Tobacco Control Act Ethics Project
O'Neill Institute for National & Global Health Law
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BACKGROUND INFORMATION TO PREPARE FOR THE JUNE 12 TCA EXPERTS MEETING

Core Questions We Will Try to Answer:

1. *Is currently available research and other evidence sufficient to support an FDA rule to reduce nicotine levels in cigarettes and possibly other smoked tobacco products and, if so, how should that rule be structured, consistent with applicable legal standards, to work most effectively to protect and promote the public health and otherwise be as ethically appropriate as possible*?

2. *What minimal standards should FDA apply to e-cigarette PMTA and MRTP applications and any related permissive orders to ensure that allowing the e-cigarettes to enter or stay on the market or to be marketed with MRTP claims will be "appropriate for the protection of the public health" and otherwise ethically appropriate?*

<u>The Tobacco Control Act's Major Substantive and Evidentiary Standards</u>

The Tobacco Control Act gives FDA extensive authorities to regulate tobacco products and their manufacture, distribution, marketing, and sale. The major limits on FDA's authorities come from the Act explicitly stating that FDA may not:
(a) Ban all tobacco products or entire types of tobacco products (e.g., all cigarettes or all cigars);
(b) Raise the federal minimum legal age for purchasing tobacco products above 18;
(c) Require that nicotine yields from any tobacco product be zero;
(d) Require a prescription to purchase tobacco products; or
(e) Prohibit the in-person sale of tobacco products in any specific category of retail outlet.[1]

In addition, the First Amendment's protections for corporate speech place significant constrains on the extent to which FDA may restrict tobacco product labeling or advertising or require tobacco product manufacturers or importers to include certain statements or images on their tobacco product labeling, packaging, or advertising.[2]

Beyond these constraints, the TCA provides FDA with broad authorities to issue tobacco product standards or other rules, including standards to reduce nicotine levels in tobacco products, so long as FDA determines that issuing the rule is "appropriate for the protection of the public health." The Act

[1] TCA § 906(d) [21 U.S.C. 387f(d)]; § 907(d)(3) [21 USC 387g(d)(3)]. For this project, we will assume (reasonably) that the TCA restrictions on FDA banning all cigarettes or requiring nicotine yields of zero do not interfere with FDA's ability to implement a nicotine-reduction rule that does not require nicotine yields or other nicotine levels of zero.

[2] These 1st Am. constraints would not likely apply to any nicotine-reduction rule, but would apply to any labeling requirements or advertising restrictions that FDA might include in a permissive PMTA or MRTP order. However, if any such restrictions or requirements worked effectively to protect the public health they could likely pass constitutional muster if the advertising restrictions were narrowly tailored and left the companies with reasonably ways to reach their legal customers and the labeling requirements did not put words in the companies' mouths and did not include controversial content. [But constitutional law is, or course, a bit more complicated than summarized here, and also somewhat fluid.]

directs FDA to make these determinations "with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product," taking into account both the increased or decreased likelihood that existing users of tobacco products will stop using such products; and the increased or decreased likelihood that those who do not use tobacco products will start using such products."[3]

The Act also establishes procedures whereby no new or substantially changed tobacco product may enter the U.S. market unless its manufacturer or importer first applies for and receives a permissive order from FDA. Applications for such orders are often referred to as Pre-Market Tobacco Product Applications or PMTAs. To issue a permissive PMTA order, FDA must determine that allowing the new or changed tobacco product on the market as proposed would be "appropriate for the protection of the public health."[4] To ensure that allowing the product on the market is "appropriate for the protection of the public health" (or to make doing so even more beneficial to the public health), any such permissive ordes may include various restrictions or requirements relating to the product or its labeling, marketing, and sale that were proposed by the applicant or added by FDA.[5]

Similarly, the TCA establishes that no tobacco product that is labeled or advertised with modified risk tobacco product (MRTP) claims -- i.e., claims that its use reduces health risks or reduced exposures to harmful of potentially harmful constituents compared to using other tobacco products -- may enter the U.S. market unless its manufacturer or importer first applies for and receives a permissive order from FDA. To issue a permissive MRTP order, FDA must determine, first, that the proposed MRTP will actually reduce risk or reduce exposure as claimed and, second, that allowing the MRTP on the market with the claim will be "appropriate for the protection of the public health."[6] As with PMTA orders, permissive MRTP orders may include various restrictions or requirements relating to the product or its labeling, marketing, and sale to ensure that allowing the product on the market with the modified risk claims is "appropriate for the protection of the public health," or to make doing so even more beneficial to the public health.[7]

For FDA tobacco product standards and other tobacco control rules, the burden of proof is on FDA. For FDA PMTA and MRTP orders, the burden of proof is on the tobacco product manufacturer or importer submitting the application – e.g., FDA must determine whether the applicant has demonstrated in its

[3] § 907(a)(3)(B) [21 U.S.C. 387g(a)(3)(B)].

[4] § 910(c)(4) [21 U.S.C. 387j(c)(4)].

[5] § 910(c)(1)(B) [21 U.S.C. 387j(c)(1)(B)].

[6] § 911(g) [21 U.S.C. 387k(g)]. The language in the TCA MRTP provisions does not use the specific "appropriate for the protection of the public health" phrase as in the PMTA and product standard provisions, but its text otherwise parallels the PMTA and product standard text, with the same focus on benefiting the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products, and also considering other behavioral impacts.

[7] § 911(h)(5) & (h)(1)&(2) [21 U.S.C. 387k(h)(5) & (h)(1)&(2)]. § 911 also states that FDA "shall require" that any advertising and labeling delivering an FDA-permitted modified-risk claim enable the public to comprehend the information and understand its relative significance in the context of total health and in relation to all the diseases and health-related conditions associated with using tobacco products. § 911(h)(1) [21 U.S.C. 387k(h)(1)].

application that issuing a permissive order would be "appropriate for the protection of the public health."[8]

Pursuant to the Administrative Procedures Act, FDA's appropriate-for-the-protection-of-the-public-health and other determinations when developing and issuing tobacco control rules or PMTA or MRTP orders must not be "arbitrary, capricious, or an abuse of discretion," and the final rule or order or its implementation must not otherwise be "arbitrary or capricious."[9]

More on the Application of the "Appropriate for the Protection of the Public Health" and "Not Arbitrary or Capricious" Standards

An earlier part of this project produced an exhaustive analysis of the Tobacco Control Act, its legislative history, and related court rulings to try to clarify some of the gray areas in the "appropriate for the protection of the public health" and "not arbitrary or capricious" standards in the TCA context.[10] It's main findings follow.

- When determining whether a specific tobacco control rule or order is "appropriate for the protection of the public health," FDA may not consider any non-health impacts. In particular, the TCA does not require or allow FDA to consider the following when determining whether a rule or order is "appropriate":
  - Technical achievability
  - Burdens on the industry
  - "Smokers' Rights" or any adult consumers' right to choose
  - Illicit trade (other than its impact on the public health).[11]

- When FDA is determining whether a specific tobacco control product standard, rule, or order is "appropriate for the protection of the public health," only the health impacts on the population *as a whole* are relevant. In particular:
  - The TCA shows little or no concern regarding specific health impacts on any sub-population or disadvantaged group, other than youth, users, and nonusers.
  - The TCA does not put a higher priority on preventing or reducing youth tobacco use or harms than it does on reducing adult use and harms.

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[8] FDA has no obligation to consider any information that might support the application or its proposed order other than what the application, itself, offers; and the TCA leaves FDA free to reject inadequate PMTA or MRTP applications and proposed orders rather than make any effort to fix them. § 910(c)(2) [21 U.S.C. 387J(c)(2)]; § 911(g)(1)&(2)&(3)(A) [21 U.S.C. 387k(g)(1)&(2)&(3)(A)]. But FDA has typically provided repeated opportunities for applicants to amend and improve their applications and often does its own related supplementary research.

[9] 5 USC 706(2)(A). TCA Sec. 912(b) [21 USC 387l(b)].

[10] Lindblom, Eric N., "Key Parameters of the 'Appropriate for the Protection of the Public Health' Standard for FDA Regulatory Action Under the U.S. Tobacco Control Act" (submitted). Confidential copies happily provided upon request (with comments welcome). Enl27@law.georgetown.edu.

[11] As outlined below, however, a rule or order that is "appropriate for the protection of the public health" could still be found legally invalid if certain non-health impacts made it "arbitrary or capricious." In addition, FDA can also exercise its discretion when deciding which tobacco control rules to implement to choose those rules with fewer or less severe non-health impacts compared to other options.

  - Such subpopulation or disparities impacts are not relevant to "appropriate" determinations.[12]

- When determining whether a tobacco control rule or order is "appropriate for the protection of the public health," FDA must consider its impact on the full range of tobacco-related behaviors over time that affect the health of the population as a whole (not just initiation and cessation but also relapse, switching, dual use, consumption level changes, etc.).

- The TCA provides FDA with enormous discretion regarding how it clarifies the remaining gray areas of the appropriate-for-the-protection-of-the-public-health standard and regarding how it handles uncertainty regarding future net impacts on the health harms and risks to the population as a whole when determining whether a tobacco control rule or order is "appropriate."

- Under the TCA, FDA has enormous discretion to determine how much research, other evidence, and certainty it needs to determine whether a tobacco control rule or permissive PMTA or MRTP order is "appropriate for the protection of the public health."

- As long as FDA follows established procedures, considers contrary analysis and options, and explains its decisions, the "not arbitrary or capricious" standard places few constraints on FDA appropriate-for-the-protection-of-the-public-health determinations, including its determinations regarding how much evidence is needed or how to handle inevitable uncertainties involved when estimating future impacts.[13]

- However, under existing case law, once FDA chooses to implement a specific final tobacco control rule that is "appropriate for the protection of the public health," it must, to avoid being found arbitrary or capricious, implement any obvious or readily available adjustments to the structure of the rule, within its FDA-chosen reach or scope, that would reduce its costs (or any equally or more undesirable secondary impacts) without impeding its ability to promote its statutory purpose (i.e., to secure a net reduction in health harms and risks to the population as a whole). This same requirement should apply equally to any final FDA PMTA or MRTP permissive orders.

- Accordingly, once FDA chooses to implement a specific final tobacco control rule or order that is "appropriate for the protection of the public health," to avoid being found arbitrary or capricious, FDA must, at a minimum, implement any obvious, readily available adjustments to the structure of

[12] But, as outlined below, a rule or order that is "appropriate for the protection of the public health" could still be found legally invalid if its health impacts on specific subpopulations or on health disparities made it "arbitrary or capricious." In addition, FDA can also exercise its discretion when deciding which tobacco control rules to implement to choose those rules with fewer or less severe sub-population health impacts or health-disparity impacts compared to other options.

[13] For example, FDA might reasonably determine that to be "appropriate for the protection of the public health," no tobacco control rule or order may produce a significant risk of producing a non-trivial net increase in public health harms. Or, alternatively, FDA might reasonably determine that that a tobacco control rule or order is "appropriate" so long as the likelihood and size of its expected net public health benefit are at least ten (or twenty) times the likelihood and size of any possible negative public health impact. Similarly, there are a number of ways that FDA may exercise its discretion and expertise to employ various reasonable ways to develop estimates of the likelihood and size of the public health and other relevant impacts of a tobacco control rule or order (including best-case and worst-case estimates) that FDA could use to guide its determinations despite inevitable research gaps and uncertainties.

the rule or order, within its reach or scope, that would reduce the likelihood or size of any public health or subpopulation or individual health risks or harms it might cause without reducing the likelihood or size of its potential net public health gains.[14]

- It is also possible that FDA has a parallel duty, to avoid being "arbitrary or capricious," to implement any obvious, readily available adjustments to the structure of the rule or order, within its reach or scope, that would increase the likelihood or size of the net reduction in health harms and risks to the population as a whole the rule or order would secure – at least so long as that does not increase any related individual or subpopulation health harms, the likelihood or size of any negative public health risks, or any other relevant undesirable impacts.

Related Ethical Standards for FDA Tobacco Control Action

Even if the "not arbitrary or capricious" standard did not require such FDA actions to reduce unnecessary secondary health harms and risks, costs, and other possible undesirable impacts from its tobacco control rules or orders, taking such action would be consistent with fundamental standards of ethical conduct.

Another part of this project is looking carefully at how such ethical perspectives as utilitarianism, public health ethics, and bioethics (with its core principles of beneficence, non-maleficence, justice, and autonomy) might guide FDA's actions to clarify the unclear aspects of the appropriate-for-the-protection-of-the-public-health standard and otherwise develop or structure its tobacco control rules or orders. While coming up with bright-line rules is difficult and, sometimes, impossible, these ethical perspectives suggest the following guidelines.

- FDA should (to the extent permitted by the White House and OMB) use its regulatory authorities within applicable legal constraints to develop and implement those measures that will secure the largest and quickest reductions to tobacco-related health harms and risks in the most ethically appropriate manner. That means choosing those product standards and other rules to implement that will quickly secure the largest net public health gains with little or no risk of:
  - Causing new health harms to innocents (those who would not otherwise be harmed)
  - Causing other underlying new health harms or risks
  - Increasing health disparities (and, ideally, reducing them, instead)
  - Causing other serious harms (esp. to innocents or vulnerable/disadvantaged subpopulations)
  - Seriously infringing on personal autonomy.[15]

[14] It does not appear that FDA took advantage of any readily available measures to minimize such risks in the permissive PMTA orders the agency issued in 2015 for several Swedish Match snus tobacco products. For example, FDA's final permissive order could have included labeling requirements about how they should be used to produce health gains (and which uses would increase health harms) and could have included advertising restrictions to ensure that the snus could not legally be advertised in ways that reached or attracted youth. So far, the snus do not appear to have been advertised in irresponsible ways. But adding certain restrictions and requirements into the final orders could have largely eliminated that risk from the start and made it easier to stop such advertising if it did occur.

[15] Although ethical debate is possible, the assumption here is that stopping the legal commercial sale of cigarettes with sufficient nicotine to develop and satisfy nicotine addictions would not, by itself, be a serious infringement on personal autonomy (especially if nicotine-delivering e-cigarettes remain a legally available way to inhale nicotine into one's lungs).

- FDA should not grant permissive PMTA or MRTP orders if FDA determines that allowing the subject tobacco product on the market will create a non-trivial possibility of producing serious new public health harms or risks -- with a possible exception if FDA determines that allowing the product on the market will also create a much stronger likelihood of producing a much larger net reduction in health harms to the population as a whole; the size and character of the possible net health harms/risks are not too large or severe (e.g., harms/risks are reversible) and cannot readily be reduced; and FDA could (and would) quickly stop any negative net impacts that might arise by pulling the product from the market or making other changes to the permissive order and possibly taking other tobacco control action.

- FDA should structure any tobacco control rules it implements and any permissive PMTA or MRTP orders it issues to maximize the likelihood and size of the net reductions to health risks and harms to the population as a whole they will secure, while also minimizing the likelihood or size of any:
  - New health harms (esp. to innocents)
  - Increases to health disparities (and, ideally, reducing them)
  - Serious new non-health harms (esp. to innocents or vulnerable/disadvantaged subpopulations)
  - Serious infringements on personal autonomy.

Ethical guidance is less clear, however, about how to balance competing ethical goals against each other when they conflict (e.g., when maximizing net reductions to smoking-caused harms would increase one or more of the harms/risks FDA should, ideally, minimize).

In rulemaking, FDA could largely avoid these ethical conflicts by thoughtfully choosing to issue those rules that would produce the largest net public health gains with little or no undesirable health or other impacts. Relevant to this project, it appears that a nicotine-reduction rule could, depending on its structure, secure large reductions in health harms and risks to the population as a whole without directly causing any significant new health harms to innocents or others, without increasing health disparities, and (arguably) without causing other serious undesirable impacts.

But FDA cannot choose which applications for permissive PMTA or MRTP orders to consider. FDA must consider all applications, and available options for how to structure any permissive PMTA or MRTP orders that might be issued are likely to raise trade-off issues between maximizing potential overall public health gains, minimizing the risk of producing any net public health harms, and creating new health harms for some specific vulnerable or disadvantaged subpopulations or other serious undesirable impacts. Most fundamentally, the only way allowing an MRTP or PMTA tobacco product on the market could have a beneficial net impact on the public health is by prompting some users of more-harmful tobacco products to switch to the less-harmful new one, and that immediately creates a risk that some switching or dual use might also prevent or delay total cessation by some users and that the product's market entry might also increase relapse by otherwise committed former tobacco users or prompt new initiation by those who otherwise would not have used any tobacco product at all.

As noted above, however, the TCA requires FDA to put a much higher priority on reducing health harms and risks to the population as a whole compared to any other beneficial or detrimental health or non-health impact its tobacco control rules or orders might produce, and that priority necessarily carries over into any related "arbitrary or capricious" analysis, thereby constraining or guiding the application of these ethical principles somewhat, as well.

In addition, applying the different ethical perspectives appears to support the same not-arbitrary-or-capricious findings that -- before getting to any remaining sticky legal or ethical questions about trade-offs that might remain -- FDA should, when implementing a final tobacco control rule or order that is "appropriate for the protection of the public health," first:

- Implement any obvious or readily available adjustments to the structure of the rule or order, within its reach or scope, that would:
  - Reduce the likelihood or size of any public health or subpopulation or individual health risks or harms it might cause, or reduce other serious undesirable impacts, without reducing the likelihood or size of its potential net public health gains; or
  - Increase the likelihood or size of the net reduction in health harms and risks to the population as a whole it would secure without increasing related individual or subpopulation health harms, the likelihood or size of any negative public health risks, or any other relevant undesirable impacts.

Application of these Legal and Ethical Standards to the Project's Two Main Questions

Applying the just-described legal and ethical standards to the project's two key project questions (see above) creates a number of more-specific questions, such as the following. But the questions provided here are only initial rough drafts. More developed discussion drafts relating to an FDA nicotine-reduction rule and to FDA's consideration of PMTA and MRTP applications for e-cigarettes will be circulated later.

For an FDA nicotine-reduction rule:

Based on available research, evidence, analysis, and common sense:

NRule (1) Could a nicotine-reduction rule for cigarettes and some or all other smoked tobacco products be developed that would be highly likely to secure large net public health gains (i.e. reduce health harms and risks to the population as a whole) with little or no risk of producing a serious net public health loss?

NRule (2) If so, how should the nicotine-reduction rule be structured to accomplish the primary goal of maximizing the likelihood and size of the potential net public health gains – while also, to the extent possible without reducing the likely net public health gains, minimizing the following undesirable secondary impacts?
  - New health harms/risks to individual persons or specific subpopulations (specially innocents and to vulnerable/disadvantaged subpopulations)
  - Other serious net harms to society or individual persons or specific subpopulations (especially innocents or vulnerable/disadvantaged subpopulations)
  - Serious new infringements on personal autonomy.

NRule (3) Are there any additional modifications to the rule available that could further reduce those undesirable secondary impacts substantially but would also reduce the likelihood or size of the potential net public health gains from the rule (yet still leave it clearly "appropriate for the protection of the public health")?

NRule (4) What complementary FDA or other federal government actions outside of the rule, itself, could increase the likelihood and size of the rule's potential net public health gains from the

rule and/or reduce its undesirable secondary impacts? Which options create any trade-off issues?

For FDA consideration of e-cigarette PMTA and MRTP applications:

Based on available research, evidence, analysis, and common sense:

PMTA (1) Would issuing a permissive PMTA order to allow an e-cigarette to enter or stay on the market inevitably produce a substantial net public health gain (i.e. reduce health harms and risks to the population as a whole -- with little or no risk of producing any significant net public health loss?

PMTA (2) If not, are there certain minimum standards for e-cigarettes seeking permissive PMTA orders and/or specific restrictions and requirements on the e-cigarettes and their labeling, advertising, other marketing, and sale that could be included in all permissive PMTA orders for e-cigarettes (thereby ultimately applying to all e-cigarettes) that would eliminate or at least minimize any risk that allowing the e-cigarettes to enter or stay on the market would produce a net increase in harms and risks to the population as a whole?

PMTA (3) Should any of these minimum standards or restrictions or requirements be eliminated or modified if FDA decided to follow a policy of issuing a permissive order whenever it determined that the likelihood and size of the potential net gain to the public health from allowing the e-cigarette to enter or stay on the market were much larger than the likelihood and size of producing a net public health loss?

PMTA (4) Are there additional modifications or additional specific restrictions and requirements on e-cigarettes and their labeling, advertising, other marketing, and sale that could be included in any permissive PMTA orders for e-cigarettes that would not increase the likelihood or size of any possible negative net public health impact from allowing the e-cigarettes to enter or stay on the market but would reduce the risk of:

(A) Causing new health harms/risks to innocents or specific vulnerable or disadvantaged subpopulations
(B) Causing increases to existing health disparities
(C) Causing serious new non-health harms/risks to society or to individual persons or subpopulations (especially innocents or vulnerable or disadvantaged subpopulations)
(D) Causing serious new infringements on personal autonomy.

MRTP (1) Parallel questions to PTMA (1) to (4) for MRTP permissive orders.

How might this MRTP and PMTA analysis change if FDA had already done the following or would soon:

1. Issue a strong nicotine-reduction rule?
2. Issue a rule to ban all flavors, including menthol, for all smoked tobacco products?
3. Not issue any strong anti-smoking rules but follow a strategy of reducing tobacco use harms primarily through supporting relative-risk-based market competition that would favor e-cigarettes and other less-harmful tobacco products over smoked tobacco products?

Any and All Questions and Comments Welcome

Eric Lindblom
Enl27@law.georgetown.edu
202-661-6688