g.,* Tobacco Act, 123 Stat. at 1777-1778 (Findings 14-27).
[21] JA 546 (Woodcock Decl. at ¶ 5).
[22] JA 549 (Woodcock Decl. at ¶ 15). *See also id.* (expressing FDA's concern that "non-smokers may initiate nicotine use through these products").

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this 23rd day of December, 2010, I caused the foregoing Brief of *Amici Curiae* to be filed with the Court in hard copy and through the ECF system, which will send notification of such filing to the following registered users:

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