**UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF COLUMBIA**

**NICOPURE LABS, LLC, *ET AL.*,**

**Plaintiffs,**

***vs.***

**U.S. FOOD AND DRUG ADMIN., *ET AL.*,**

**Defendants.**

**Civ. No. 1:16-cv-0878-ABJ**

**BRIEF OF *AMICI CURIAE* CLIVE BATES AND FIFTEEN OTHERS IN IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT**

Respectfully submitted:

Eric R. Stanco
(D.C. Bar No. 555538)
Stanco & Robinson LLP
2390 Tamiami Trail North
Suite 216
Naples, FL 34103
(239) 263-7755
(239) 263-8955 (facsimile)
erstanco@suretylaw.com

Counsel for *Amici Curiae*,
Clive Bates and Fifteen Others

## THE AMICI

Philip Alcabes, Professor of Public Health College of Nursing and Public Health, Adelphi University, Garden City, New York;

Edward Anselm MD, Assistant Professor of Medicine Icahn School of Medicine at Mount Sinai, New York. Senior Fellow, R Street Institute, Washington DC;

Clive Bates (lead author), Director Counterfactual. Former Director, ASH (UK);

Ernest Drucker PhD, Research Scientist and Professor of Public Health, College of Global Public Health, New York University;

Konstantinos Farsalinos, M.D. Research Scientist, Onassis Cardiac Surgery Center, Athens, University of Patras, Greece;

William T. Godshall, MPH, Founder and Executive Director, Smokefree Pennsylvania;

Jacques Le Houezec, Consultant in Public Health, Président SOVAPE, Paris, France;

Bernd Mayer, PhD, Professor & Chair, Dept. Pharmacology, University of Graz, Austria;

Jeff Nesbit, Executive Director, Climate Nexus, New York. Former Associate Commissioner, Food and Drug Administration;

Joel L. Nitzkin, MD, MPH, DPA, Chief Executive Officer, JLN MD Associates, Senior Fellow for Tobacco Policy, R Street Institute, Washington, DC;

Riccardo Polosa, MD, PhD, Full Professor of Internal Medicine, University of Catania;

Gilbert L. Ross, MD, Diplomate, American Board of Internal Medicine Board-certified in Internal Medicine and Rheumatology. Jersey City, NJ;

Sally L. Satel MD, Resident Scholar, American Enterprise Institute, Washington DC;

Michael B. Siegel, MD, Professor, Community Health Sciences, Department of Community Health Sciences, Boston University School of Public Health. MA;

Andrzej Sobczak PhD, Professor, Head of Department Chemical Hazards and Genetic Toxicology, Inst. Occupational Medicine and Environmental Health, Sosnowiec, Poland;

David Sweanor, JD, Centre for Health Law, Policy and Ethics, University of Ottawa.

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## I. INTRODUCTION

The *Amici* respectfully submit this *amici curiae* brief in support of the Plaintiffs, Right to be Smoke-Free Coalition, *et al.*, and their challenge to the U.S. Food and Drug Administration's (FDA) Deeming Rule, 81 Fed. Reg. 28,973 (May 10, 2016).[1]

A comment was provided by *Amicus* Clive Bates during the consultation stage of the rule-making process[2] criticizing FDA's draft cost-benefit analysis under three headings:

- No attempt to assess the key benefit – the reduction in smoking – that would arise from greater uptake of e-cigarettes in the population.
- No attempt to assess how regulation *itself* may reduce or eliminate the benefits.
- No attempt to assess risks rising from real world reactions to excessive regulation proposed by FDA.

These failings have persisted in the final Deeming Rule and Regulatory Impact Analysis, yet they represent major and fatal weaknesses in the analysis. Amici contend that health consequences – both positive and negative - dominate the true costs and benefits, but have not been adequately assessed in the cost-benefit analysis shown in the Regulatory Impact Analysis[3].

## II. STATEMENT OF INTEREST

The primary interest of the *Amici* is in public health, science and regulation, with a focus on the concept of tobacco harm reduction - the replacement of high-risk nicotine products like cigarettes with low-risk products like e-cigarettes. *Amici* are concerned by the impact that scientific judgments and regulatory practice adopted in the United States will have on the health of American citizens and the influence they will have in setting *de facto* norms internationally.

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[1] Pursuant to FRAP 29(c), the *Amici* state that Clive Bates is the sole author of this Brief; no money or other consideration was received by him or by any member of his group from a party or its counsel to fund the preparation or submission of this Brief; the drafting of this Brief was not funded by any third person or entity, although CASAA's attorney, at CASAA's expense, conformed the Brief to the requirements of this Court and filed it on the Project's behalf.

[2] Bates C., Comment FDA-2014-N-0189-80077 on Proposed Rule 79 Fed. Reg. 23,141 [link]

[3] FDA, Deeming Rule, FDA-2014-N-0189: Final Regulatory Impact Analysis, 10 May 2016 [link]

## III. ARGUMENT

**THE CLAIMED BENEFITS OF THE DEEMING RULE ARE MORE LIKELY TO BE COSTS. THE MOST IMPORTANT COSTS HAVE NOT BEEN ASSESSED. THE REGULATORY IMPACT ANALYSIS IS UNSOUND AND THE RULE IS UNJUSTIFIED.**

### A. ENDS Are An Alternative Way To Use Nicotine With A Risk To Health That Is Unlikely To Exceed Five Percent Of The Risk Of Smoking And Is Likely To Be Substantially Lower Than That Figure. If ENDS Substitute For Smoking, There Are Important Public Health Gains That Could Be Jeopardized By Poorly Designed Regulation.

On 28 April 2016, the Royal College of Physicians (London) published a major assessment of the public health implication of electronic nicotine delivery systems (ENDS), such as e-cigarettes, and the strategy of tobacco harm reduction. In response to widespread public misperception of the relative risk of smoking and e-cigarette use, it provided the following carefully formulated statement:[4]

> "Although it is not possible to precisely quantify the long-term health risks associated with e-cigarettes, the available data suggest that they are unlikely to exceed 5% of those associated with smoked tobacco products, and may well be substantially lower than this figure". (Section 5.5 page 87).

The statement is grounded in an assessment of the scientific literature that covers the toxicology of e-cigarette aerosol and cigarette smoke, which has been subject to several high quality assessments[5] [6] [7]. Many hazardous agents in cigarette smoke are not detectable in ENDS

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[4] Tobacco Advisory Group of the Royal College of Physicians (London) *Nicotine Without Smoke: Tobacco Harm Reduction*, 28 April 2016 [link]

[5] Burstyn I., *Peering through the mist: systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks*, BMC Public Health 2014;**14**:18. [Link]

[6] Farsalinos KE, Polosa R., *Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review*. Ther Adv Drug Saf 2014;**5**:67–86. [Link ]

[7] Hajek P, Etter JF, Benowitz N, *et al. Electronic cigarettes: Review of use, content, safety, effects on smokers and potential for harm and benefit*. Addiction 2014;**109**:1801–10. [link]

vapor or are only present at much lower exposures, typically significantly below 1 percent. The risks are so markedly different because ENDS do not involve combustion processes.

However, FDA has approached the regulation as if the health impacts of ENDS are unknown: "*We do not currently have sufficient data about e-cigarettes to determine what effects they have on the public health.*" [79 Fed. Reg. 23,157], while citing a selection of studies suggesting presence of some hazardous agents [81 Fed. Reg. 29,029], but without quantification of magnitude (i.e. establishing material risk) or an overall synthesis. The Royal College of Physicians assessment is a synthesis based on current knowledge. This leads to a reasonable working assumption that ENDS are *much* less (95-100 percent less) harmful to health than cigarettes.

The population data are consistent with low-risk ENDS use displacing high-risk cigarette smoking – a change in how nicotine is used that would be beneficial. There are two further findings relevant to the costs and benefits of the Deeming Rule.

First, adult smoking prevalence has fallen rapidly as ENDS use has increased. The National Health Interview Survey[8] shows that U.S. adult smoking prevalence has fallen from 18.9 percent in 2011 to a record low 15.1 percent in 2015. The impact of ENDS on the cigarette trade is becoming substantial: in 2015, there were approximately 37.5m smokers, but there were 8.3m ENDS users of whom 2.5m were ex-smokers[9].

Though there were 4.9m 'dual users' (2015) who were both smoking and vaping, this is observation is encouraging, not a cause for concern. This is because most dual users will be reducing their risk to some degree and many will be undergoing a transition away from smoking

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[8] National Center for Health Statistics, *National Health Interview Survey, 1997–2015,* Sample Adult Core component. Figure 8.1. Prevalence of current cigarette smoking among adults aged 18 and over: United States, 1997–2015. [link]

[9] CDC, *National Health Interview Survey, 2015 Data Release* [link]; Cited in Rodu B. *How Many Americans Vape? CDC Data Show Fewer Vapers & Smokers in 2015*, Tobacco Truth 17 July 2016 [link]

via dual use over time. Studies of pathways followed by smokers do suggest that dual users have a higher probability of becoming ex-smokers[10]. Almost all attempts to quit smoking involve some form of 'dual use' whatever method is used, often by repeated attempts to quit followed by relapse to smoking. Very few smokers using any method quit permanently on their first attempt.

Second, adolescent smoking has also been falling rapidly. The National Youth Tobacco Survey (CDC) [11] shows that between 2011 and 2015, current use of cigarettes by high school students fell from 15.8 percent to 9.3 percent, and use of cigars and pipes also fell.

Further, the data suggest that ENDS use is less habitual and more characterized by experimentation, and much adolescent e-cigarette use does not involve nicotine at all. Almost half (45.4 percent) of those counted as e-cigarette users used e-cigarettes on only two days or fewer in the survey month[12]. The University of Michigan Monitoring the Future survey showed that of the 16.3 percent of 12th graders who used e-cigarettes in the last 30 days, only just over 1 in 5 (22 percent) of them had used nicotine liquids the last time they used an e-cigarette[13].

### B. FDA Claims Five Main Benefits For The Deeming Rule, But These Are Weak Or Unsubstantiated And More Likely To Turn Out To Be Costs.

FDA has not demonstrated any material health, consumer protection or other problems arising from ENDS to which the Deeming Rule is a proportional response. FDA summarizes Deeming Rule benefits in a list of five claims in the Final Regulatory Impact Analysis[14].

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[10] Manzoli L, Flacco ME, Ferrante M, Vecchia CL, Siliquini R, Ricciardi W, et al. *Cohort study of electronic cigarette use: effectiveness and safety at 24 months.* Tobacco Control. 2016 [link]

[11] Singh T, Arrazola RA, Corey CG, et al. *Tobacco Use Among Middle and High School Students — United States, 2011–2015*. MMWR Morb Mortal Wkly Rep 2016;65:361–367. [link]

[12] Neff LJ, Arrazola RA, Caraballo RS, *et al. Frequency of Tobacco Use Among Middle and High School Students--United States, 2014*. MMWR Morb Mortal Wkly Rep 2015;**64**:1061–5 [link]

[13] National Institute on Drug Abuse, *Monitoring the Future Figures 2015: Substance Vaporized Last Time E-cigarette Used*. December 2015. [link]

[14] FDA, Deeming Rule Docket No. FDA-2014-N-0189: Final Regulatory Impact Analysis, 10 May 2016, page 67 [link]

Claim 1: "*premarket review, which will result in fewer harmful or addictive products from reaching the market than would be the case in the absence of the rule*".

Response 1: FDA cannot claim this as a benefit. The reason is that the highly harmful and addictive products that dominate the market, cigarettes, are unaffected by the Deeming Rule, and largely unaffected by the Tobacco Control Act due to 'grandfathering' of all cigarette products on the market on 15 February, 2007 (21 USC §387j(a) *Application for review of certain tobacco products*). In reality, the rule will result in *far fewer of the much safer alternatives* (ENDS) to the most harmful and addictive products (cigarettes) reaching the market. The quality of ENDS products reaching the markets could have been assured more simply by standard-setting (21 USC §387g *Tobacco product standards***)** rather than product by product authorization.

Claim 2: "*youth access restrictions and prohibitions on free samples, which can be expected to constrain youth access to tobacco products and curb rising uptake*."

Response 2: There is near universal support for banning sales of ENDS to minors. However, FDA's intervention provides no additional benefit, and some cost, because 48 states and the District of Columbia have already implemented age restrictions, some with age limits of 19 or 21. In the two remaining states, Pennsylvania and Michigan, both legislative bodies have approved bills banning sales of ENDS to minors. The free samples available in vape shop settings have no bearing on youth access, but a ban represents a detriment to commercial freedom and adult free choice and, by denying trial opportunities, may prevent adults switching from smoking to vaping, thereby causing a health detriment.

Claim 3: "*health warning statements, which will help consumers understand and appreciate the risks of using tobacco products*."

Response 3: The health warning envisaged in the Deeming Rule is "*WARNING: This product contains nicotine. Nicotine is an addictive chemical.*". [4. Required Warning Labels 81 Fed. Reg. 28,988 (May 10, 2016)] It is important consumers are informed about the presence of nicotine and have a realistic perception of its risks. However, FDA does not report any consumer evaluation of this warning for positive impact on existing behavior or perceptions. It follows that FDA has no basis for claiming it will be beneficial. If its actual impact is to deter consumers from trying ENDS as alternatives to smoking, it may be a cause of harm.

Claim 4: "*prohibitions against false or misleading claims and unsubstantiated MRTP claims lead to better-informed consumers and help prevent the use of misleading campaigns targeted to youth populations.*"

Response 4: Consumers form their perceptions of the relative riskiness of smoking and vaping from many sources, not primarily from manufacturers. These include the statements of public bodies, activists, media-savvy academics and their press officers, journalists, hearsay and direct experience. Surveys of adult consumers show that perceptions of the relative risks of ENDS and smoking are wildly misaligned with expert assessment, and in a way that increases harm by diminishing the perceived health gains of switching. The National Cancer Institute surveyed perception of risk in 2015[15] and found only 5.3 percent of American adults correctly identified electronic cigarettes as 'much less harmful' than cigarettes – which is the answer that most closely matches expert judgment (see section A above). However, 37.5 percent thought e-cigarettes were just as harmful or more harmful – thus holding a view that no experts believe is remotely close to the reality.

[15] National Cancer Institute, *Health Information National Trends Survey*, FDA Survey 2015. [link]

FDA also claims it will "*prevent misleading campaigns targeted to youth populations*". All parties support this aim. However, FDA can only claim a benefit arising from the Deeming Rule if there is a material problem to which its powers to intervene are an effective response. FDA has not taken powers to control e-cigarette advertising in general, rather only in the narrow and rare circumstances where a false or misleading and unauthorized modified risk claim is made (i.e. not simply where advertising is targeted to appeal to adolescents). See 81 Fed. Reg. 29,041 (May 10, 2016) "*additional provisions in part 1140 (including minimum pack size and restrictions on self-service displays, sale and distribution of nontobacco items, and sponsorship of events) will not apply to the newly deemed products at this time.*"

Claim 5: "*other institutional changes, such as FDA monitoring of product developments and changes and required ingredient listings, which will enable FDA to propose more informed regulations appropriate for the protection of the public health*."

Response 5: FDA's burdensome and time consuming PMTA is required for every significant new innovation. In this way, from 8 August 2016, the Deeming Rule creates a *de facto* block on new innovations that would benefit health. Such innovations may come in two forms: (1) improvements to the safety of the device itself such as temperature control, changes to coil design, new liquid formulation, better refilling mechanisms or other safety features; and (2) improvements that make the product more attractive to smokers and thereby promote switching from high-risk to low-risk nicotine use. Such innovations may relate to ease-of-use (especially important for novices) or convenience (for example small forms based on new batteries).

### C. FDA Has Failed To Consider The Likelihood That Its Own Intervention, Through The Deeming Rule, Will Have Harmful Unintended Consequences That Create Major Public Health Costs And These Have Not Been Assessed In The Cost-Benefit Or Breakeven Analysis.

FDA makes the following claim in the Deeming Rule. [81 Fed. Reg. 28,984]

> Whether ENDS generally may eventually be shown to have a net benefit on or harm to public health at the population level—and there have not yet been long-term studies conducted to support either claim at this time—*regulation* of ENDS will still benefit public health. (original emphasis)

FDA cannot simply assume that its regulation will benefit public health. In doing so, FDA has not acknowledged a major concern with the Deeming Rule, namely that *the rule itself* will have serious harmful effects if it fundamentally changes the structure of the market to favor cigarettes at the expense of e-cigarettes. The Royal College of Physicians (London)[16] recognizes the potential danger to health arising from ENDS regulation itself:

> 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. (Section 12.10, page 187)

It is "getting this balance right" that should pre-occupy regulators because the consequences of getting it wrong are increased death and disease attributable to FDA's intervention. However, FDA has not actually recognized there is this balance to strike, or that the health consequences – positive or negative – dominate the main underlying costs and benefits.

Small increases in population smoking behavior create large costs for three reasons: (1) the value attributed to life is high ($472,000-$785,000 per quality adjusted life-year "QALY" in

[16] Tobacco Advisory Group of the Royal College of Physicians (London) *Nicotine Without Smoke: Tobacco Harm Reduction,* 28 April 2016 [link]

FDA's cost-benefit analysis); (2) the populations involved are large (37.5m smokers, 8.3m ENDS users); and (3) the loss of life caused by smoking may be several years (a lifelong male smoker typically loses 10 years of life compared to a non-smoker and stopping smoking at age 60, 50, 40, or 30 years gains, respectively, about 3, 6, 9, or 10 years of life expectancy[17]).

FDA confirms the sensitivity of its estimates to health impacts by arguing that the quantified costs of the Deeming Rule are justified by a relatively small number of QALYs[18]:

> The rule would need to save only between 2,080 and 4,187 QALYs to breakeven depending on the discount rate. These numbers can be compared to the estimated 34.9 million adults and youth who currently use the tobacco products to be deemed and roll-your-own tobacco.

However, the more complete interpretation of this statement is that the underlying costs and benefits calculation is highly sensitive to, and dominated by, any changes in the patterns of tobacco use and resulting health impact (QALYs gained or lost) – and not the administrative costs and burdens that are the focus of the Regulatory Impact Analysis. It follows that any *increases* in smoking that arise from unintended consequences of regulation (summarized in the Royal College of Physicians citation above but unacknowledged by FDA) will also dominate.

As an illustrative example, consider the following hypothetical scenario: (1) that the behavior of just one percent of the current 8.3 million U.S. ENDS users changes adversely to increased smoking due to the Deeming Rule's unintended consequences, and (2) that this creates an average of just one QALY health detriment per person affected. In that case, a detriment of 83,000 QALYs should be included in the RIA. At the value of $472,000-785,000 per QALY used in the RIA (Table 3) that would create a cost of $39-$65 billion undiscounted.

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[17] Doll R, Peto R, Boreham J, *et al. Mortality in relation to smoking: 50 years' observations on male British doctors*. *BMJ* 2004;**328**:1519 [link]

[18] FDA, Deeming Rule Docket No. FDA-2014-N-0189: Final Regulatory Impact Analysis, 10 May 2016 page 17 [link]

This is a very large cost relative to all others in the cost-benefit analysis[19], yet it built on modest assumptions about smoking behavior change. *Amici* contend that without assessing the potentially negative impact on changes in patterns of cigarette smoking arising from application the Deeming Rule to ENDS, FDA's justification omits potentially very large non-financial health detriment that it is required consider, and monetize if possible, in a credible cost-benefit analysis.

## IV. CONCLUSION

Amici argue that the cost-benefit analysis for the Deeming Rule overstates benefits and ignores a major category of cost. The analysis is fundamentally flawed and not a sufficient justification for the Deeming Rule. It is the view of the *Amici* that applying the Deeming Rule to ENDS is likely to cause more harm to health than it prevents.

Respectfully submitted:

/s/ Eric R. Stanco

Eric R. Stanco
Counsel for *Amici Curiae*,
Clive Bates and Fifteen Others

[19] FDA, Deeming Rule Docket No. FDA-2014-N-0189: Final Regulatory Impact Analysis, 10 May 2016, Table 32 page 114 [link] The total cost included for ENDS is $573m to 675m discounted.