No. 22-1112

IN THE

Supreme Court of the United States

AVAIL VAPOR, LLC,
BLACKSHIP TECHNOLOGIES DEVELOPMENT, LLC,
BLACKBRIAR REGULATORY SERVICES, LLC,
Petitioners,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,
Respondent.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Fourth Circuit

BRIEF OF *AMICI CURIAE* PUBLIC HEALTH EXPERTS IN SUPPORT OF PETITIONERS

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INTEREST OF *AMICI CURIAE*

Amici are public health experts with extensive experience related to tobacco products and particularly electronic cigarettes (Electronic Nicotine Delivery Systems or "ENDS").[1] *Amici* believe that policy decisions related to those products should be grounded in sound science and good regulatory practice and that reducing *cigarette smoking* remains the primary goal of any tobacco policy. *Amici* are concerned that poor regulation of ENDS based on flawed scientific reasoning will lead to unintended consequences and could do more harm than good for public health.

David B. Abrams, Ph.D. is a Professor of Social and Behavioral Sciences at New York University School of Global Public Health. He previously directed the Office of Behavioral and Social Sciences Research ("OBSSR") at the National Institutes of Health ("NIH") and directed The Schroeder International Institute of Tobacco Research and Policy Studies at the Truth Initiative in Washington, D.C. Over a 50-year career, Dr. Abrams published over 300 papers on nicotine, led an NIH Center of Excellence, authored *The Tobacco Dependence Treatment Handbook: A Guide to Best Practices*, and served on the Board of Scientific Advisors, National Cancer Institute. He has researched ENDS since 2009.

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[1] This brief was not authored in whole or in part by counsel for any of the parties; no party or party's counsel contributed money for preparing or submitting this brief; and no one other than *amici* and its counsel have contributed money for preparing or submitting this brief. Notice was timely provided to counsel for Petitioner pursuant to Rule 37. Notice was provided to counsel for Respondent on June 9, 2023, inside the 10-day notice period. On June 12, 2023, counsel for all parties, including Respondent, provided consent for the filing of this brief. Respondent's response brief is due July 14, 2023.

Scott D. Ballin, J.D. has 50 years of experience in the field of tobacco policy and science. He is the former Vice President and Legislative Counsel to the American Heart Association and former Chairman of the Coalition on Smoking OR Health, which brought together the major health non-profits to advocate for a strengthened response to smoking. He is an advisor to the University of Virginia Institute for Engagement and Negotiation and convenor of the Morven dialogues, promoting civil dialogue and consensus-building on tobacco and nicotine policy.

Clive D. Bates, M.Sc. is Director of Counterfactual, a consultancy focused on sustainability and public health. He was previously the Director of Action on Smoking and Health (UK) ("ASH"), the UK's leading anti-smoking non-profit. He has written extensively on tobacco policy and science, and has reviewed hundreds of scientific papers related to tobacco harm reduction over the past ten years.

Martin J. Jarvis, D.Sc. O.B.E. is Emeritus Professor of Health Psychology at University College London. He was previously Principal Scientist with Cancer Research UK. He has published 200 papers on tobacco smoking in peer-reviewed journals. He served as Chair of the UK government's Technical Advisory Group on Tobacco and Health, Deputy Chair of the Scientific Committee on Tobacco and Health, and Specialist Adviser to the Health Select Committee of the UK parliament. He served on the World Health Organisation's study group on Tobacco Product Regulation.

Raymond S. Niaura, Ph.D. is Professor of Social and Behavioral Sciences and Epidemiology, and Chair of the Department of Epidemiology at the School of Global Public Health, New York University. From 2009-2017, he was Director of Research at the

Schroeder Institute, Truth Initiative in Washington D.C. He has extensive expertise in tobacco dependence and treatment, and has published over 400 peer-reviewed articles and several book chapters in this area. He has been the Principal Investigator or co-Investigator of over 70 NIH-funded grants, and is the former President of the Society of Nicotine and Tobacco Research.

Thomas J. Miller, J.D. served for 40 years as Iowa's Attorney General and was one of the leaders in the landmark settlement with the tobacco companies to recover billions of dollars in healthcare costs associated with treating smoking-related illnesses. He served for nine years, two as chairman, of the Truth Initiative, which was instrumental in significantly reducing youth smoking. He has been involved in tobacco harm reduction for 12 years.

Steven A. Schroeder, M.D. is Distinguished Professor Emeritus of Health and Health Care at the University of California, San Francisco ("UCSF"). He qualified as an M.D. in 1964 at Harvard Medical School and followed a career in internal medicine and public health. He served as the president and CEO of the Robert Wood Johnson Foundation from 1990 to 2002. Until recently, he headed the Smoking Cessation Leadership Center at UCSF. Dr. Schroeder has received many honors and six honorary doctoral degrees. He has served on the board of the James Irvine Foundation, the editorial board of the *New England Journal of Medicine*, and as president of the Harvard Medical Alumni Association.

David T. Sweanor, J.D. is Adjunct Professor of Law and Chair of the Advisory Board of the Centre for Health Law, Policy and Ethics at the University of Ottawa, and a Member of the Global Leadership

Council, Boston University School of Public Health. He was the first lawyer in the world to work full-time on policy measures to reduce cigarette smoking. His 40-plus year career has included achieving many global policy precedents, testifying on risk reduction issues before the U.S. Congress, authoring dozens of publications, and speaking at tobacco public policy events around the world.

SUMMARY OF ARGUMENT

Since the first electronic cigarettes (Electronic Nicotine Delivery Systems or "ENDS") were commercialized over a decade ago, a tremendous amount of academic research and public policy work has sought to inform decisions made by the U.S. Food and Drug Administration ("FDA"), which is tasked with regulating ENDS at a federal level under the Family Smoking Prevention and Tobacco Control Act, state and local governments, and international bodies. No doubt much of this is being driven by the fact that in the United States alone almost a half-million adults die annually from smoking combustible cigarettes. And the stakes could not be higher. Today, ENDS are the most popular method of quitting traditional cigarettes in this country. Indeed, many researchers and public health experts view ENDS as key to "harm reduction," in which adults who are unable or unwilling to immediately stop using nicotine have access to much safer nicotine products as an alternative to deadly cigarettes.

Importantly, a growing body of scientific and behavioral research confirms that ENDS must be front and center of any harm reduction efforts. As discussed by *amici* below, there is now a virtual consensus that ENDS pose much less risk to human health than combustible cigarettes. And while debate continues over other salient issues, decision-makers must account

for studies and other work demonstrating, on both a population and individual user level, that ENDS as an overall category provide significant benefits, even if this is challenging to show for each individual product. Not only are adult smokers successfully using ENDS to reduce or kick their smoking habits, they are relying on non-tobacco flavored ENDS (e.g., mint or fruit) to effectively do so. At the same time, while preventing youth use of ENDS must always be part of the equation, recent evidence shows that underage use rates have significantly declined from a peak in 2019, youth are not attracted to the types of ENDS devices that many adults rely upon, and that, on balance, ENDS are not a gateway to underage smoking. Since ENDS were first introduced, youth cigarette smoking rates have also fallen dramatically.

All of this, therefore, raises serious questions about an FDA policy that makes it less likely that smokers will switch to ENDS and more likely that ENDS users will return to smoking, a policy with potentially life-threatening consequences for millions of Americans. Accordingly, *amici* request that this Court grant the Petition.

ARGUMENT

I. ENDS Are, Beyond Reasonable Doubt, Much Safer Than Cigarettes.

Compared to traditional cigarettes, ENDS expose users to far fewer harmful chemicals and generally at much lower levels. Almost all the harm caused by smoking arises from inhaling toxic products of combustion (tar and toxic gases that constitute the smoke from burning tobacco leaf). ENDS instead use electricity to heat a liquid into an aerosol of liquid droplets and do not involve combustion.

As ENDS are a relatively recent innovation, we do not have conclusive data on long-term health outcomes. However, there is a rich body of proxy evidence from biomarkers of exposure (measures of toxicants in the blood, saliva, or urine of users) and biomarkers of potential harm (signs of damage to the body). Indeed, FDA relies on biomarker data in its decision-making about impacts of ENDS on human health:

> To evaluate the acute and chronic health effects associated with the product, FDA recommends including studies, other scientific evidence, or both, that identify biomarkers of exposure, biomarkers of harm, and health outcome measurements or endpoints…While long term studies are most useful for identifying chronic effects associated with use of a product, such studies are not routinely expected.[2]

In 2018, the National Academies of Science, Engineering, and Medicine ("NASEM") completed a comprehensive review of relevant literature, concluding that "*While e-cigarettes are not without health risks, they are likely to be far less harmful than combustible tobacco cigarettes*."[3] Many other similar assessments have reached similar conclusions. In 2022, England's Office for Health Improvement and Disparities ("OHID") concluded that *"vaping poses*

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[2] FDA, *Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (Revised): Guidance for Industry* (March 17, 2023), at 40-41, https://tinyurl.com/3f6ht2a6.

[3] National Academies of Sciences, Engineering, and Medicine ("NASEM"), *Public Health Consequences of E-Cigarettes*, NATIONAL ACADEMIES PRESS (2018), Summary at 1, https://bit.ly/3qzJLhf.

only a small fraction of the risks of smoking,"[4] and the Royal College of Physicians ("RCP") concluded that *"the hazard to health arising from long-term vapour inhalation… is unlikely to exceed 5% of the harm from smoking tobacco."*[5] Not only are the harmful exposures lower in ENDS, but there is also evidence for an *improvement* in the health of smokers who switch to ENDS. An analysis of biomarkers among U.S. adults concluded that, *"Former smokers who currently use e-cigarettes only have levels of biomarkers…that are comparable to…never tobacco users."*[6] Other research has demonstrated a health improvement in smokers who switch completely to ENDS. For example, smokers with chronic obstructive pulmonary disease ("COPD") who either completely stopped or substantially reduced smoking with ENDS experienced significant improvements in objective and subjective COPD outcomes after five years.[7]

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[4] Office for Health Improvement and Disparities ("OHID") (formerly Public Health England), *Nicotine Vaping in England: 2022 evidence update summary* (2022), at ch. 16, https://tinyurl.com/3njz34fd.

[5] Royal College of Physicians ("RCP"), *Nicotine without Smoke: Tobacco Harm Reduction* (2016), at 189, https://tinyurl.com/22a2cz7x.

[6] Carol H. Christensen, et al., *Biomarkers of Inflammation and Oxidative Stress Among Adult Former Smoker, Current E-Cigarette Users – Results from Wave 1 PATH Study*, CANCER EPIDEMIOL. BIOMARKERS PREV. 30(10): 1947-1955 (2021), at 9, https://tinyurl.com/nh7p6fu9.

[7] Ricardo Polosa, et al., *COPD smokers* who *switched to e-cigarettes: health outcomes at 5-Year follow-up*, THER. ADV. CHRONIC DIS. Vol. 11:1-15 (2020), at 10, https://tinyurl.com/3a75as5t.

II. ENDS Help Adult Smokers Quit And Can Reach Many Adults Who Would Not Otherwise Quit Smoking.

ENDS are effective in helping adult smokers quit. They outperform the current FDA-approved cessation method, nicotine replacement therapy ("NRT") (e.g., nicotine gums and patches). The latest Cochrane systematic review – widely considered the gold standard of systematic reviews – concluded, *"There is high-certainty evidence that [e-cigarettes] with nicotine increase quit rates compared to NRT..."*[8]

Notably, the above evidence base captures smokers who *a priori* decide to quit smoking and actively seek out support. However, this only describes a minority of smokers – the majority (~70%) do not plan to quit smoking in the next 30 days,[9] and many of those (~28%) do not end up making a quit attempt;[10] NRT is not likely to reach these people. However, *ENDS can*; specifically, by functioning as an alternate consumer product. Adult smokers who do not intend to quit nevertheless often end up completely switching away from smoking after taking up ENDS[11] – a phenomenon

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[8] Jamie Hartmann-Boyce, et al., *Electronic cigarettes for smoking cessation (Review),* Cochrane Database of Systematic Reviews (2022), Abstract at 2, https://tinyurl.com/22jbyw52.

[9] Richard J. O'Connor, et al., *Internalized smoking stigma in relation to quit intentions, quit attempts, and current e-cigarette use*, SUBSTANCE ABUSE Vol. 38, No. 3, 330-336 (2017), Table 1 at 332, https://tinyurl.com/25mvup7v.

[10] Lauren Arancini, et al., *Age as a predictor of quit attempts and quit success in smoking cessation: findings from the ITC 4-Country Survey*, ADDICTION Vol. 116, Issue 9, 2509-2520 (2021), Table 3 at 6, https://tinyurl.com/2p89ww34 (no free access).

[11] Nicholas I. Goldenson, et al., *Switching away from Cigarettes across 12 Months among Adult Smokers Purchasing*

known as "accidental switching" – including among adults who initially *never* planned to quit smoking.[12]

As such, ENDS have the potential for a substantial positive public health *impact* (a function of reach × efficacy), given that ENDS are both more efficacious and have a greater reach than current FDA-approved cessation methods. Indeed, there is evidence that ENDS have made such an impact at the population level, in terms of sharper declines in cigarette smoking than originally expected. For example, adult smoking prevalence is now lower than anticipated from pre-ENDS era trends – with the largest declines in smoking occurring in the age groups with higher uptake of ENDS (i.e., adults under 44 years of age).[13] Similarly, national retail data show that higher ENDS sales are accompanied by lower cigarette sales. In one review, every additional ENDS unit sold per capita was associated with a shortfall of 1.4 cigarette packs per capita.[14]

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the JUUL System, AM. J. HEALTH BEHAV. 2021;45(3):443-463, Figure 2 at 452, https://tinyurl.com/5ye5exh4.

[12] Karin A. Kasza, et al., *E-Cigarette use and change in plans to quit cigarette smoking among adult smokers in the United States: Longitudinal findings from the PATH Study 2014–2019*, ADDICT. BEHAV. VOL. 124 (2021), Abstract at 1, https://tinyurl.com/2cdkuc7s.

[13] David T. Levy, et al., *US Nicotine Vaping Product SimSmoke Simulation Model: The Effect of Vaping and Tobacco Control Policies on Smoking Prevalence and Smoking-Attributable Deaths*, INT. J. ENVIRON. RES. PUBLIC HEALTH (2021), 18, 4876, Results at 8, https://tinyurl.com/2utw4u62.

[14] A. Selya, et al., *Sales of Electronic Nicotine Delivery Systems (ENDS) and Cigarette Sales in the USA: A Trend Break Analysis*, J. CONSUM. POLICY (2023) 46:79-93, at 79, https://tinyurl.com/bdfdwmys.

III. ENDS Flavors Are Important To Adults Trying To Quit Smoking.

A common misperception about ENDS products is that, like cigarettes, they are inherently tobacco-flavored. But the base ingredients used in ENDS do not impart a tobacco or any characterizing flavor. Rather, all flavors in ENDS, including tobacco-flavor, must be added to the e-liquid. To date, the FDA has authorized only tobacco-flavored ENDS products; however, most adult smokers use non-tobacco flavors, including fruit, mint/menthol, and candy/dessert.[15] Using non-tobacco ENDS flavors may help adult smokers switch away from cigarettes. For instance, Mok, et al. analyzed a nationally-representative survey of adult smokers and concluded, *"Those using flavored e-cigarettes, particularly menthol or mint, are more likely to quit successfully."*[16] Similarly, Friedman & Xu found that adult smokers who used non-tobacco-flavored ENDS were significantly more likely to subsequently switch away from smoking.[17]

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[15] Mari S. Gades, et al., *The Role of Nicotine and Flavor in the Abuse Potential and Appeal of Electronic Cigarettes for Adult Current and Former Cigarette and Electronic Cigarette Users: A Systematic Review*, NICOTINE TOBACCO RESEARCH (2022), 24, 1332-1343, Flavor at 1136, https://tinyurl.com/5n6j7yhh.

[16] Yoonseo Mok, et al., *Associations between E-Cigarette Use and E-Cigarette Flavors with Cigarette Smoking Quit Attempts and Quit Success: Evidence from a U.S. Large, Nationally Representative 2018-2019 Survey*, NICOTINE TOBACCO RESEARCH 2023, 25, 541-552, at 541, https://tinyurl.com/2j79rdjr.

[17] Abigail S. Friedman, et al., *Associations of Flavored E-Cigarette Uptake with Subsequent Smoking Initiation and Cessation*, JAMA NETWORK OPEN 2020;3(6):e203826, at 9, https://tinyurl.com/3khzp8ym.

Beyond the potential advantage of mint/menthol flavored ENDS in particular, non-tobacco flavors in general – and especially a variety of such flavors – may confer a benefit to adult smokers. One systematic review concluded that *"the availability of a variety of flavors in e-cigarettes might facilitate complete substitution for cigarettes."*[18] We discuss the possible unintended consequences of a *de facto* ban on non-tobacco flavors in section VII below.

IV. Youth Vaping Has Declined Markedly Since 2019, With Most Youth Vaping Being Infrequent, Non-Addictive, And Temporary, And More Frequent And Intense Vaping Generally Limited To Adolescents Who Are Otherwise Likely To Smoke.

Youth vaping is a concern; however, important context can help to mitigate some of this concern. Youth vaping peaked in 2019 and has subsequently declined. In 2019,[19] 20% of middle and high school students used ENDS at least once in the past 30 days, according to the Centers for Disease Control's ("CDC") National Youth Tobacco Survey ("NYTS"); this has since declined to 9.4% in 2022[20] – a more than 50%

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[18] Gades, et al., *supra* note 15, at 1332.

[19] Teresa W. Wang, et al., *Tobacco Product Use and Associated Factors Among Middle and High School Students – United States, 2019*, MMWR Surveillance Summaries 68(12);1-22 (Dec. 2019), Table 2 at 13, https://tinyurl.com/47f62ecx.

[20] Maria Cooper, et al., *Notes from the Field: E-Cigarette Use Among Middle and High School Students – United States, 2022*, MMWR Weekly Report 71(40);1283-1285, Table at 1284, https://tinyurl.com/ycedn68e.

decline. Similar declines have been reported by other U.S. national surveys.[21]

The majority of youth vaping seems to be experimental in nature rather than indicative of regular or addictive patterns of vaping. According to NYTS 2022,[22] the majority (57.7%) of youth users vaped *in*frequently (i.e., on fewer than 20 days out of the past 30). There were also substantially *fewer* frequent youth vapers in 2022 than in 2019 (1.08 vs. 1.63 million, respectively).[23]

Additionally, youth vaping – especially frequent vaping – is concentrated in adolescents who use other tobacco products. For instance, Jarvis, et al. found adolescents with an established history of tobacco use were more than five times as likely to have used ENDS in the past 30 days."[24] *Frequent* vaping was even more strongly concentrated in those with a history of other tobacco product use – only 2.1% of tobacco-naïve youth vaped frequently.[25] Thus, it is highly likely that youth who vape frequently would have otherwise likely

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[21] Richard A. Miech, et al., *Monitoring the Future: National Survey Results on Drug Use, 1975–2022: Secondary School Students*, University of Michigan Institute for Social Research (2023), at Table 5-5c at 150, https://tinyurl.com/y2x2s6nw; CDC, *Youth Risk Behavior Survey: Data Summary & Trends Report* (2023), at 35, https://tinyurl.com/2wazwjax.

[22] Cooper, et al., *supra* note 20, Table at 1284.

[23] Wang, et al., *supra* note 19, Table 3 at 14; Cooper, et al., *supra* note 20, Table at 1284.

[24] Martin Jarvis, et al., *Epidemic of youth nicotine addiction? What does the National Youth Tobacco Survey 2017-2019 reveal about high school e-cigarette use in the USA?*, QEIOS (2020), Findings at 1, https://tinyurl.com/3j6sbw8r.

[25] *Id.* at 6.

smoked cigarettes.[26] Adolescents who vape have individual characteristics and circumstances that are also associated with a higher likelihood of cigarette smoking, including using other substances, poor mental health, risk-seeking personality traits, and a family history of tobacco use.[27]

Overall, while no youth should use ENDS, it is important to understand the context of substantial declines in youth vaping in recent years, including *frequent* vaping. Vaping is concentrated in youth with a history of other tobacco use and those who otherwise are likely to have smoked cigarettes.

V. Young People Do Not Generally Use The Refillable Tank Devices Sold In Vape Shops, But Instead Use More Mass-Market Products.

The ENDS market is diverse and includes a variety of device types. Refillable tanks, referred to as "open" systems, involve refilling a device with a separately bottled e-liquid. In contrast, pre-packaged or "closed" systems include pods/cartridges and disposable ENDS with internal reservoirs that are pre-filled with e-liquid and discarded after use. Open systems such as refillable tanks are primarily sold in age-restricted specialist vape shops or online. They are rarely sold

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[26] Natasha A. Sokol, et al., *High School Seniors Who Used E-Cigarettes May Have Otherwise Been Cigarette Smokers: Evidence From Monitoring the Future (United States, 2009–2018)*, NICOTINE TOBACCO RESEARCH 2021, 11, 1958-1961, Conclusions at 1958, https://tinyurl.com/3fczmuvm (no free access).

[27] Peter N. Lee, et al., *Considerations related to vaping as a possible gateway into cigarette smoking: an analytical review*, F1000RESEARCH 2019, 7:1915, Association of smoking with other risk factors at 5 and Table 2 at 6, https://tinyurl.com/bdfc34fm.

in other physical retail settings (e.g., convenience stores, etc.). According to an analysis of national retail data through 2022 conducted by CDC authors, including Dr. Brian King, now Director of FDA's Center for Tobacco Products,[28] bottled e-liquid products accounted for <1% of ENDS sales from tracked[29] channels (i.e., excluding online and specialty vape store sales), in which disposable and pre-filled pods/cartridges dominate. The NYTS 2021 data show most youth obtained their ENDS products from social sources, either without buying them (37.2%) or buying from a friend, relative, or someone else (21.5%).[30]

Youth use rates vary widely across ENDS device types, but the use of refillable tanks has remained consistently low among youth despite many large-scale changes in the ENDS market. Youth rarely use refillable tank products as their usual device type – this was only 6.7% of past-month youth vapers in NYTS 2022[31] – corresponding to only 160,000 youth out of the 2.55

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[28] Fatma M. Romeh, et al., *Trends in US E-cigarette Sales and Prices by Nicotine Strength, Overall and by Product and Flavor Type, 2017-2022*, NICOTINE TOBACCO RESEARCH 2023, 25, 1052-1056, Measures at 1053, https://tinyurl.com/2p892cve.

[29] Tracked retail data from Information Resources, Incorporated ("IRI") include sales from convenience stores, gas stations, grocery stores, drug stores/pharmacies, mass merchandiser outlets, retail chain stores, club stores, dollar stores, and military sales; and exclude sales from specialty vape/tobacco stores and online. *Id.* at Data Source at 1053.

[30] Andrea S. Gentzke, et al., *Tobacco Product Use and Associated Factors Among Middle and High School Students – National Youth Tobacco Survey, United States, 2021*, MMWR Surveillance Summaries 71(5);1-29, Table 7 at 23, https://tinyurl.com/8jyacwxp.

[31] Cooper, et al., *supra* note 20, Table at 1284.

million who vaped in the past 30 days.[32] In contrast, the majority of youth vapers (55.3%) used disposables, and 25.2% used pre-filled pods/cartridges.[33] At the same time, refillable tank ENDS products are overwhelmingly used by adults and represent a minimal threat to youth, who much more often use pre-packaged or closed ENDS products. Paradoxically, pre-packaged or closed-device systems have so far been the only type of ENDS products to be granted a marketing order through FDA's premarket review process.

VI. Claims That Vaping Is A Gateway To Smoking Are Based On A Misunderstanding Of The Evidence.

Some concerns have been raised that ENDS act as a "gateway" to cigarette smoking among youth, based on findings that youth who use ENDS are also more likely to later initiate cigarette smoking.[34] However, this is to confuse correlation and causation. Youth who vape and youth who smoke share many of the same underlying risk factors (e.g., other substance use, poor mental health, risk-seeking personality traits, family history of tobacco use), suggesting instead that a general "common liability" or propensity for tobacco use (regardless of the specific tobacco product) better

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[32] *Id.*

[33] *Id.*

[34] NASEM, *supra* note 3, Summary at Conclusion 16-1 at 10; Samir Soneji, et al., *Association Between Initial Use of E-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults: A Systematic Review and Meta-Analysis*, JAMA PEDIATR. 2017;171(8):788-797, Abstract at 788, https://tinyurl.com/yjaz8wfz (no free access); Jessica L. Barrington-Trimis, et al., *E-Cigarettes and Future Cigarette Use*, PEDIATR. 2016:138(1), Abstract at 1, https://tinyurl.com/2fr5nc3t (no free access).

explains the overlap between ENDS use and smoking. A well-known limitation of the available data on youth vaping (which is observational rather than experimental for ethical reasons) is the difficulty of separating out "confounding factors," which can better explain the observed association. Specifically, it is difficult to statistically separate the hypothesized unique, *causal* effect of ENDS use on subsequent smoking initiation (the gateway effect) from the pre-existing propensity to use tobacco (i.e., the user would have likely become a smoker in the absence of ENDS).

While studies that purport to show a gateway effect do attempt to account for pre-existing propensity to use tobacco products, they can never do this sufficiently. One review article identified 34 risk factors common to both ENDS use and cigarette smoking, which must be accounted for when attempting to isolate the hypothesized causal gateway effect.[35] However, none of the studies published at the time of the review examined even half of these risk factors.[36] These unaccounted-for risk factors can create quite strong correlations, but they do not show that ENDS caused subsequent smoking.[37] In support of this, the apparent gateway association becomes successively weaker as

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[35] Lee, et al., *supra* note 27, Data Availability, Additional File at 1, Table A1-2 at 17-20, https://osf.io/xg2hz. The table lists 34 risk factors considered in 15 studies.

[36] *Id*.

[37] Sooyong Kim, et al., *The Relationship Between Electronic Cigarette Use and Conventional Cigarette Smoking Is Largely Attributable to Shared Risk Factors*, NICOTINE TOBACCO RESEARCH 2020, 7, 1123-1130, Abstract at 1123, https://tinyurl.com/mr2v8hwk (no free access).

more shared risk factors are accounted for.[38] Ultimately, the association between ENDS use and smoking initiation becomes non-significant in some studies[39] – that is, youths' pre-existing propensity to use tobacco products may *entirely* explain why youth who vape are also more likely to smoke. Thus, there does not seem to be a unique causal effect of ENDS use on youth smoking initiation, above and beyond what is explained by the pre-existing propensity to use tobacco products.

Population-level trends also provide another line of research with which to "triangulate" evidence in support of or in opposition to the gateway hypothesis.[40] If a gateway effect were real, we might expect increased smoking to follow increased vaping. However, the population-level smoking prevalence trends show the opposite. Several studies have demonstrated that smoking declined *faster* after ENDS use became common,[41]

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[38] *Id.* at Discussion at 6; Adam M. Leventhal, et al., *Association of Electronic Cigarette Use with Initiation of Combustible Tobacco Product Smoking in Early Adolescence*, JAMA 2015;314(7):700-707, Table 4 at 705, https://tinyurl.com/yn6mxa6t; Ruoyan Sun, et al., *Is Adolescent E-Cigarette Use Associated with Subsequent Smoking? A New Look*, NICOTINE TOBACCO RESEARCH 2022, 24, 710-718, Abstract at 710, https://tinyurl.com/ywdc3rjw.

[39] Kim, et al., *supra* note 37, Abstract at 1123; Sun, et al., *supra* note 38, Abstract at 710.

[40] Lion Shahab, et al., *Unpacking the Gateway Hypothesis of E-Cigarette Use: The Need for Triangulation of Individual - and Population-Level Data*, NICOTINE TOBACCO RESEARCH 2022, 24, 1315-1318, at 1315, https://tinyurl.com/2p8zb39t.

[41] David T. Levy, et al., *Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check*, TOBACCO CONTROL 2019;28:629-635, Abstract at 629, https://tinyurl.com/ydu7jhuz; Rafael Meza, et al., *Trends in Tobacco Use Among Adolescents by Grade, Sex, and Race, 1991-*

and that there is more likely a displacement effect whereby ENDS use occurs among youth who are predisposed to use tobacco and would have otherwise smoked.[42] U.S. public health objectives are codified in the U.S. Department of Health and Human Service's Healthy People ("HP") targets for reduced tobacco product use. These underscore how drastic and unexpected the decline in past-month youth smoking has been. The HP 2030 target for youth cigarette smoking prevalence in 2030 (3.4%) had been *achieved by 2020* (3.3%), down from the 2018 baseline of 5.4%.[43] The 2020 cigarette smoking prevalence of 3.3% – was far lower than the HP 2020 target of 16% that was set in 2010.[44]

It is theoretically possible for both a gateway and displacement effect to occur simultaneously;[45] however, if there is a gateway effect, it is comparatively weak, and there must be a net diversion effect to explain observed declines in smoking prevalence.

2019, JAMA NETWORK OPEN 2020;3(12):1-14, Abstract at 2, https://tinyurl.com/34f57znx.

[42] Arielle S. Selya, et al., *Trends in electronic cigarette use and conventional smoking: quantifying a possible 'diversion' effect among US adolescents*, ADDICTION 116 1848-1858 (2021), Discussion at 1854, https://tinyurl.com/mupdw8c9.

[43] U.S. Health and Human Services, Healthy People 2030, Tobacco Use Objectives, TU-06, https://tinyurl.com/yc744wt4.

[44] U.S. Health and Human Services, Healthy People 2020, Tobacco Use Objectives, archive, https://tinyurl.com/2p83fmrd.

[45] Carl V. Phillips, *Gateway Effects: Why the Cited Evidence Does Not Support Their Existence for Low-Risk Tobacco Products (and What Evidence Would)*, INT. J. ENVIRON. RES. PUBLIC HEALTH 2015, 12, 5439-5464, 2.8 Magnitude Matters at 5450, https://tinyurl.com/2p85a33d.

The existing evidence overwhelmingly supports a common liability explanation rather than a gateway explanation. This means there are characteristics of young people and their circumstances that incline them to both vaping and smoking, so the two behaviors are seen together, but one does not cause the other.

VII. Because Smoking And Vaping Are Linked, Measures Like E-Liquid Flavor Bans Can Cause More Smoking Or Other Damaging Unintended Consequences.

Several lines of evidence show that ENDS function as substitutes for cigarettes. Population-level evidence shows that smoking prevalence declined faster as ENDS use became common among both youth and adults,[46] with the largest declines occurring among groups with the highest ENDS uptake. National sales data similarly show a shortfall in cigarette sales that correlates with ENDS sales, such that cigarette sales decline by 1.4 packs per capita for every additional per-capita ENDS unit sold – with evidence supporting ENDS, rather than cigarettes, as the driving factor.[47] Additionally, quasi-experimental studies show that ENDS function as economic substitutes for cigarettes. For instance, higher cigarette prices are associated with *lower* cigarette purchases but *higher* ENDS purchases.[48] Likewise, there is some evidence that

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[46] Levy, et al., *supra* note 13, Figure 1 at 9 and Table 3 at 11-12; Levy, et al., *supra* note 41, Abstract at 629; Meza, et al., *supra* note 41, Abstract at 2; Selya, et al., *supra* note 42, Figure 3 at 1852.

[47] Selya, et al., *supra* note 14, Results at 85.

[48] Chad Cotti, et al., *The effects of e-cigarette taxes on e-cigarette prices and tobacco product sales: Evidence from retail panel data*, J. HEALTH ECON. (2022), Abstract at 1, https://tinyurl.com/bdz6r8pe (no free access); Tingting Yao, et al., *The impact of e-cigarette*

higher ENDS prices are associated with higher *cigarette* purchases[49] (though this association is weaker and not always significant, likely due to the cigarette market being approximately ten times as large as the ENDS market),[50] as well as increased cigarette smoking prevalence among adults.[51]

With this well-established substitution between ENDS and cigarettes, it is plausible that restrictions imposed on the ENDS market could have the harmful unintended effect of driving tobacco users back to cigarettes, which are far more harmful to health. In fact, there is evidence of this unintended consequence occurring. Friedman showed that *youth smoking rates increased* following San Francisco's ban on flavored tobacco products, which included nearly all ENDS

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and cigarette prices on e-cigarette and cigarette sales in California, PREV. MED. REP. (2022), Conclusion at 5, https://tinyurl.com/mrxd8djj; Yuqing Zheng, et al., *U.S. Demand for Tobacco Products in a System Framework*, HEALTH ECON. 2017, 26, 8, 1067-1086, Abstract at 1067, https://tinyurl.com/4kvt4zhd (no free access).

[49] Cotti, et al., *supra* note 48, Results at 27; Arielle Selya, et al., *Meta-analysis of E-Cigarette Price Elasticity*, F1000RESEARCH 2023, Abstract at 1, https://tinyurl.com/3tys2xu6.

[50] Selya, et al., *supra* note 49, Discussion at 16; Selya, et al., *supra* note 14, Figure 1 at 82.

[51] Michael F. Pesko, et al., *The effects of traditional cigarette and e-cigarette tax rates on adult tobacco product use*, J. RISK UNCERTAINTY 60, 229-258 (2020), Abstract at 1, https://tinyurl.com/2c5kk8ty (no free access); Henry Saffer, et al., *E-Cigarettes and adult smoking: Evidence from Minnesota*, J. RISK UNCERTAINTY 60, 207-228 (2020), Abstract at 1, https://tinyurl.com/yxztny5u (no free access); Abigail S. Friedman, et al., *Young adult responses to taxes on cigarettes and electronic nicotine delivery systems*, ADDICTION 117, 12 (2022), Abstract at 3121, https://tinyurl.com/yn3a8yka.

varieties.[52] A substitution effect was also shown to result from changes in ENDS prices. For example, every additional $1 in ENDS price was associated with users smoking three additional packs over the past 30 days.[53] As described above, several other studies also show increased cigarette smoking prevalence or intensity associated with ENDS price increases.[54] Thus, restrictions on the ENDS market – which can include state-level or local price increases and flavor bans, or FDA regulatory practice that creates a *de facto* federal flavor ban – are likely to have harmful unintended consequences of driving tobacco users towards cigarettes. Given the substantially higher health risks posed by cigarettes, these restrictions may result in a substantial net detriment to public health, outweighing the gains of reduced ENDS use.

In its 2016 report, the Royal College of Physicians (London) signaled its concern about the potentially

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[52] Abigail S. Friedman, *A Difference-in-Differences Analysis of Youth Smoking and a Ban on Sales of Flavored Tobacco Products in San Francisco, California*, JAMA PEDIATR. 2021;175(8):865-867, Figure 1 at 864, https://tinyurl.com/56z35ka7; Abigail S. Friedman, *Clarification and Correction of Survey Wave Collection Dates in an Analysis of Youth Smoking and a Ban on Sales of Flavored Tobacco Products in San Francisco, California*, JAMA PEDIATR. 2022;176(9):1-4, at 1, https://tinyurl.com/2p89r9cn.

[53] Michael F. Pesko, et al., *Re-exploring the early relationship between teenage cigarette and e-cigarette use using price and tax changes*, HEALTH ECON. 2022;31:137-153, Results at 143, https://tinyurl.com/mr3z96vx.

[54] Pesko, et al., *supra* note 51, Abstract at 1; Saffer, et al., *supra* note 51, Abstract at 1; Friedman, et al., *supra* note 51, Abstract at 3121.

perverse consequences of otherwise well-intentioned ENDS regulation:[55]

> A risk-averse, precautionary approach to e-cigarette regulation can be proposed as a means of minimising the risk of avoidable harm, e.g., exposure to toxins in e-cigarette vapour, renormalisation, gateway progression to smoking, or other real or potential risks.
>
> However, if this approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it causes harm by perpetuating smoking. Getting this balance right is difficult.

An increase in smoking is not the only plausible adverse response to aversive ENDS regulation. There may also be switching to well-organized illicit sources, the creation of an informal economy of home mixing and small-scale trading, or a rise in cross-border trade.

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[55] RCP, *supra* note 5, at 187.

CONCLUSION

Based on the foregoing, this Court should grant the Petition.

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