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EIGHT TOBACCO HARM REDUCTION PROPOSALS FOR THE FEDERAL GOVERNMENT

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EXECUTIVE SUMMARY

In 2015, 36.5 million Americans, or 15 percent of U.S. adults, combined to smoke 264 billion cigarettes. Cigarette smoking causes more than 480,000 deaths each year in the United States – more than HIV, illicit drugs, alcohol, motor vehicles and guns combined. Smoking-related illness in the United States costs more than $300 billion annually, including nearly $170 billion for direct medical care for adults and more than $156 billion in lost economic productivity.[1] Smoking creates a massive health and economic burden.

Yet despite very large expenditures and sweeping federal powers, perverse tobacco policy is failing the American public and will soon destroy thousands of small and medium-sized businesses that are part of the solution, not part of the problem. The vast majority of health harms attributed to smoking arise from burning tobacco cigarettes and inhaling the smoke into the lungs, not from nicotine use. The 2014 Surgeon General's Report[2] confirmed: "Death and disease from tobacco use in the United States is overwhelmingly caused by cigarettes and other burned tobacco products." Where there is no combustion—as with smokeless tobacco, e-cigarettes and other vaping products or heated tobacco products—the risks of nicotine use inevitably will be much lower (representing from 2 percent to 10 percent of the risk of cigarettes) because the physical processes are so different. None of these products are perfectly safe, as very little is, but they are very much safer.

These products with radically reduced risk create opportunities for major health and economic gains through substitution. However, U.S. policy has actively denied and stymied this opportunity:

- U.S. tobacco policy suffers from an "abstinence-only" ideology. This intolerant approach rarely works well in any branch of public health. There is opportunity to move to a market-based "harm reduction" approach, in which people who want to use nicotine or are not sufficiently motivated to quit nicotine can use products that are much less harmful than combustible cigarettes.
- New regulations coming into effect between now and August 2019 will have the effect of taking 90 to 99 percent of vaping products off the market, and for bureaucratic rather than safety reasons. This will dramatically limit consumers' options to switch from high-risk to low-risk products. It also will serve to obstruct innovation.

1. CDC. Centers for Disease Control and Prevention. Smoking & Tobacco Use. Fact sheets. Accessed 11 Jan, 11, 2017. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/index.htm

2. Surgeon General. The Health Consequences of Smoking—50 Years of Progress. 2014. https://www.surgeongeneral.gov/library/reports/50-years-of-progress/fact-sheet.html

- Such rules will cause harm to people, as they predictably return to smoking. They also will cause harm to American businesses, as consumers instead seek black-market supplies from international vendors over the internet.
- American consumers have been systematically misled and denied truthful information about the relative risks of noncombustible products.
- The system of tobacco-science funding in the United States works to support expansion of federal bureaucracies and an abstinence-only ideology, rather than in the public interest.

Concern about children. Much of the rhetoric used by activists and regulators to justify poor or excessive regulation has been based on emotive appeals to protect children. However, the data show a sharp decline in teenage smoking, coinciding with the rise in popularity of vapor products. Between 2011 and 2015, current use of cigarettes by high school students fell rapidly from 15.8 percent to 9.3 percent, and use of cigars and pipes also fell.[3] Nonsmoking high school students are highly unlikely to use e-cigarettes; among those who do, most use them very infrequently.[4] Further, only a small minority of teenage vaping involves nicotine,[5] and much of the use is occasional and experimental, rather than an entrenched habit.[6] Sales of vapor products to minors were already banned in every state before the Food and Drug Administration asserted jurisdiction in 2016. It is unlikely that teenagers are harmed by the emergence of products much safer than cigarettes. However, it is likely that both teenagers and adults will be harmed by excessive regulation or de facto prohibition of low-risk products that substitute for smoking.

Proposed response. To address these policy failures, we suggest eight proposals for discussion, summarized below and set out in concise briefing form in the subsequent sections. The proposals are as follows:

1. **Seize the huge opportunity presented by low-risk nicotine products.** Revolutionize tobacco and nicotine policy, reduce health-care spending and improve health by exploiting the very large difference in risks to human health that stem from combustible and smoke-free products. Make appointments and provide direction and funding to embed this approach in federal agencies, such as the Food and Drug Administration, Centers for Disease Control and Prevention, National Institutes of Health and Office of the Surgeon General, as well as at the highest levels of the Department of Health and Human Services. This will require a concerted approach on many fronts.
2. **Cancel the FDA deeming rule before it destroys the U.S. vaping market.** An emergency response is required to prevent the near complete and needless destruction of the U.S. vapor industry by crudely designed and wholly inappropriate regulation. The following approaches should be part of this urgent response:
    a. Put the implementation process on hold and quickly pass legislation that changes the Tobacco Control Act predicate date to Aug. 8, 2016, for nicotine products that do not contain tobacco.
    b. Replace the costly, opaque and politicized product-by-product authorization regime with a standards-based regime, as outlined in Recommendation 3, to make clear what is required of manufacturers.
    c. Add a range of interim safeguards concerning common-ground issues, such as battery and fluid safety. These should be applied by Congress through the legislative instrument it uses to effect the above changes.
3. **Establish a standards-based regime for low-risk nicotine products.** Regulate low-risk tobacco and nicotine products by setting product standards (chemical, mechanical, thermal, electrical) that reduce individual risk to users while promoting innovation and ensuring the products are an attractive alternative to smoking. These standards would ensure average exposures were at least 90 percent lower than smoking and would make further public-health-benefit tests unnecessary.
4. **Use new labels to inform consumers about relative risk.** Using its rulemaking powers, the FDA should allow manufacturers to apply an accurate harm-reduction message to all non-combustible tobacco or nicotine products: "This product presents substantially lower risks to health than cigarettes," or other truthful and non-misleading communications.
5. **Stop using the public health test to protect the cigarette trade.** The public health test in the Tobacco Control Act does not protect public health, but it

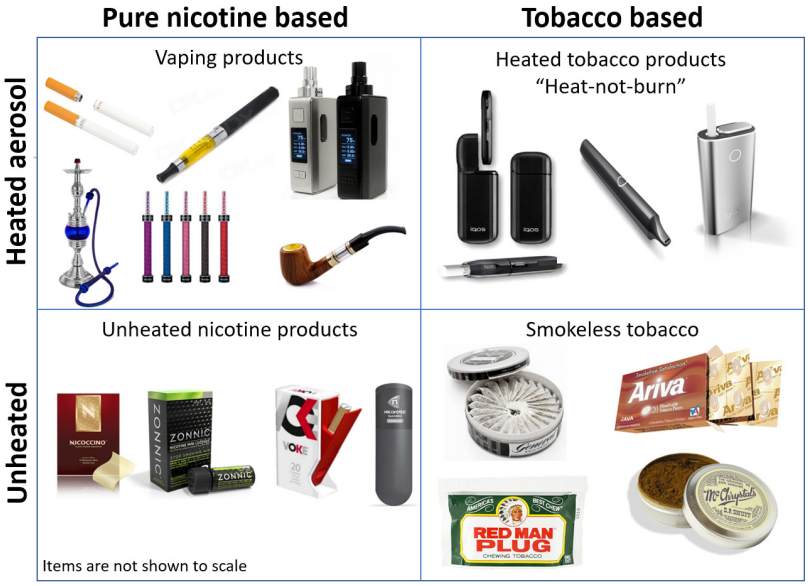
3. Singh T, Arrazola RA, Corey CG, et al. Tobacco Use Among Middle and High School Students — United States, 2011–2015. *MMWR Morb Mortal Wkly Rep* 2016; 65:361–367. https://www.cdc.gov/mmwr/volumes/65/wr/mm6514a1.htm?s_cid=mm6514a1_w

4. Warner KE. Frequency of E-Cigarette Use and Cigarette Smoking by American Students in 2014. *Am J Prev Med*. August 2016; 51(2):179–84. http://www.ajpmonline.org/article/S0749-3797(15)00782-5/abstract

5. Miech R, Patrick ME, O'Malley PM, Johnston LD. What are kids vaping? Results from a national survey of US adolescents. *Tob Control*.; 2016. http://tobaccocontrol.bmj.com/content/early/2016/07/21/tobaccocontrol-2016-053014

6. Villanti AC, Pearson JL, Glasser AM, Johnson AL, Collins LK, Niaura RS, et al. Frequency of youth e-cigarette and tobacco use patterns in the U.S.: Measurement precision is critical to inform public health. *Nicotine Tob Res.* December 2016. https://academic.oup.com/ntr/article-abstract/doi/10.1093/ntr/ntw388/2738979/Frequency-of-Youth-E-Cigarette-and-Tobacco-Use

FIGURE 1: REDUCED-RISK CONSUMER NICOTINE MARKET



does protect the cigarette trade from competition. It should not be applied to non-combustible tobacco or nicotine products. These should be evaluated according to their product characteristics and risks to individual users, not unknowable post-market population effects.

6. **Restore honesty and candor to public-health campaigns.** Require that the FDA, CDC and other relevant federal agencies act to bring public perceptions closer to reality. Set a goal that, by 2020, at least 75 percent of Americans believe that e-cigarettes, smokeless tobacco and heated tobacco products are, correctly, each "very much less harmful" than cigarettes. This campaign could be realized either through enabling language and funding included in the president's budget proposal or by executive order.

7. **Refocus tobacco science on the public interest, not bureaucratic expansion.** Overall, the imperative should be to change the incentive structures in tobacco-related research to stress objectivity in the public interest, not to justify expanded bureaucratic intervention.

    - Congressional oversight hearings should examine the state of tobacco science.
    - The FDA's Center for Tobacco Products should commission replications, counterfactuals, quality reviews and contrarian analysis to challenge its own thinking.
    - The CDC should commission tobacco-use surveillance, but outsource conduct and analysis to independent third parties and practice open data principles.
    - The NIH should produce guidelines on conduct and reporting of tobacco-related research (e.g., inclusion of comparisons with smoking and materiality of risk, rather than drawing policy conclusions).
    - Encourage establishment of a "Center for Nicotine and Tobacco Science in the Public Interest" to act as a defender of the public interest.

8. **Challenge vapor and smokeless prohibitions under World Trade Organization rules.** The United States should initiate complaints under WTO agreements about wholly unjustified prohibitions of low-risk nicotine products in jurisdictions outside the United States. This would represent a win-win for public health and American exporters, while challenging the negligence of the World Health Organization and some of its member states.

SEIZE OPPORTUNITY OF LOW-RISK NICOTINE PRODUCTS

RECOMMENDATION 1: Revolutionize tobacco and nicotine policy, reduce health-care spending and improve health by exploiting the very large difference in risks to human health that stem from combustible and smoke-free products. Make appointments and provide direction and funding to embed this approach in federal agencies, such as the FDA, CDC, NIH and Office of the Surgeon General, as well as at the highest levels of HHS.

Current tobacco policy is mired in obsolete themes, confusion about goals and denial about highly positive developments

in the marketplace.[7] The overwhelming majority of the risk associated with tobacco use comes from tobacco smoke and combustion, not from nicotine. Nicotine is a mildly psychoactive drug that can be addictive, but addictiveness depends on how fast, in what form and how much of the drug is delivered. Nicotine itself is not particularly harmful. It is the tobacco smoke that holds and transports the nicotine to the lungs that is the cause of cancer, cardiovascular and respiratory illnesses. While combusted tobacco smoke is the most effective delivery system for nicotine, there are products that deliver a nicotine experience nearly as satisfying without the smoke, and therefore with greatly reduced health risks. These products have four main generic forms:

1. E-cigarettes and vaping products. These create much lower exposures to toxic agents[8,9,10] and are likely to be at least 95 percent lower risk than smoking.[11,12]
2. Heated tobacco products, in which a vapor is created by heating, but not burning, tobacco. These products are likely to be at least 90 percent lower risk than smoking.[13,14,15,16]
3. Novel nicotine products, such as lozenges, films, inhalers and some forms of pharmaceutical nicotine-replacement therapy (NRT). These are likely to approximate NRT in their risk profile.
4. Smokeless tobacco, including well-established products like snus, which is likely to be at least 98 percent lower risk than smoking.[17] Snus has been responsible for the lowest levels of smoking in the developed world in Sweden,[18] as well as significant health gains.[19]

These smoke-free nicotine products have become viable consumer-market competitors to smoking, with a small fraction of the risk. They may not be completely safe—very little is—but the fundamental physical and chemical processes involved mean these products will be much less harmful than smoking. Therein lies a vast untapped opportunity both for health and potentially to reduce health-care costs by billions of dollars.[20] As a study of the fiscal effects of tobacco harm reduction focused on the state of Indiana concluded:

> Making [e-cigarettes] more expensive for or unavailable to consumers is misguided because switching to [e-cigarettes] from combustible cigarettes leads to improved health outcomes for cigarette smokers. Over time, this will lower the substantial amount of state funds that are spent on public health-care programs such as Medicaid.[21]

7. Kozlowski LT, Abrams DB. Obsolete tobacco control themes can be hazardous to public health: the need for updating views on absolute product risks and harm reduction. *BMC Public Health*. England: BioMed Central; May 24, 2016;16(1):432. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4878038/

8. 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. http://www.biomedcentral.com/1471-2458/14/18/abstract

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11. Public Health England. E-cigarettes around 95% less harmful than tobacco estimates landmark review. E-cigarettes: an evidence update Aug. 19, 2015. https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update

12. Royal College of Physicians (London), Nicotine without smoke: tobacco harm reduction. April 28, 2016. https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction-0

13. Gilchrist M. Heat-not-Burn Products: Scientific Assessment of Risk Reduction. Presentation to Global Tobacco and Nicotine Forum, Phillip Morris International, September 2015. https://www.pmiscience.com/library/heat-not-burn-products-scientific-assessment-risk-reduction-0

14. Lüdicke, F., G. Baker, J. Magnette, P. et al (2016). Reduced exposure to harmful and potentially harmful smoke constituents with the Tobacco Heating System 2.1. *Nicotine and Tobacco Research* (2016). http://ntr.oxfordjournals.org/content/early/2016/07/01/ntr.ntw164.abstract?keyty

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16. British American Tobacco, Controlled aerosol release to heat tobacco: product operation and aerosol chemistry assessment. Poster presentation SRNT March 2016, Chicago. http://www.bat-science.com/groupms/sites/BAT_9GVJXS.nsf/vwPagesWebLive/DOA7MJCN/$FILE/SRNT_SP_2016_(2).pdf?openelement

17. Lee PN. Epidemiological evidence relating snus to health - an updated review based on recent publications. *Harm Reduct J.* England; 2013;10(1):36. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4029226/

18. European Commission. Eurobarometer Special Survey 429: Attitudes of Europeans towards Tobacco and Electronic Cigarettes. 2015. http://ec.europa.eu/public_opinion/archives/ebs/ebs_429_en.pdf. Ramström L, Borland R, Wikmans T. Patterns of Smoking and Snus Use in Sweden: Implications for Public Health. *Int J Environ Res Public Health*; 2016 Nov 9;13(11):1110. https://www.ncbi.nlm.nih.gov/pubmed/27834883

19. Ramström L, Wikmans T. Mortality attributable to tobacco among men in Sweden and other European countries: an analysis of data in a WHO report. *Tob Induc Dis.* January 2014;12(1):14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4154048/?tool=pmcentrez

20. Moody JS. Heartland Institute, E-cigarettes poised to save Medicaid billions, State Budget Solutions, March 2015 https://www.heartland.org/publications-resources/publications/e-cigarettes-poised-to-save-medicaid-billions

21. Meyer J. The Fiscal Effects of Tobacco Harm Reduction: A Case Study of Indiana, Economics 21, Dec. 1, 2016. http://economics21.org/html/fiscal-effects-tobacco-harm-reduction-case-study-indiana-2173.html

CANCEL FDA DEEMING RULE

RECOMMENDATION 2: An emergency response is required to prevent the near complete and needless destruction of the U.S. vapor industry by crudely designed and wholly inappropriate regulation. The following approaches should be part of this urgent response:

a. Put the implementation process on hold and quickly pass legislation that changes the Tobacco Control Act predicate date to Aug. 8, 2016, for nicotine products that do not contain tobacco.

b. Replace the costly, opaque and politicized product-by-product authorization regime with a standards-based regime, as outlined in Recommendation 3, to make clear what is required of manufacturers.

c. If agreement on a standards-based regime will take time to realize, add a range of interim safeguards concerning common-ground issues, such as battery and fluid safety. These should be applied by Congress through the legislative instrument it uses to effect the above changes.

In May 2016, the Food and Drug Administration published a 134-page regulation[22] deeming e-cigarettes and some tobacco products to fall under the regulatory regime set out by the Family Smoking Prevention and Tobacco Control Act of 2009. In doing so, the FDA applied extremely burdensome regulatory burdens and an opaque authorization regime, the Pre-Market Tobacco Application (PMTA),[23] to many thousands of products made by thousands of businesses, the vast majority being small-scale American enterprises. Arguments against this rule are laid out in proceedings brought against the FDA by Nicopure Labs,[24] and in a supportive *amici curiae* brief by public-health experts.[25] Broadly, the arguments can be summarized as follows:

- There is no problem to which the proposed rule provides a solution. In fact, recent experience with e-cigarettes and nicotine vapor products is one of public-health success, with adult[26] and youth smoking[27] falling to record lows and at rapid rates.
- Despite alarmist claims about youth vaping, most teenage vaping does not involve nicotine[28] and is occasional or experimental[29] Frequent use is concentrated among young people who already are smokers.[30]
- The claimed benefits of these regulations[31] are, in fact, null or negative when examined[32].
- The costs and burdens of the regulations are so large that they will destroy nearly the entire vaping market, while leaving the cigarette market intact. All vaping products currently on the market, which serves more than 8 million Americans,[33] will be taken off the market by default. To regain market access, the products' makers will be required to comply with the PMTA authorization process, at a cost estimated to be between $182,000 and $2.01 million per-application for liquids and between $286,000 and $2.62 million per-application for devices.[34] Some experts believe these costs are understated.
- The FDA will need to create a vast bureaucracy of scientists and evaluators to process the 6,000 to 7,000 PMTA applications it expects to receive. This volume

22. Food and Drug Administration, Deeming Tobacco Products To Be Subject to the Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act, 81 FR 28973, May 10, 2016. https://www.federalregister.gov/documents/2016/05/10/2016-10685/deeming-tobacco-products-to-be-subject-to-the-federal-food-drug-and-cosmetic-act-as-amended-by-the

23. Pre-market Tobacco Application. FDA information. http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/ucm304506.htm. FDA, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry. May 2016. http://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM499352.pdf

24. Nicopure Labs et al vs Food and Drug Administration et al, Motion for Summary Judgement, July 8, 2016. http://www.clivebates.com/documents/NicopureMSJ.pdf

25. Brief of *amici curiae* of Clive Bates and other in support of plaintiffs' motion for summary judgement, Aug. 5, 2016. http://www.clivebates.com/documents/AmicusTHR.pdf

26. 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. https://www.cdc.gov/nchs/nhis/releases/released201605.htm#8

27. 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. http://www.cdc.gov/mmwr/volumes/65/wr/mm6514a1.htm?s_cid=mm6514a1_w

28. Miech R, Patrick ME, O'Malley PM, Johnston LD (2016) What are kids vaping? Results from a national survey of US adolescents. Tob Control tobaccocontrol-2016-053014. http://tobaccocontrol.bmj.com/content/early/2016/07/21/tobaccocontrol-2016-053014

29. 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 Table 35. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6438a1.htm

30. Warner KE, Johnston LD, O'Malley PM, et al (2016) Frequency of E-Cigarette Use and Cigarette Smoking by American Students in 2014. *Am J Prev Med* 51:179–184. http://www.ajpmonline.org/article/S0749-3797(15)00782-5/abstract

31. FDA, Deeming Rule Docket No. FDA-2014-N-0189: Final Regulatory Impact Analysis, 10 May 2016, 5. *Willingness To Pay for Benefits of Rule*, page 67. http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/UCM500254.pdf

32. Brief of *amici curiae* of Clive Bates and fifteen other in support of plaintiffs' motion for summary judgement, Aug. 5, 2016. http://www.clivebates.com/documents/AmicusTHR.pdf. See page 4-7 for short critique of each benefit claimed by FDA.

33. CDC, National Health Interview Survey, 2015 Data Release, https://www.cdc.gov/nchs/nhis/nhis_2015_data_release.htm. Analysis by Rodu B. How Many Americans Vape? CDC Data Show Fewer Vapers & Smokers in 2015, Tobacco Truth, July 17, 2016. http://rodutobaccotruth.blogspot.com/2016/07/how-many-americans-vape-cdc-data-show_7.html

34. FDA cost estimates for PMTA costs are set out in its final Regulatory Impact Analysis, May 2016 (http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/reports/economicanalyses/ucm500254.pdf – table 11 & 12 from page 85). The figures show here are for the first application.

does not include that portion of the industry that will exit the market altogether, and not because there is anything wrong with their products. Rather, it will be because they cannot afford the costs and uncertainty of the FDA's PMTA process and do not have the compliance experience that will be necessary.

- Vaping and other alternatives to cigarettes create new pathways out of smoking for people who do not wish to quit or find quitting difficult.[35] The FDA has failed to assess the likely impact of its own highly burdensome intervention on the resulting patterns of vaping and smoking. There are many scenarios in which its rules could increase smoking and cause harm by reducing the relative appeal of vaping products. The FDA's regulations are reckless and amount to an unjustified and harmful protection of the cigarette trade.
- The FDA's intervention is certain to stimulate cross-border internet shopping, as users try both to source the products they currently use and to take advantage of new innovations the FDA will obstruct from entering the U.S. market. In doing so, it will pile costs onto American businesses while subjecting them to cutthroat price competition from foreign internet vendors.
- Though regulation is supposed to be proportionate to risk, the most toxic products (cigarettes) were given a broad exemption from the authorization regime. The regulation of vaping products is not just disproportionate, but it is "anti-proportionate," perverse and unfair, compared to the treatment of cigarettes.

Safeguards can be introduced rapidly, pending the development of a full standards-based regime. These could be similar to those added to the Cole-Bishop amendment to 2016's agricultural appropriations bill.[36]

STANDARDS-BASED REGIME FOR NICOTINE PRODUCTS

RECOMMENDATION 3: Regulate low-risk tobacco and nicotine products by setting product standards (chemical, mechanical, thermal, electrical) that reduce individual risk to users while promoting innovation and ensuring the products are an attractive alternative to smoking. These standards would ensure average exposures were at least 90 percent lower than smoking and would make further public-health-benefit tests unnecessary.

There are many problems with the FDA's proposed authorization regime for vaping products. It should be replaced with a regime that defines transparent industrywide standards. This would allow everyone involved to understand what is expected of them and how to comply, which is normal practice.

- The FDA's process is extremely burdensome, with demanding evidentiary requirements and costly paperwork. This is compounded by evaluation costs and lengthy delays at the FDA.
- It is an opaque procedure in which the applicant does not know how the application will be evaluated or how flexible the FDA's evaluators will be. For example, it's unknown how high evidentiary bars will be set; how trade-offs will be made; and how inevitable uncertainties will be reconciled. Authorization decisions rest with the FDA and its staff. But like any agency, it is vulnerable to politicized decision-making and the biases of its decision makers.
- The authorization requires a "public health benefit test" to be passed before a product may be placed on the market.[37] Taken literally, this standard involves proving a negative and would be almost impossible to meet.[38] Even for products that prove very beneficial, it is hard to prove these benefits before the product is available for sale. The public-health-benefit test could even harm public health by erecting bureaucratic hurdles that keep beneficial products from the market (see Recommendation 5).
- Even obviously beneficial improvements—like hardware upgrades or better temperature control—must go through new authorizations. The regime acts as a barrier to innovation. Yet innovation is necessary to attract more smokers away from cigarettes, and to make continuing improvements in e-cigarette safety.

35. Levy DT, Cummings KM, Villanti AC, Niaura R, Abrams DB, Fong GT, et al. A framework for evaluating the public health impact of e-cigarettes and other vaporized nicotine products. *Addiction*. April 25, 2016; https://www.ncbi.nlm.nih.gov/pubmed/27109256

36. See description at: Keller and Heckman LLP, The Cole-Bishop Amendment to the Agricultural Appropriations Bill Amending the Grandfather Date for "Deemed" Tobacco Products Passes House Committee - What Next? April 29, 2016. https://khlaw.com/9094

37. FDA Pre-Market Tobacco Application (PMTA) http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/ucm304506.htm#2

38. FDA. Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (ENDS) – draft guidance, May 2016. http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm499351.htm

- Combustible cigarettes, the most dangerous products, have escaped this regime completely.[39]

The alternative is to employ an approach used for most regulated products on the market in the United States – setting industrywide standards. Noncombustible products should comply with standards that govern chemical, thermal, electrical and mechanical risks. To achieve the optimum public-health outcome, standards should be set carefully and in ways that neither increase the likelihood that consumers will relapse to smoking nor that fewer smokers will switch.

- **Combustion products.** Combustible products (cigarettes, rolling tobacco, cigars, etc.) could continue to be regulated under the existing framework of the Tobacco Control Act.
- **Vaping products.** Set standards for testing methods and product characteristics that mitigate the main residual risks and allow these standards to adapt to new knowledge and advances in technology. There already are precedents from which the United States may draw. The French standards-setting body—the Association Française de Normalisation, or AFNOR—has published a range of standards.[40] The British Standards Institute has defined optional standards.[41] Meanwhile, the European standardization body—the Comité Européen de Normalisation, or CEN—has commenced work on a four-part standard.[42] Elements of a standards regime could include blacklisted ingredients where there are known health risks;[43] maximum concentrations for contaminants; limits to products of thermal decomposition measured in vapor; and battery-safety standards, including covers on loose batteries and battery-charger compatibility.[44] To the extent permitted under the First Amendment, limits could be placed on marketing designed to appeal to or disproportionately reach those under age 18. For example, U.K. guidelines aim to strike a balance between protecting young people and the commercial freedom to market smoking alternatives to adults.[45]
- **Heated tobacco products.** The approach would be similar to that for vaping products, though with different standards to reflect the different ingredients and chemical processes involved.
- **Smokeless tobacco/nicotine products.** Set standards for residual toxins, such as tobacco-specific nitrosamines. This approach and an outline standard was recommended by the World Health Organization's expert group[46] and the snus maker Swedish Match has established standards to which it holds its own products.[47] Standards should be moderate to start, with the aim to remove outliers and tighten standards with experience.

The FDA is empowered to set such standards under Section 907 of the Tobacco Control Act.[48] In all cases, standard consumer protection legislation should be used to address concerns to the extent possible.

NEW LABELS TO INFORM CONSUMERS ABOUT RELATIVE RISK

RECOMMENDATION 4: Using its rulemaking powers, the FDA should allow manufacturers to apply an accurate harm-reduction message to all non-combustible tobacco or nicotine products: "This product presents substantially lower risks to health than cigarettes," or other truthful and non-misleading communications.

39. Tobacco products on the market at Feb. 15, 2007 were 'grandfathered' when the Tobacco Control Act was introduced in 2009. Tobacco Control Act §910. http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm262073.htm

40. AFNOR (France) Electronic cigarettes and e-liquids Part 1: Requirements and test methods for e-cigarettes XP D90-300-March 1, 2015. https://www.boutique.afnor.org/norme/xp-d90-300-1/cigarettes-electroniques-et-e-liquides-partie-1-exigences-et-methodes-d-essai-relatives-aux-cigarettes-electroniques/article/823264/fa059565
Part 2: Requirements and test methods for e-cigarette liquid XP D90-300-March 2, 2015. http://www.boutique.afnor.org/norme/xp-d90-300-2/cigarettes-electroniques-et-e-liquides-partie-2-exigences-et-methodes-d-essai-relatives-aux-cigarettes-e-liquides-/article/823265/fa059566 and Part 3: Requirements and emission-related test methods XP D90-300-July 3, 2016. https://www.boutique.afnor.org/norme/xp-d90-300-3/cigarettes-electroniques-et-e-liquides-partie-3-exigences-et-methodes-d-essais-relatives-aux-emissions/article/868678/fa186224

41. BSI PAS 54115:2015 Vaping products, including electronic cigarettes, e-liquids, e-shisha and directly-related products - Manufacture, importation, testing and labelling – Guide. http://shop.bsigroup.com/ProductDetail/?pid=000000000030303130 July 2015

42. European Centre for Standardisation, CEN/TC 437 - Electronic cigarettes and e-liquids. https://standards.cen.eu/dyn/www/f?p=204:29:0::::FSP_ORG_ID,FSP_LANG_ID:1958025,25&cs=1865F42A0756525EE7843AAC9C463EF2C#1

43. A blacklist would target carcinogenic, mutagenic, reprotoxic substances and respiratory sensitizers. There are known ingredients of concern, for example: diacetyl (a buttery flavouring), cinnamaldehyde and benzaldehyde. The evidence does not so far support a material health risks at typical exposures, but there is a case for requiring alternatives to be used where these are available.

44. International electrical safety standards are available: IEC 60335-1 (safety of household appliances); IIEC 60335-2-29 (safety of battery chargers); IEC 62133 (safety of portable batteries); IEC 61558 (safety of AC adaptors); IEC 61000 series; and EN 55022 & EN 55024 (for USB chargers & cables)

45. Committee on Advertising Practice (UK), UK Code of Broadcast Advertising: 33. E-cigarettes Broadcast. https://www.cap.org.uk/Advertising-Codes/Broadcast/Code-Item.aspx?cscid=%7Bb8ec097d-cfaf-4dfa-96e8-7a231f7339a0%7D#.VodZNRp96bU; UK Code of Non-broadcast Advertising, Sales Promotion and Direct Marketing (CAP Code): 22. E-cigarettes. https://www.cap.org.uk/Advertising-Codes/Non-Broadcast/CodeItem.aspx?cscid=%7B49028fdc-fc22-4d8a-ba5b-ba7ccc3df99a%7D#.VodYYx-p96bU

46. WHO Study Group on Tobacco Product Regulation Report on the Scientific Basis of Tobacco Product Regulation: WHO Technical Report Series, no. 951, 2008. http://www.who.int/tobacco/global_interaction/tobreg/publications/tsr_951/en/

47. Swedish Match, GOTHIATEK® limits for undesired components. https://www.swedishmatch.com/Snus-and-health/GOTHIATEK/GOTHIATEK-standard/

48. Food and Drug Administration, Section 907 of the Federal Food, Drug, and Cosmetic Act - Tobacco Product Standards (2009) http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm263053.htm

Given that combustible cigarettes are between 10 and 100 times riskier than noncombustible products, how should this highly valuable health information be conveyed to consumers? The statutory warnings that cover e-cigarettes, heated tobacco products, some novel products[49] and smokeless tobacco[50] are shown in Table 1.

TABLE I: STATUTORY WARNINGS ON E-CIGS AND SMOKELESS TOBACCO

PRODUCT	WARNINGS
E-cigarettes, etc.	This product contains nicotine. Nicotine is an addictive chemical
Smokeless tobacco	This product can cause mouth cancer. This product can cause gum disease and tooth loss. This product is not a safe alternative to cigarettes. Smokeless tobacco is addictive.

These warnings provide virtually no valuable, actionable or even truthful information to consumers.

- **Misleading about nicotine addiction.** Nicotine itself is not particularly dangerous to health. How addictive it is will depend on how rapidly and how high a peak exposure is reached in the brain, as well as the interaction with other chemical agents in smoke; addiction is strongly product- and user-dependent. The term "addictive" itself is understood only vaguely. It covers many forms of dependence. For example, nicotine is not addictive in the same way that opioids are, even if it does meet almost all clinical definitions of an addictive substance for at least a portion of the population.
- **Misleading about health.** The evidence for smokeless tobacco causing mouth cancer, gum disease and tooth loss is very thin and may not apply to some forms of smokeless tobacco, such as snus.[51,52] The specific health warnings do not convey the magnitude of these risks, either in comparison to smoking or to other risks, such as those arising from dietary choices.
- **Misleading about safety.** The most damaging warning claims smokeless tobacco is "not a safe alternative to cigarettes." Though technically true, this is profoundly misleading. It has been strongly criticized by experts for withholding the most crucial information about risk differentials.[53]

A 2011 citizen petition filed on behalf of Reynolds American[54] urged the FDA to initiate administrative rulemaking to replace the safety warning with the following text:

> WARNING: No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes

Though this warning contains truthful information and isn't misleading, the FDA determined it would not promote better understanding. It rejected the petition in November 2015.[55]

Despite this setback, the makers of these products do have a route by which they can make truthful health claims. It is the FDA's Modified Risk Tobacco Product application process (MRTP),[56] which was established to validate reduced-risk marketing claims. To date, this process has been a total failure and, despite 33 applications, has yet to approve any modified risk claims,[57] despite huge variations in the real-world risk presented by different products. In June 2014, the snus company Swedish Match applied[58] to have the same warning, as proposed by Reynolds, applied to eight of its own products. Despite a 130,000-page submission and more than two years of deliberation, the FDA made a Dec. 14, 2016 announcement of further prevarication.[59] The agency's explanation for this

49. FDA. "Covered" Tobacco Product and Roll-Your-Own/ Cigarette Tobacco Labeling and Warning Statement Requirements accessed Dec. 14, 2016. http://www.fda.gov/TobaccoProducts/Labeling/Labeling/ucm524470.htm This warning applies, *inter alia*, to vaporizers, e-cigarettes, and other electronic nicotine delivery systems (ENDS), dissolvables, gels and heated tobacco products.

50. FDA. Smokeless Tobacco Labeling and Warning Statement Requirements, accessed Dec. 14, 2016. http://www.fda.gov/TobaccoProducts/Labeling/Labeling/ucm2023662.htm

51. Lee PN. Summary of the epidemiological evidence relating snus to health. *Regul Toxicol Pharmacol*. 2011;59(2). http://www.sciencedirect.com/science/article/pii/S0273230010002229

52. Lee PN. Epidemiological evidence relating snus to health - an updated review based on recent publications. *Harm Reduct J.* England; 2013;10(1):36. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24314326/

53. Kozlowski LT, Sweanor DS. Withholding differential risk information on legal consumer nicotine/tobacco products: The public health ethics of health information quarantines. *Int J Drug Policy.* Elsevier. http://www.ijdp.org/article/S0955395916300925/fulltext

54. FDA. Docket FDA-2011-P-0573, Initiate a Rulemaking Procedure to Adjust the Text of a Smokeless Tobacco ("ST") Product Warning Label Statement. https://www.regulations.gov/docket?D=FDA-2011-P-0573 Petition denied May 11, 2015.

55. FDA. FDA takes action on applications seeking to market modified risk tobacco products, Dec. 14, 2016. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm533219.htm

56. FDA. Modified Risk Tobacco Products, accessed Dec. 14, 2016. http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm304465.htm

57. FDA. Modified Risk Tobacco Products - Summary of MRTP Application Actions. Accessed Jan. 4, 2017. http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm304465.htm

58. FDA. Swedish Match North America, Inc. MRTP Applications. http://www.accessdata.fda.gov/Static/widgets/tobacco/SMNA_MRTPA_FDA-2014-N-1051.html. Swedish Match press release, June 11, 2014. https://www.swedishmatch.com/Media/Pressreleases-and-news/Press-releases/2014/Swedish-Match-submits-a-Modified-Risk-Tobacco-Product-MRTP-application/

59. FDA. FDA takes action on applications seeking to market modified risk tobacco products. Dec. 14, 2016. http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm263069.htm

decision[60] revealed the FDA's willingness to make up the rules as the process unfolds. In doing so, it creates new barriers to candid communication of risks in a way that consumer groups argue works against the consumer interest.[61]

- The FDA cherry-picked studies showing adverse effects rather than looking at the science as a whole.[62]
- The FDA insisted the company prove its product could not cause an adverse health effect before it would be permitted to make a reduced-risk claim.
- The FDA insisted the company show the product has lower risks for all possible health impacts, however trivial, not just the major causes of tobacco-related disease.

The FDA has a thoroughly flawed approach to risk communication:

- It relies on a tobacco company to find it commercially advantageous to apply in the first place. That is a bizarre and wholly inadequate basis for providing important risk information to the public.
- It relies on allowing tobacco companies to be the primary communicators of relative risk to the public, even though these companies are among the least-trusted organizations in modern life.
- It applies only to that company's products, though near-identical products may be on the market and would be labelled differently.
- The FDA does not have to justify its own warning regime or show it does not mislead consumers. The status quo is granted immunity from scrutiny or any requirement to meet a public-health-benefit test.
- Messages should inform consumers, not aim to manipulate their behavior to achieve some desired outcome. For example, if the undisclosed purpose of these warnings was to deter all nicotine use, they may perversely mislead citizens into continued smoking even where they might otherwise have switched to smokeless tobacco to reduce risks.

60. FDA. Perspective: Lessons Learned from the First Review of MRTP Applications. Dec. 16, 2016. http://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm533753.htm

61. CASAA. Swedish Match gets trapped in FDA's hall of mirrors. December 2016. http://casaa.org/news/swedish-match-gets-trapped-in-the-fdas-regulatory-house-of-mirrors/

62. Rodu B. FDA Rejects Plea to Correct Smokeless Tobacco Warnings; A Closer Look at Flawed Interpretations, Tobacco Truth. Dec. 21, 2016. http://rodutobaccotruth.blogspot.com/2016/12/fda-rejects-plea-to-correct-smokeless.html

STOP USING PUBLIC HEALTH TEST TO PROTECT CIGARETTE TRADE

RECOMMENDATION 5: The public health test in the Tobacco Control Act does not protect public health, but it does protect the cigarette trade from competition. It should not be applied to non-combustible tobacco or nicotine products. These should be evaluated according to their product characteristics and risks to individual users, not unknowable post-market population effects.

One of the main failings of U.S. tobacco policy is the so-called "public health test" built into 2009's Tobacco Control Act, which guides the FDA's regulatory determinations. Before a new tobacco or consumer-nicotine product may be brought to market, the vendor must show its release would be appropriate to protect public health. The test uses the following formulation:[63]

> **Basis for Finding**. For purposes of this section, the finding as to whether the marketing of a tobacco product for which an application has been submitted is appropriate for the protection of the public health shall be determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product, and taking into account:
>
> A. the increased or decreased likelihood that existing users of tobacco products will stop using such products; and
>
> B. the increased or decreased likelihood that those who do not use tobacco products will start using such products.

It may sound reasonable, but this test does not serve public health. Its main effect is to create near-insurmountable market barriers-to-entry for products that are much safer than cigarettes, while it does not apply to thousands of cigarette products already on the market. The test is problematic not because new products really are inappropriate for public health, but because the burden of proof to meet this test is so great, especially in advance of the product being placed on the market. Consider the following:

- The public health impact of a product is *not a characteristic of the product itself*, but an emergent property of the complex web of behavioral influences that guide the product's use. Many of these are extremely difficult predict or even completely unknowable

63. Federal Food, Drug, and Cosmetic Act - Application for Review of Certain Tobacco Products Section 910(c)4, 2009. *http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm262073.htm*

in advance, and they are beyond the control of the manufacturer.

- There is no experience with a new product until it has been placed on the market, so the applicant has no relevant concrete data to offer from real-world use to support an application – a Catch-22. If data exists, it applies to older products, past market conditions, a different regulatory environment, a different communications environment and different consumer preferences.
- It is hard enough to find consensus about entire categories, let alone specific products. Consider the disputed evidence and ideologically based arguments about e-cigarettes regarding relative risk, gateway effects, renormalizing smoking and reducing quitting. If there is no consensus at the level of the entire category, then how can an individual manufacturer make a case for a specific product?
- It is impossible to set up meaningful trials, because there are so many uncontrollable variables in real-world use.
- The impact of one product depends on other products (competitors) and rival strategies (cessation or different harm reduction approaches).
- The public health impact of a product cannot be known until all consumer behavioral transitions have worked through, a process that may take decades.

These problems are not merely technical; they have bureaucratic, legal and political dimensions.

- *Bureaucratic*. If a harmful product is incorrectly approved, there is risk that the regulator will be shown to be wrong. However, if a beneficial product is not approved, there is no way to check if the decision was wrong or whether harms may have been avoided. This asymmetry in accountability and reputational risk is an incentive to reject applications.
- *Legal*. A legal challenge from a manufacturer to a rejection will be easier to fight in court than a legal challenge from an interest group to an approval, given the inherent uncertainties and that the burden of proof rests with the manufacturer.
- *Political*. Where there is inherent difficulty in establishing a cast-iron case to approve a product, there is scope for decisions to be made for reasons other than relevant evidence – for example, reasons of ideology, to pacify or impress interest groups or simply to look and feel "tough."

These forms of bias can emerge because manufacturers face the daunting task of predicting future use of a new product in changing market conditions, in a changing product landscape and with constantly evolving behavioral influences. They have little to do with inherent product characteristics. Further, there are ethical concerns with relying on population health assessments, even if these could be done reliably, which they cannot. It can mean denying market access to products that are much safer than cigarettes. It means that one person may be denied access to a product that would be highly beneficial for them because of concerns about how someone else may use the product.

The public-health test was included in the Tobacco Control Act because, at the time, it was thought the regulatory challenge would arise from re-engineered combustible products or "safer cigarettes."[64] The concern was that changes in behavior or false reassurance could easily overwhelm the benefits of reduced individual risk. This becomes much less of a concern if the reduced-risk product is orders of magnitude lower risk than smoking,[65] as is the case with non-combustibles. The test is applied elsewhere in the act,[66] thus creating barriers to setting reasonable product standards (see Recommendation 3) and to making truthful and non-misleading claims to consumers (see Recommendation 4).

The appropriate approach for non-combustible products is for regulators to focus determinations, standard-setting and risk communication on actual product characteristics and risk to individuals, not on the unknown (and unknowable) ways in which the product may be used in the marketplace. If population effects are a concern, they should be a matter for post-market surveillance. If harmful effects emerge, a regulator or manufacturer may be able to take corrective action at that time.

64. Stratton K, Shetty P, Wallace R, Bondurant S. Committee to assess the science base for tobacco harm reduction, Institute of Medicine. Clearing the smoke: Assessing the science base for tobacco harm reduction. National Academy Press. 2001. https://www.nap.edu/catalog/10029/clearing-the-smoke-assessing-the-science-base-for-tobacco-harm?onpi_webextra1

65. Kozlowski LT, Strasser AA, Giovino GA, Erickson PA, Terza J V. Applying the risk/use equilibrium: use medicinal nicotine now for harm reduction. *Tob Control.* BMJ Publishing Group Ltd; September 2001;10(3):201–3. http://tobaccocontrol.bmj.com/content/10/3/201.long

66. See Tobacco Control Act Section 907(a)3 on Tobacco Product Standards, http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm263053.htm and Section 911((g)4 on Modified Risk Tobacco Applications, http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm262077.htm

RESTORE HONESTY TO PUBLIC HEALTH CAMPAIGNS

RECOMMENDATION 6: Require that the FDA, CDC and other relevant federal agencies act to bring public perceptions closer to reality; for example, to set a goal that, by 2020, at least 75 percent of Americans believe that e-cigarettes, smokeless tobacco and heated tobacco products are, correctly, each "very much less harmful" than cigarettes. This campaign could be realized either through enabling language and funding included in the president's budget proposal or by executive order.

When asked how risky vaping or smokeless tobacco is compared to cigarettes, American adults gave answers in a 2015 survey by the National Cancer Institute that are summarized in Table 2.[67]

TABLE 2: NATIONAL CANCER INSTITUTE SURVEY ON E-CIGARETTES (%)

Compared to smoking cigarettes, would you say that electronic cigarettes are…		Do you believe that some smokeless tobacco products, such as chewing tobacco and snuff, are less harmful than cigarettes?	
Much less harmful	5.3	Yes	10.9
Less harmful	20.6	No	66.2
Just as harmful	32.8	Don't know	22.0
More harmful	2.7	Other	0.9
Much more harmful	2.0		
I've never heard of e-cigarettes	1.2		
I don't know enough about these products	33.9		

SOURCE: National Cancer Institute

The only remotely correct answers are that e-cigarettes are "much less harmful" and that, "yes," smokeless tobacco products are less harmful than cigarettes. These are thus shocking results, showing a dramatic misalignment of perception and reality in a way that implicitly favors continued smoking. There also is evidence that these misperceptions are worsening over time, despite constantly improving specialist knowledge. A May 2016 survey[68] found 47 percent of respondents said vaping "was not healthier than smoking conventional cigarettes," compared with 38 percent a year earlier. If America's 38 million smokers are basing their choices, at least in part, on these perceptions of risk, then many will miss the opportunity to reduce their risk radically by switching to a noncombustible product.

The question therefore arises: what is the cause of this misperception? The problem has its origins in misleading and misguided promotional activity by key federal agencies and their senior officials. These bodies strongly signal norms and expectations to the wider research, health and activist community. Three examples of misleading federal messengers suffice, but the problem is replicated at the state level.

Centers for Disease Control and Prevention. The lead public-health agency has led highly negative abstinence-only campaigns against vaping[69,70] and smokeless tobacco, denying or ignoring possible benefits to smokers[71] and exaggerating risks,[72,73] while falsely claiming there are gateway effects.[74,75]

Food and Drug Administration. The main federal drug regulator undertook a sustained campaign to extend its bureaucratic reach to include e-cigarettes. It has, therefore, a bias to justify its expanded role by finding problems to which its involvement could be proffered as a solution.[76,77] It has joined in the largely unfounded panic about youth vaping and ignored or underplayed the benefits to adults. The FDA relentlessly conflates and confuses smoking, tobacco use and nicotine use, creating the impression these are all essentially

67. National Cancer Institute, Health Information National Trends Survey, FDA Survey 2015. E-cigarettes. http://hints.cancer.gov/question-details.aspx?PK_Cycle=8&qid=1282; Smokeless tobacco, https://hints.cancer.gov/question-details.aspx?PK_Cycle=8&qid=864

68. Reuters, U.S. e-cigarette use stalls as health concerns grow: Reuters/Ipsos poll, May 2014. http://www.reuters.com/article/us-usa-ecigarettes-poll-idUSKCN0YF0DE

69. See CDC. E-cigarette Ads and Youth, https://www.cdc.gov/vitalsigns/ecigarette-ads/index.html. E-cigarette study sparks national attention around e-cigarettes and nicotine toxicity. https://www.cdc.gov/nceh/hsb/success_stories/ecigarette_study.htm

70. *Los Angeles Times*. CDC director explains what he hates about electronic cigarettes, April 29, 2014. http://www.latimes.com/science/sciencenow/la-sci-sn-why-tom-frieden-hates-electronic-cigarettes-cdc-20140429-story.html

71. Rodu B. How Many Americans Vape? CDC Data Show Fewer Vapers & Smokers in 2015, Tobacco Truth. July 7, 2016. http://rodutobaccotruth.blogspot.com/2016/07/how-many-americans-vape-cdc-data-show_7.html

72. Siegel M. CDC Director Apparently Fabricating More "Scientific Evidence" to Demonize Electronic Cigarettes, Rest of the Story, May 12, 2014. http://tobaccoanalysis.blogspot.com/2014/05/cdc-director-apparently-fabricating.html

73. Satel S. Their Product Is Doubt--Deceptive Government Campaign Against Electronic Cigarettes, *Forbes*. April 14, 2015. http://www.forbes.com/sites/sallysatel/2015/04/14/their-product-is-doubt-deceptive-government-campaign-against-electronic-cigarettes/

74. Siegel M. CDC is Running a Dishonest Campaign Against E-Cigarettes Which is Re-Normalizing Smoking, Rest of the story, April 20, 2014. http://tobaccoanalysis.blogspot.com/2015/04/cdc-is-running-dishonest-campaign.html

75. Rodu B. The CDC Buries the Lead: Teen E-cigarette Use Rises as More Dangerous Cigarette Use Plummets, Tobacco Truth, Oct. 13, 2015. http://rodutobaccotruth.blogspot.com/2015/10/the-cdc-buries-lead-teen-e-cigarette.html

76. CDC (with FDA comment). E-cigarette use more than doubles among U.S. middle and high school students from 2011-2012. September 2013. https://www.cdc.gov/media/releases/2013/p0905-ecigarette-use.html

77. FDA. Regulation of Electronic Nicotine Delivery Systems (Including E-Cigarettes) and the Continuum of Nicotine-Delivering Products 81 FR 29028. https://www.federalregister.gov/d/2016-10685/p-625

the same.[78,79] Though calling for a debate on nicotine,[80] it has used newspaper articles to make alarmist statements about vaping,[81] which are easily shown to be baseless or misleading.[82] Its extremely burdensome deeming rule has, of course, pre-empted any "debate" and it has done little to sponsor a genuine open-minded discussion about the role of nicotine in society.

Office of the Surgeon General. The recent report of the surgeon general on youth vaping avoided drawing obvious conclusions or plausible hypotheses from the data[83] and misrepresented the available science to create unjustified alarm.[84] The surgeon general drew policy conclusions that were flawed for youth protection, but failed even to consider harmful unintended consequences for adults.[85] Although most of the established media followed the surgeon general's contrived narrative, it subsequently has started to attract much more critical analysis.[86,87]

REFOCUS TOBACCO SCIENCE ON THE PUBLIC INTEREST

RECOMMENDATION 7: Overall, the imperative should be to change the incentive structures in tobacco-related research to stress objectivity in the public interest, not to justify expanded bureaucratic intervention.

- Congressional oversight hearings should examine the state of tobacco science.
- The FDA's Center for Tobacco Products should commission replications, counterfactuals, quality reviews and contrarian analysis to challenge its own thinking.
- The CDC should commission tobacco-use surveillance, but outsource conduct and analysis to independent third parties and practice open data principles.
- The NIH should produce guidelines on conduct and reporting of tobacco-related research (e.g., inclusion of comparisons with smoking and materiality of risk, rather than drawing policy conclusions).
- Encourage establishment of a "Center for Nicotine and Tobacco Science in the Public Interest" to act as a defender of the public interest.

A dysfunctional science system. The science system for tobacco policy in the United States is failing the American people. Over years of conflict with Big Tobacco, tobacco-control science has developed a culture with strong cognitive biases toward problem-finding and alarm-sounding, justifying abstinence-only approaches and a tendency toward policy proposals that go far beyond what a science paper can support. This culture was never right or justifiable, even if it felt necessary to those involved. When it comes to reduced-risk products, such activist bias is a scientific and public-health disaster. Several skilled experts now monitor the literature. A tour of their work[88] or PubMed Commons[89] reveals how bad the situation has become. The types of error widely propagated in the literature have been summarized in a guide to bad vaping science that's replicated in Appendix 1.[90] A devastating critique[91] of a recent WHO paper drew heavily on poor science that originated in the United States. Overall, the

78. Bonhomme MG, Holder-Hayes E, Ambrose BK, Tworek C, Feirman SP, King BA, et al. Flavoured non-cigarette tobacco product use among US adults: 2013-2014. *Tob Control*; 2016 Nov;25(Suppl 2):ii4-ii13. http://tobaccocontrol.bmj.com/content/early/2016/10/28/tobaccocontrol-2016-053373.full

79. FDA. Overview of the Center for Tobacco Products: Consumer Fact Sheet. http://www.fda.gov/TobaccoProducts/NewsEvents/ucm265521.htm

80. *New York Times*. Smoking, Vaping and Nicotine (Interview with FDA Center for Tobacco Products Director Mitchell Zeller), May 26, 2015. http://www.nytimes.com/2015/05/26/opinion/joe-nocera-smoking-vaping-and-nicotine.html

81. *New York Times*. A Lobbyist Wrote the Bill. Will the Tobacco Industry Win Its E-Cigarette Fight? Sept. 2, 2016. http://www.nytimes.com/2016/09/03/us/politics/e-cigarettes-vaping-cigars-fda-altria.html

82. Bates CD. Lehrer E. Letter to Mitch Zeller on FDA e-cigarette rules. R Street, Sept. 8, 2016. http://www.rstreet.org/outreach/letter-to-mitch-zeller-on-fda-e-cigarette-rules/

83. Bates CD. Five questions to put to the US Surgeon General on e-cigarette science, Counterfactual, Dec. 7, 2016. http://www.clivebates.com/?p=4574

84. Farsalinos K. US Surgeon General declares e-cigarettes are a public health concern. But where is the evidence of harm? E-cigarette Research, Dec. 9, 2016. http://www.ecigarette-research.org/research/index.php/whats-new/whatsnew-2016/250-sg

85. Bates CD. Bad science, poor insights and likely to do harm - rapid reaction to the Surgeon General's terrible e-cigarette report, Counterfactual. Dec. 8, 2016. http://www.clivebates.com/?p=4593

86. Satel S. & Sweanor D. Dear Surgeon General and Public Health Agencies, Anti-Vaping Polices Are Bad for Public Health, Real Clear Health, Dec. 19, 2016. http://www.realclearhealth.com/articles/2016/12/19/dear_surgeon_general_and_public_health_agencies_anti-vaping_polices_are_bad_for_public_health_110332.html

87. Redmond H. The Surgeon General's Pack of Lies About E-Cigarettes Is Likely to Cost Lives, The Influence, Dec. 19, 2016. http://theinfluence.org/the-surgeon-generals-pack-of-lies-about-e-cigarettes-is-likely-to-cost-lives/

88. Siegel M. The rest of the story, http://tobaccoanalysis.blogspot.co.uk/; Rodu B. Tobacco Truth, http://rodutobaccotruth.blogspot.co.uk/; Farsalinos K. E-cigarette research http://www.ecigarette-research.org/research/index.php; Phillips CV. Anti-THR Lies https://antithrlies.com/; Bates CD. The Counterfactual http://www.clivebates.com/

89. See for example collection of critical PubMed Commons reviews by Clive Bates and others http://www.ncbi.nlm.nih.gov/sites/myncbi/clive.bates.1/collections/50103881/public/

90. Bates CD. The critic's guide to bad vaping science. Dec. 3, 2016. http://www.clivebates.com/documents/BadScienceBriefing1.pdf

91. UKCTAS, Commentary on WHO report on ENDS and ENNDS, October 2016. http://ukctas.net/news/commentary-on-WHO-report-on-ENDS&ENNDS.html

problem is an obsessive focus on minor or hypothetical risks, combined with indifference to or denial of opportunities.

A wall of money in favor of regulation. The system of funding starts with deep biases. For example, an NIH request for applications for grant funding[92] stated:

> The overall goal is to develop an evidence base to inform smokeless tobacco control efforts, and to develop effective ways to limit the spread and promote cessation of smokeless tobacco use.

The idea that smokeless tobacco might be a valuable low-risk substitute for smoking is excluded and the research subordinated to support control efforts. The FDA's Center for Tobacco Products funds a major tobacco regulatory-research program and 14 Tobacco Centers of Regulatory Science.[93] These research centers will receive more than $273 million in grants between 2013 and 2018. It should be obvious that so much science funded by a regulator will be biased toward finding reasons to regulate. Further, it will create supposedly independent advocates for FDA regulation. This establishes giant conflicts of interest that are never acknowledged by those involved. Dr. Brad Rodu of the University of Louisville School of Medicine has analyzed overall NIH spending on tobacco-related research. He notes:[94]

> In 2014, the NIH (mainly the National Cancer, Heart Blood Lung, Drug Abuse and Mental Health Institutes) dispensed $623 million (total costs) in 1,300 grants to over 1,000 PIs at almost 300 universities, medical centers and other institutions. That works out to about $600,000 for each investigator. Few researchers will jeopardize grants of that size by doing or saying anything that conflicts with NIH dogma.

Even the most basic data on youth tobacco and nicotine use is controlled and interpreted by the CDC and has been routinely misrepresented to create a moral panic.[95] But when full data are eventually released, the results appear much more positive, suggesting any gateways to vaping might be exits from smoking.[96] The Truth Initiative's Schroeder Institute has been one bright spot in a dismal U.S. landscape, with recent in-depth and credible reviews on e-cigarette science[97] and nicotine.[98] This is the sort of impartial and robust analysis that should be informing U.S. tobacco policy, rather than reports designed to support activism or more regulation.

Amplification of bias. The initial bias and perverse incentives are then amplified through various mechanisms, including grant-seeking behavior by researchers; publicity-seeking by university press offices; impact-seeking by journals and editors; groupthink and common cause by peer reviewers; sensation-seeking by news outlets; and the rise of "clickbait" as a driver of news values.

The case of "hidden formaldehyde." A letter published in the *New England Journal of Medicine* claimed e-cigarettes could produce five to 15 times greater formaldehyde-related cancer risk than smoking.[99] This created huge global media coverage.[100] The experiment was deeply flawed; it operated e-cigarettes at temperatures no human would ever use.[101] Yet in terms of critical response, the journal published only a 125-word response three months later.[102] It declined to correct or withdraw the original letter, even though it has no relevance to human health and despite the damage that such false information causes.[103] Nine months later, the team at Portland State University who authored the letter were awarded a $3.5 million grant from the NIH and FDA.[104]

92. NIH. Measures and Determinants of Smokeless Tobacco Use, Prevention, and Cessation (R01) Request for Applications (RFA) Number: RFA-CA-08-024, July 3, 2008. https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-024.html

93. FDA. Tobacco Regulatory Science Program (TRSP) https://prevention.nih.gov/tobacco-regulatory-science-program, FDA. Tobacco Centers of Regulatory Science (TCORS) http://www.fda.gov/TobaccoProducts/PublicHealthScienceResearch/Research/ucm369005.htm

94. Rodu B. NIH Funding Stifles Tobacco Harm Reduction Research and Support in Academia, Feb. 17, 2015. http://rodutobaccotruth.blogspot.co.uk/2015/02/nih-funding-stifles-tobacco-harm.html

95. CDC. Youth and tobacco use. April 2016. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/youth_data/tobacco_use/

96. Villanti AC, Pearson JL, Glasser AM, Johnson AL, Collins LK, Niaura RS, et al. Frequency of youth e-cigarette and tobacco use patterns in the U.S.: Measurement precision is critical to inform public health. *Nicotine Tob Res*. 2016. http://ntr.oxfordjournals.org/content/early/2016/12/24/ntr.ntw388.abstract

97. Glasser AM, Collins L, Pearson JL, Abudayyeh H, Niaura RS, Abrams DB, et al. Overview of Electronic Nicotine Delivery Systems: A Systematic Review. *Am J Prev Med*. Nov. 30, 2016. http://www.ajpmonline.org/article/S0749-3797(16)30573-6/abstract

98. Naiura RS. Rethinking nicotine and its effects, Truth Initiative, Schroeder Institute, Dec. 2, 2016. http://truthinitiative.org/news/re-thinking-nicotine-and-its-effects

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100. See Jensen et al media coverage summary at *New England Journal of Medicine* http://www.nejm.org/doi/full/10.1056/NEJMc1413069#t=metrics

101. Bates CD, Farsalinos KE. Research letter on e-cigarette cancer risk was so misleading it should be retracted. *Addiction*. Oct. 9, 2015;110(10):1686–7. http://onlinelibrary.wiley.com/doi/10.1111/add.13018/full and supporting material (complaint under COPE guidelines. http://onlinelibrary.wiley.com/store/10.1111/add.13018/asset/supinfo/add13018-sup-0001-Supplementary.pdf?v=1&s=4f57349e6de3ca1fce6b8e533eeb85d7b0350b82

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103. Bates CD. More on *New England Journal of Medicine* fake formaldehyde scandal. Counterfactual http://www.clivebates.com/?p=3441

104. Portland State University. Portland State nets $3.5 million NIH grant to help clear the air on hazards of e-cigarettes, Sept. 10, 2015. https://www.pdx.edu/news/portland-state-nets-35-million-nih-grant-help-clear-air-hazards-e-cigarettes

CHALLENGE PROHIBITIONS UNDER WTO RULES

RECOMMENDATION 8: The United States should initiate complaints under WTO agreements about wholly unjustified prohibitions of low-risk nicotine products in jurisdictions outside the United States. This would represent a win-win for public health and American exporters, while challenging the negligence of the World Health Organization and some of its member states.

There are many countries that have taken a highly counterproductive and harmful approach to low-risk nicotine products, especially vapor products. Several have banned the manufacture, sale or import of these products, either explicitly or by default, through excessive regulation. In the European Union, snus is banned other than in Sweden,[105] even though the product has had very significant health benefits[106] and even though chewing tobacco or nasal snuff is allowed on the market. A 2016 survey reports the prohibitions of e-cigarettes in the following jurisdictions:[107]

> Sale of all types of e-cigarettes is banned in 26 countries: Argentina, Bahrain, Brazil, Brunei Darussalam, Cambodia, Colombia, Greece, Jordan, Kuwait, Lebanon, Lithuania, Mauritius, Mexico, Nicaragua, Oman, Panama, Qatar, Saudi Arabia, Seychelles, Singapore, Suriname, Thailand, Turkey, United Arab Emirates, Uruguay and Venezuela.

In these countries, much more harmful combustible tobacco products such as cigarettes are freely available. Incredibly, the World Health Organization has encouraged these prohibitions via its submission to parties to the Framework Convention on Tobacco Control.[108] WHO Director-General Margaret Chan even called for e-cigarettes to be prohibited in China.[109] This represents an unethical[110] and, at best, confused approach to the health of more than 1 billion current smokers worldwide.[111]

There is no basis for snus or e-cigarette prohibition on public health, scientific or ethical grounds. Such bans may also be unlawful under existing international trade law. Trade law prohibits discriminatory treatment of "like products" based on their country of origin. From a trade law perspective, e-cigarettes and cigarettes may be considered "like products" based on four criteria (i) the physical properties of the products; (ii) their end-uses; (iii) consumer preferences and (iv) the international classification of the products for customs purposes.[112] If products are recognized as "like products" in the meaning of trade law, two key anti-discriminatory principles apply under the WTO General Agreement on Tariffs and Trade (GATT):[113]

1. **Most-favored-nation (MFN) principle** ("treating different foreigners equally"). Where a country allows market access to imported cigarettes from one trading partner, it must extend this "advantage" to the "like products" of other trading partners, including low-risk nicotine products. Failure to do so would constitute a violation of Article I:1 of the GATT.[114]

2. **National treatment principle** ("treating foreigners and locals equally"). If regulatory prohibitions prevent low-risk nicotine products from entering the market—while cigarettes can be produced, distributed and sold domestically—the conditions of competition discriminate against the imported product, thereby constituting less favorable treatment under Article III:4 of GATT.[115]

- **Public health exception will not apply.** It is possible to override these anti-discriminatory measures on public-health grounds under the General Exception provisions of Article XX of GATT.[116] However, the country imposing the prohibition on the low-risk product would need to justify the use of this exception. It is hard to see how they could make this case; certainly not by relying on the WHO's scientific

105. European Union, Tobacco Products Directive, 2014/40/EU, Article 17. http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32014L0040

106. Ramström L, Borland R, Wikmans T. Patterns of Smoking and Snus Use in Sweden: Implications for Public Health. *Int J Environ Res Public Health*. Multidisciplinary Digital Publishing Institute (MDPI); Nov 9, 2016;13(11). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5129320/

107. Institute for Global Tobacco Control. Country Laws Regulating E-cigarettes: A Policy Scan. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health. January 2016. http://globaltobaccocontrol.org/node/14052

108. WHO. Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems (ENDS/ENNDS), FCTC/COP/7/Aug. 11, 2016. http://www.who.int/fctc/cop/cop7/FCTC_COP_7_11_EN.pdf– see especially WHO's policy proposals (para 29-32) which start by assuming prohibition is the norm.

109. *China Daily*, Tougher controls urged for e-cigarettes, Oct. 13, 2015. http://www.chinadaily.com.cn/china/2015-10/13/content_22168321_2.htm

110. Hall W, Gartner C, Forlini C. Ethical issues raised by a ban on the sale of electronic nicotine devices. *Addiction* 2015;110:1061–7. http://onlinelibrary.wiley.com/doi/10.1111/add.12898/abstract

111. Bates CD. Who or what is the World Health Organization at war with? Counterfactual, May 23, 2016. http://www.clivebates.com/?p=4071

112. Foltea M, Markitanova A. The "Likeness" of New and Conventional Tobacco Products in the WTO. In: Society of International Economic Law (SIEL), 2016. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2844044

113. WTO. Principles of the trading system: trade without discrimination. Accessed Dec. 20, 2016. https://www.wto.org/english/thewto_e/whatis_e/tif_e/fact2_e.htm

114. WTO General Agreement on Tariffs and Trade, 1994 Article I:1: https://www.wto.org/english/res_e/booksp_e/analytic_index_e/gatt1994_01_e.htm#article1

115. WTO General Agreement on Tariffs and Trade, 1994 Article III:4: https://www.wto.org/english/res_e/booksp_e/analytic_index_e/gatt1994_02_e.htm#article3

116. WTO General Agreement on Tariffs and Trade, 1994 Article XX:(b): https://www.wto.org/english/res_e/booksp_e/analytic_index_e/gatt1994_02_e.htm#article3

assessment, which has been comprehensively discredited[117].

- **Prohibition through excessive regulation.** Where technical regulations create discrimination via a de facto prohibition (for example, in Australia), they may violate Articles 2.1 and 2.2 of the WTO's Technical Barriers to Trade (TBT) agreement,[118] which respectively prohibit technical regulations that favor like products of national origin over like products from a foreign country, and require that "technical regulations shall not be more trade-restrictive than necessary to fulfil a legitimate objective [including...] protection of human health."
- **WHO Framework Convention on Tobacco Control (FCTC).** The WHO's tobacco-control treaty does allow parties to take tobacco-control measures that go beyond the terms of the FCTC, but only if these "are in accordance with international law" (Article 2), including WTO commitments. [119]

The Office of the United States Trade Representative (USTR) monitors and secures U.S. trade interests.[120] The issue could come to the newly established White House National Trade Council for consideration.[121] The Doggett Amendment should not apply, nor be disapplied for vapor products.

117. Britton, J, McNeill, A, Bauld L, Bogdanovica I Commentary on WHO report on Electronic Nicotine Delivery Systems and Electronic Non-Nicotine Delivery Systems, UK Centre for Alcohol and Tobacco Studies, Oct. 26, 2016. http://ukctas.net/news/commentary-on-WHO-report-on-ENDS&ENNDS.html

118. WTO Agreement on Technical Barriers to Trade Article 2: Preparation, Adoption and Application of Technical Regulations by Central Government Bodies. https://www.wto.org/english/docs_e/legal_e/17-tbt_e.htm#articleII

119. WHO. Framework Convention on Tobacco Control, 2003 Article 2. http://www.who.int/fctc/text_download/en/

120. Office of the United States Trade Representative, Enforcement. Accessed Dec. 20, 2016. https://ustr.gov/issue-areas/enforcement

121. "Doggett Amendment" Omnibus Appropriations Act, Public Law 113-76, 113th Congress, Jan. 17, 2014. https://www.tobaccocontrollaws.org/files/live/United%20States/United%20States%20-%20Doggett%20Amendment%20-%20national.pdf

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APPENDIX I: CHALLENGING COMMON SOURCES OF ERROR IN SCIENTIFIC PAPERS ON VAPING

1. Toxic chemicals have been identified in e-cigarette vapor or e-liquids.

A. Did they show potentially harmful exposure not just the *presence* of a chemical? "The dose makes the poison."

B. How risky is the exposure compared to smoking?

C. How risky is the exposure compared to other risks, such as those accepted under occupational health limits?

D. Were measurements made in realistic human operating conditions or overheated or at very high concentrations?

E. Are inappropriate proxies being used for risk – for example, effects that are also seen with coffee or exercise?

F. Are flawed analogies being used – for example, assuming all ultrafine particles are equally toxic?

2. Adverse health effects from e-cigarettes are reported

A. Was vaping the real cause?

B. Was the person suffering from adverse impacts of beings a smoker before using e-cigarettes?

C. Is the study just observing the effect of nicotine on the body (though no serious disease is caused by nicotine)?

D. Is there evidence of actual harm or is it just a *change* in the body or brain?

E. Is it based on a cell culture study and are the limitations recognized and was exposure a realistic proxy for human use?

F. Is it based on an animal study and are the limitations recognized?

3. Claims second-hand vapor is toxic and indoor vaping should be banned.

A. Are vapor exposures to bystanders potentially harmful given they pose little risk to direct users?

B. Is the difference between risk or harm and nuisance or personal preference recognized?

C. Have false choices been proposed? E.g., between a ban and laissez-faire, when it could be left to owners to decide?

4. Nicotine damages the adolescent brain.

A. What is the specific nature of the detriment to human health?

B. Where is the evidence for the brain damage from nicotine in the longstanding human population of smokers?

C. How does this compare to damage from alcohol, cannabis or caffeine?

5. More children using e-cigarettes and gateway effects.

A. Did they characterize use properly? For example, "ever use" of an e-cigarette is really a marker of experimentation.

B. Could the rising use of e-cigarettes be a good thing if it is displacing smoking?

C. High level of smoking associated with vaping – but is this due to independent common factors (confounding)?

D. Have they defined a gateway effect?

E. Are they assuming prior behavior caused the later behavior?

6. E-cigarettes keep people smoking and reduce quit rates.

A. Has vaping been wrongly conceptualized as though it is a medical intervention?

B. Has the importance of the product's consumer appeal been recognized?

C. Was "dual use" described as problematic – any cutting down is beneficial and may be part of a longer transition?

D. Did they claim there are no benefits to cutting down?

E. Not enough randomized controlled trials (RCTs)? RCTs are a poor way to measure impact of diffusion of technology.

7. Flavors and e-cigarette marketing aimed at children.

A. Do they assume it is just obvious that childish names appeal to kids?

B. Why would adolescents try to emphasize their childishness?

C. Have *preferences* for particular flavors been misrepresented as a *cause* of vaping?

D. Could it be a benefit that some flavors are attractive to adolescents if it means they don't smoke?

E. Is an e-cig advertising in effect an anti-smoking ad?

8. Citing uncertainty and appeal to the "precautionary approach."

A. Have they understood what is known and recognized that the physical processes in vaping are different to smoking?

B. Are they asking the impossible? For example, by saying we will only know the risks when we have 40 years of data?

C. Do they realize that 'precautionary approach can do harm to health if it stops people accessing beneficial technology?

9. Tobacco industry involvement implies inevitable harm

A. Is the malign influence of tobacco companies assumed or demonstrated?

B. Is there over-reliance on decades-old industry statements, documents or behaviors?

C. Is there a proper understanding of how the nicotine and tobacco market works?

D. Are the authors concerned about the right things? For example, are they fighting ill health or capitalism?

10. Policy recommendations in a scientific paper.

A. Do policy recommendations go beyond what their research justifies?

B. Have policymaking disciplines been followed – options generation, impact assessment, consultation, etc.?

C. Are the authors' policy positions revealing their biases and priors?

D. Have unintended consequences been ignored? Many e-cigarette policy proposals could lead to more smoking.