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Should FDA try to move smokers to e-cigarettes or other less-harmful tobacco-nicotine products and, if so, how?

Introduction & Framing for Other Panel Presentations by Moderator, Eric Lindblom

1. For the purposes of this panel, e-cigarettes are defined as any tobacco-nicotine product through which consumers can inhale nicotine directly into their lungs without any combustion that cause lesser health harm and risks to exclusive users than smoking.
2. Many see e-cigarettes as being much more attractive, viable, and direct less-harmful substitutes for smoking than other non-combustible tobacco products (e.g., smokeless tobacco) or non-tobacco nicotine-delivery products (e.g., nicotine gum or patches) because e-cigarettes enable smokers to feed their addiction by inhaling nicotine directly into their lungs, just like smoking. That raises the possibility of securing significant public health gains by shifting ongoing smokers to using e-cigarettes, instead.
3. FDA is generally allowed to take action relating to non-medical tobacco/nicotine products when doing so is “appropriate for the protection of the public health.”¹
 - A. But FDA is not required by law to initiate any new tobacco control regulations, public education campaigns, or even most enforcement actions – no matter how “appropriate for the protection of the public health” taking those actions might be. Hence, this panel’s question: *Should FDA try to move smokers to e-cigarettes or other less-harmful tobacco-nicotine products and, if so, how?*
 - B. The panelists or others (including FDA officials) could have a wide range of non-health reasons for thinking that FDA should or should not try to move smokers to e-cigs or should take certain specific actions to do so (e.g., political or legal concerns, wanting to avoid industry burdens, cost to the government, availability of more effective options to reduce tobacco harms). But, regardless of any non-health reasons for choosing to take any specific action, before actually taking the action FDA must, generally, be able to determine that taking the action is “appropriate for the protection of the public health” (and not be “arbitrary or capricious” or “abuse its discretion” in making that determination).²
4. There is considerable debate among researchers and others about how much less harmful exclusive e-cigarette use is compared to smoking. But this panel is not going to get into that debate, much less try to resolve it. Instead, the panel is basing its analyses and recommendations on the following core research-based facts:
 - A. Exclusive e-cig use is less harmful/risky to users than smoking.
 - B. Exclusive e-cig use is more harmful/risky to users than not using e-cigs or any other non-medical tobacco or nicotine product at all.
 - C. Switching to dual use from smoking is not less-harmful to users than just smoking unless the dual use reduces smoking levels substantially (e.g., to very low levels).
 - D. Exposure to e-cig use is less harmful/risky to non-users than exposure to smoking (including harms to newborns from maternal e-cig use only vs. maternal smoking during pregnancy).
 - E. Exposure to e-cig use is more harmful/risky to non-users (including newborns) than not being exposed to any smoking or e-cig use at all.

5. Based on those core facts, moving smokers to using e-cigarettes could produce health gains in the following ways:
 - A. Less harm to exposed non-users to extent exposure to smoking is replaced by exposure to e-cig use or otherwise reduced significantly.
 - B. Less harm to smokers if they switch completely to using e-cigs, instead.
 - C. Dual use with large reductions to former smoking levels might reduce health harms/risks.
 - D. Complete switching to e-cigs could be pathway to total cessation; and incomplete switching (dual use) could be pathway to complete switching to e-cig use, with related harm reductions.
 - E. Youth who experiment with e-cigarettes instead of with smoking and move on to initiate regular use would be initiating into less-harmful form of tobacco/nicotine use. Also possible that experimenting with e-cigs instead of smoking might be less likely to result in regular/addicted use.
6. At the same time, moving smokers to using e-cigarettes could produce health harms in the following ways:
 - A. Some smokers who would have otherwise quit all tobacco-nicotine use could switch to using e-cigs, alone or via dual use, instead -- preventing or delaying total cessation.
 - B. Some smokers who would otherwise have quit all smoking could switch to dual use, instead – thereby preventing or delaying smoking cessation.
 - C. In many cases, dual use could be more harmful than just smoking.
 - D. Efforts to move smokers to e-cigs could prompt youth or adults who would not otherwise use any tobacco-nicotine product to start regular/addicted e-cig use, and some might move on to regular/addicted smoking.
7. The extent to which any of those beneficial and harmful behavior changes occur will depend on how the e-cigarettes and smoked tobacco products are marketed and regulated. For example, a recent journal article projected that *if virtually all cigarette smoking were replaced with e-cigarette use over the next ten years* that could, under its conservative assumptions (e.g., e-cigs only 5% as harmful as cigarettes, low residual smoking, low initiation by otherwise nonsmokers), prevent 1.6 million premature deaths and could, under its optimistic assumptions (e.g., e-cigs 40% as harmful, higher residual smoking, more initiation), prevent 6.6 million premature deaths.³ An earlier modeling study found both positive and negative net health impacts, depending on a wide range of different assumptions about switching, dual use, cessation, and initiation trends, as well as about relative harmfulness (but none assuming that smoking would be largely eliminated).⁴ The study's most optimistic scenarios (e.g., considerable total switching, low or no cessation delays or initiation by otherwise nonsmokers) produced net health benefits even when e-cigarettes were assumed to be 50% as harmful as cigarettes, and its most pessimistic scenarios (e.g., considerable dual use with cessation delays, little total switching, increased initiation) produced net health harms even when e-cigarettes were assumed to be only 1% as harmful as cigarettes – with other, in-between scenarios having net positive or negative impacts depending on the what relative-harm assumptions were used.
8. Current situation under federal law: Manufacturers of e-cigs on the U.S. market must register and make various reports to FDA; e-cigs may not be sold to persons under the age of 18; no free samples; liquid nicotine must be in child-proof packaging; packages must have nicotine/addictive warning label by August 2018; e-cigs currently on U.S. market (as of 8/8/16) must submit an application to obtain an FDA new product or substantial equivalence order by August 2022 to stay on market; any brand-new e-cigs

(or existing e-cigs that are significantly changed) must obtain a new product order before entering the market; and manufacturers may not make reduced-risk claims about their e-cigs without first obtaining a permissive Modified Risk Tobacco Product (MRTTP) order from FDA.⁵

9. Possible FDA goals from a Tobacco Control Act or public health perspective:

- A. Take action to move smokers to e-cigs if doing so would produce substantial net public health gains -- compared to taking no action or to taking readily available alternative actions to prevent or reduce tobacco use harms. [Or FDA could both take the action to move smokers to e-cig use and take one or more of the other readily available alternative actions at same time, if doing that would secure even larger net public health gains.]
- B. If action is taken to move smokers to e-cigarettes, structure the action, to the extent possible, to reduce any risks that it will also produce new health harms – at least so long as reducing those risks does not significantly reduce the likely net public health gains from taking the action.

10. Available FDA tools for moving smokers to using e-cigarettes.

- A. Include relative-risk information or encouragement for smokers to switch in FDA public statements, website pages, reports, documents, press releases, etc.
- B. Public education campaigns (which could be targeted to maximize reaching smokers and minimizing reaching youth and non-smokers).⁶
- C. New rules to inform smokers about relative risks through required warning labels or inserts/onserts for cigarettes and other smoked tobacco products and/or for e-cigs.⁷
- D. New rules to make cigarettes and other smoked tobacco products less addictive or attractive.⁸
- E. New rules to make e-cigarettes more attractive to smokers.⁹
- F. Not issue any new rules that place new restrictions or requirements on e-cigarettes or their advertising or other marketing which are as or more strict, costly, or burdensome as those placed on cigarettes or other smoked products.
- G. New Product Orders. For example: Provide expedited pathways to enable innovative new e-cigs to get on FDA order to allow them on the market (e.g., if they are less harmful/risky than existing e-cigs or serve as better smoking substitutes).
- H. MRTTP Orders. For example: Provide expedited pathways to enable manufacturers to advertise certain e-cigs to smokers with reduced-risk claims.¹⁰
- I. Enforcement discretion.¹¹ For example:
 - (1) Put a top priority on enforcing existing TCA provisions and related rules against cigarettes and other smoked tobacco products.
 - (2) Postpone or forgo enforcement of the TCA and related rules against e-cigarettes.

[FDA does not have authority to establish [or increase tax rates on any tobacco-nicotine products. Nor does FDA have authority to change, overrule, or impose state or local smoke-free laws.]

11. As noted above, in most cases FDA cannot take action to move smokers to using e-cigarettes unless it determines that doing so is “appropriate for the protection of the public health.” It is also quite possible that when deciding whether to take action and what action(s) in might take, FDA might follow some versions of the medical maxim to “do no harm” or the precautionary principle (which basically says that when an activity raises threats of harm to human health, precautionary measures should be

taken even if there is no scientific certainty that the harms will occur).¹² Accordingly, the panelists have been urged to try to ensure that any actions they think FDA should take to move smokers to e-cigarettes would not only work effectively to move ongoing smokers to using only e-cigs, instead, but would also be structured, to the extent possible, to reduce any related risks of promoting health-harming behavior changes (such as those listed above), at least so long as that can be done without sharply reducing the number of smokers moved to e-cigs.¹³

12. Two major options FDA might consider (which panelists will comment on):

A. *Minimizing nicotine levels in cigarettes and similarly smoked tobacco products.* FDA Commissioner Scott Gottlieb has announced that FDA is considering this possibility and authored a related article with FDA Center for Tobacco-Products Director Mitch Zeller.¹⁴ Possible elements of such a nicotine-minimizing rule:

- (1) Applies to cigarettes, RYO tobacco, and similarly smoked tobacco products (excludes large, premium cigars) – to prevent cigarette smokers from simply switching to smoking cigarette-like or otherwise actively inhalable cigars.
- (2) No phase-in (which prompts compensation at non-minimal levels). Minimal nicotine level must be met by effective date.
- (3) Minimal level set at lowest level that is readily achievable by existing processes and technologies (e.g., no higher than 0.4 mg/gm or 0.6 mg/cigarette) -- to ensure no addictive or addiction-satisfying potential.
- (4) Industry given time to re-tool to meet standard and then sell off its inventories of full-nicotine cigarettes, etc. (with provisions to stop pre-effective date stockpiling).

[Availability of legal e-cigarettes, which provide for inhaling nicotine into the lungs, likely to reduce demand for illicit non-complying cigarettes appearing, further reducing the feasibility of any major new illicit market appearing.]¹⁵

B. *MRTP Fast-Track to enable manufacturers to obtain MRTP orders from FDA more quickly and easily, allowing them to market e-cigarettes with reduced-risk claims.* Some think that smokers should be encouraged to switch to using e-cigarettes largely through market competition. But a major impediment to that is that e-cigarette manufacturers cannot compete against cigarettes and smoking by telling smokers that e-cigarettes are less harmful without first getting a permissive MRTP order from FDA, which can be costly, difficult, and time consuming. Possible elements of an MRTP fast-track:

- (1) *Eligible Products:* Non-combustible tobacco-nicotine products that are significantly less harmful to exclusive users (and exposed nonusers) than smoking (e.g., e-cigs, smokeless) and are not clearly more harmful or risky than other tobacco-nicotine products of the exact same type that are currently on the market. In particular, the product would have to: (a) meet minimal standards re contamination; (b) not include or create any harmful or potentially harmful constituents not necessary to the product's operation (e.g., can contain and deliver nicotine); and (c) not have any characterizing flavor other than menthol, tobacco, or neutral (to minimize the risk of attracting new youth or other users, while still enabling the products to serve readily as direct alternatives to cigarettes). [Under existing law, would also have to have child-proof packaging of any nicotine liquids.]
- (2) *Eligible Reduced Risk Claims* (with possible FDA template): Must be accurate, non-misleading statements about reduced harms/risks to self and others from switching from smoking to using the lesser-harm product – and must also include accurate, not-misleading statements

meant to prevent less-beneficial behavior change regarding: (a) the harms/risks from dual use; (b) the harms/risks from just exclusive lower-harm product use; and (c) how complete cessation of all tobacco-nicotine use is the best way to maximize reduced risks and protect one's health.

- (3) *Restrictions on Delivery of Reduced-Risk Claims*: May be made only through direct communications (e.g., mail, email, social media) only to pre-verified adult smokers. [These restrictions are meant to enable reduced-risk claims to be marketed directly to their target audience while minimizing the risk that the reduced-risk claims could also reach and attract youth or current adult nonusers].¹⁶

¹ See, e.g., *Family Smoking Prevention and Tobacco Control Act* (FSPTCA), Sec. 906(d)(1) [21 USC 387f(d)(1)] and 907(a)(3) [21 USC 387g(a)(3)]. The FSPTCA also specifically forbids FDA from taking certain actions under its tobacco control authorities, including banning all cigarettes (or certain other entire types of tobacco products), requiring the reduction of nicotine yields of a tobacco product to zero, requiring that tobacco products be sold only by prescription, prohibiting face-to-face sales of tobacco products in any specific category of retail outlets (e.g., no sales in pharmacies), or establishing a minimum age of sale of tobacco products older than 18 years of age. FSPTCA Sec. 907(d)(3) [21 USC 387g(d)(3)]; Sec. 906(d)(1&3) [21 USC 387f(d)(1&3)].

² FSPTCA Sec. 912(b) [21 USC 387], incorporating by reference 5 USC 706(2)(A).

³ Levy, DT, et al., "[Potential deaths averted in USA by replacing cigarettes with e-cigarettes](#)," *Tobacco Control* (ePub. October 2, 2017).

⁴ Kalkhoran, S & Glantz, SA, "[Modeling the Health Effects of Expanding e-Cigarette Sales in the United States and United Kingdom: A Monte Carlo Analysis](#)," *JAMA Internal Medicine* 175(10): 1671-80 (Oct. 1, 2015).

⁵ FDA, [Deeming Tobacco Products to be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products](#) ("Deeming Rule"), 81 Fed. Reg. 28,974 (May 10, 2016) [21 C.F.R. pts. 1100, 1140, & 1143]; FDA, [Guidance: Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule \(Revised\)](#) (August 4, 2017).

⁶ For examples of the kinds of public education campaigns FDA's Center for Tobacco Products has initiated, targeting specific subpopulations, see the FDA website, Tobacco Products, [Public Education Campaigns](#), www.fda.gov/tobaccoproducts/publichealtheducation/publiceducationcampaigns, accessed October 7, 2017.

⁷ See, e.g., Lindblom, EN, et al., "[FDA-Required Tobacco Product Inserts & Onserts – and the First Amendment](#)," *Food & Drug Law Journal* 72(1): 1-25 (March 2017).

⁸ See, e.g., Campaign for Tobacco-Free Kids, Report, [Designed for Addiction: How the Tobacco Industry has Made Cigarettes More Addictive, More Attractive to Kids and Even More Deadly](#) (June 23, 2014).

⁹ See, e.g., Pechacek, TF, et al., "[The Potential That Electronic Nicotine Delivery Systems Can be a Disruptive Technology: Results From a National Survey](#)," *Nicotine & Tobacco Research* 18(10): 1989–97 [Concluding that e-cigarettes must become more attractive to smokers, or cigarettes made less attractive, for e-cigarettes to realize their potential as a disruptive technology that replaces conventional cigarettes.] But see Eshnrt, TL, et al., "[Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users](#)," *Tobacco Control* 26(e1):e23-e28 (March 2017)[on industry developing e-cigarettes that deliver nicotine even more like cigarettes, making them more attractive as substitutes].

¹⁰ See, e.g., Lindblom, Eric N., "[Effectively Regulating E-Cigarettes and Their Advertising— and the First Amendment](#)," *Food and Drug Law Journal* 70(1): 57-94 (March, 2015).

¹¹ On enforcement discretion in general, see, e.g., *Heckler v. Chaney*, 470 U.S. 821, 831 (1985)[Supreme Court declines to review FDA's decision not to take enforcement action, stating that it has "recognized on several occasions over many years that an agency's decision not to prosecute or enforce, whether through civil or criminal process, is a decision generally committed to an agency's complete discretion."] See, also, Rechtschaffen, C, "[Promoting Pragmatic Risk Regulation: Is Enforcement Discretion the Answer?](#)," *Univ. of Kansas Law Review* 52:1327 (March 2004). On enforcement discretion by FDA in the context of e-cigarettes, see Lindblom, Eric N., "[Effectively Regulating E-Cigarettes and Their Advertising— and the First Amendment](#)," *Food and Drug Law Journal* 70(1): 57-94 (March, 2015). FDA exercised its enforcement discretion to a considerable extent in its tobacco control [deeming rule](#) and its subsequent [guidance extending the deadlines](#) for e-cigarettes to meet various statutory deadlines that FDA had set in the deeming rule through its enforcement discretion. *Supra*, note 4.

¹² On "do not harm," generally, see, e.g., Sokol, D, "[First, do no harm' revisited](#)," *BMJ* 347:f6426 (October 25, 2013). On "do not harm" in the regulatory context, see, e.g., Warren, EW & Marchant, GE, "[More Good Than Harm': A First Principle for Environmental Agencies and Reviewing Courts](#)," *Ecology Law Quarterly* 20: 379 (1993). On the precautionary principle in policy making, see, e.g., Martuzzi, M, "[The Precautionary Principle: in Action for Public Health](#)," Goldstein, BD, "[Problems in Applying the Precautionary Principle to Public Health](#)," Kriebel, D, "[The Reactionary Principle: Inaction for Public Health](#)," and Rushton, L, "[The Precautionary Principle in the Context of Multiple Risks](#)," in *Occupational & Environmental Medicine* 64(9) (Sept. 2007), at : 569–574. See, also, Saitta, D, et al., "[A Risk Assessment Matrix for Public Health Principles: The Case for E-Cigarettes](#)," *Int'l Jnl of Environmental Research & Public Health* 14(4): 363 (April 2017).

¹³ See, e.g., Saitta, D, et al., "[A Risk Assessment Matrix for Public Health Principles: The Case for E-Cigarettes](#)," *Int'l Jnl of Environmental Research & Public Health* 14(4): 363 (April 2017).

¹⁴ FDA News Release, "[FDA announces comprehensive regulatory plan to shift trajectory of tobacco-related disease, death: Agency to pursue lowering nicotine in cigarettes to non-addictive levels and create more predictability in tobacco regulation](#)" July 28, 2017). Gottlieb, S & Zeller, M, "[A Nicotine-Focused Framework for Public Health](#)," *New England Journal of Medicine* 377: 1111-14 (Sept. 21, 2017). See, also, Clarke, T, "[Philip Morris International CEO cheers U.S. FDA tobacco proposal](#)," *Reuters* (August 22, 2017).

¹⁵ For more on the nuts and bolts of establishing a law or rule to minimize nicotine levels, see Lindblom, EN, "[Filling in the Blanks on Reducing Tobacco Product Addictiveness in the FCTC Partial Guidelines for Articles 9 & 10](#)," O'Neill Institute for National & Global Health Law Working Paper No. 1 (November 17, 2014). For subsequent related research, see, e.g., Smith, TT, et al., "[Impact of smoking reduced nicotine content cigarettes on sensitivity to cigarette price: further results from a multi-site clinical trial](#)," *Addiction* 112(2):349-359 (Feb. 2017); Hatsukami, DC, et al, "[Reduced nicotine content cigarettes and use of alternative nicotine products: exploratory trial](#)," *Addiction* 112(1):156-67 (Jan. 2017). Donny, EC, et al., "[Randomized Trial of Reduced-Nicotine Standards for Cigarettes](#), *New England Journal of Medicine* 373(14):1340-49 (Oct. 2015).

¹⁶ For a similar proposal for expedited review of e-cigarette new product and MRTP applications, see, e.g., Lindblom, Eric N., "[Effectively Regulating E-Cigarettes and Their Advertising— and the First Amendment](#)," *Food and Drug Law Journal* 70(1): 57-94, March, 2015. See, also, O'Brien, EK, et al, "[U.S. Adult Interest in Less Harmful and Less Addictive Hypothetical Modified Risk Tobacco Products](#)," *Nicotine & Tobacco Research* (ePub. Sept. 28, 2017). In that study, about half of smokers and 1/10th of former and never smokers reported being interested in trying a less-harmful tobacco product when asked "If a tobacco product made a claim that it was less harmful than other tobacco products, how likely would you be to use that product?" Further research is needed to see if the results might be even more favorable toward trying if the question had asked specifically about e-cigarettes making less-harmful-than-smoking claims.