SUPPLEMENTAL FILE

The "appropriate for the protection of the public health" standard

Analysis of FDA's IQOS marketing authorisation and its policy impacts

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The Tobacco Control Act's[1] legislative history states, in reference to the "appropriate for the protection of the public health (APPH) standard, that: "'Appropriate for the protection of public health' is used because tobacco products are not 'safe' or 'safe and effective,' the standards used by FDA for foods, drugs, and medical devices. The public health standard is intended to be a flexible standard that focuses on the overall goal of reducing the number of individuals who die or are harmed by tobacco products."[2] Thus, although the Tobacco Control Act does not explicitly define the "appropriate for the public health" (APPH) standard,[3] the law explicitly requires applicants to demonstrate both individual and population health impacts.

To obtain FDA authorization to market a new tobacco product, Tobacco Control Act Section 910(c)(4) provides that a new tobacco product applicant has the burden of demonstrating with sufficient scientific studies that the proposed new product would be "appropriate for the protection of the public health," taking into account "the risks and benefits to the population as a whole, including users and nonusers of the tobacco product." FDA's Guidance for Industry on Applications for Premarket Review of New Tobacco Products[4] recommends the kinds of studies that applicants should submit to demonstrate that their proposed new tobacco product is APPH.

At its essence, the APPH standard "requires the applicant to demonstrate that, on balance, allowing the sale of the new product would likely *reduce* tobacco-related harms [emphasis added]."[5]

However, as we discuss in the main text of our paper, in considering the IQOS PMTA, instead of determining whether the applicant (Philip Morris) demonstrated that the sale of its proposed new product (IQOS) would likely *reduce tobacco-related harms*, FDA turned this standard on its head and based its decision to authorize sales of IQOS on its finding that IQOS was not proven to be *more dangerous than cigarettes.* In other words, although the law squarely puts the burden on the applicant to demonstrate that its product confers public health benefits, FDA's IQOS decision established a new, weaker *de facto* standard: a new tobacco product is APPH if the FDA cannot clearly determine, based on the information submitted in the application, that the proposed product is more dangerous than cigarettes.

FDA should not have only considered the relative health effects of IQOS as compared to *cigarettes*; rather, FDA should have considered the relative health effects of IQOS as compared to *any and all other tobacco products currently on the market,* including e-cigarettes and/or other heated tobacco products, which may be less harmful than cigarettes and less harmful than IQOS. Tobacco Control Act section 910(b)(1)(A) provides that a PMTA application *"shall contain"* (i.e., *must* provide) all information concerning "the health risks of such [proposed new] tobacco product and whether such tobacco product *presents less risk than other tobacco products."* There

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is no rational basis for FDA to limit its consideration to how IQOS compared to only cigarettes because the law required Philip Morris to demonstrate that IQOS "presents less risk than *other tobacco products*."

If the law intended applicants and FDA to limit their consideration of health impacts to cigarettes only, rather than to any and all "other tobacco products," the law would have explicitly stated that. Indeed, a fundamental principle of statutory interpretation is to look at the plain meaning of the language used in the text of the statute. The statute uses the term "tobacco product," which is defined as "any product made or derived from tobacco,"[6] not "cigarette" which is more limited in scope and defined as "(A) any roll of tobacco wrapped in paper or in any substance not containing tobacco, and (B) any roll of tobacco wrapped in any substance containing tobacco which, because of its appearance, the type of tobacco used in the filler, or its packaging and labeling, is likely to be offered to, or purchased by, consumers as a cigarette described in subparagraph (A)."[7]

The Tobacco Control Act gives FDA authority to regulate "tobacco products." This general category was defined to apply to cigarettes, cigarette tobacco, roll-your-own tobacco, smokeless tobacco, *and also* "to any other tobacco products that the Secretary by regulation deems to be subject to this chapter."[8] The "Deeming Rule"[9] explicitly extended FDA's authority in 2016 to regulate all products that meet the statutory definition of "tobacco products," including e-cigarettes and heated tobacco products.

Philip Morris submitted to FDA its PMTA for IQOS in May 2017 at a time when e-cigarettes and other non-cigarette tobacco products were widely available on the market. A fundamental canon of statutory interpretation is that "general terms are to be given their general meaning and afforded their full and fair scope, without being arbitrarily limited. This canon is based on the reality that it is often useful to create categories (e.g. "dangerous weapons") without knowing or anticipating everything that may fit or come to fit within that category."[10]

Another fundamental principle of statutory construction is that FDA should not insert into the statute a term or provision that is obviously not there. Congress deliberately used the term "cigarettes" and not "tobacco products" in section 907 of the Tobacco Control Act that set product standards for cigarettes only, not for all tobacco products. Had Congress intended to limit the requirements for PMTA applications in section 910(b)(1)(A) to cigarettes, it would have explicitly used the term "cigarettes," not "tobacco products." FDA should have applied the normal rule of statutory construction that "identical words used in different parts of the same act are intended to have the same meaning."[11]

The clear intent of the Tobacco Control Act in general was to *improve* public health and the intent of the premarket authorization requirements of TCA section 910 in particular was to ensure that no new tobacco products of any type are introduced into the market that harm public health. This Congressional intent is laid out in the Findings section[12] of the TCA. TCA section 2(36) states: "It is also essential that manufacturers, prior to marketing such [tobacco] products, be required to demonstrate that such products will meet a series of rigorous criteria, and will benefit 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." This clear statement of

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Congressional intent regarding the Act's premarket authorization requirements is directed at all "tobacco products" and is not limited to "cigarettes." (In contrast, for example, Findings sections 2(18) and 2(24), explicitly describe "cigarette" advertising.) The law takes into account the dynamic nature of the tobacco products market. To protect public health, FDA must ensure that manufacturers demonstrate that any new tobacco product that they seek to bring to market "will benefit the health of the population as a whole" compared to the *status quo at the time that the new product is submitted for approval,* not just compared to cigarettes and older generations of tobacco products.

Additionally, Philip Morris and FDA did not adequately consider the health effects of using IQOS concurrently with cigarettes and/or e-cigarettes and/or other tobacco products ("dual- or poly-use").

FDA's decision on IQOS therefore deviated from the clear dictates of the law in at least four ways: (1) FDA shifted the burden away from requiring the applicant to prove something to allowing the FDA to aver the absence of something; (2) FDA minimized the required burden of proof from a showing that the proposed new product would likely *reduce* tobacco-related harms (i.e., confer a public health *benefit*) to merely a showing that the proposed new product would be no more harmful than cigarettes, the most toxic product on the market; (3) FDA only considered the health effects of IQOS as compared to cigarettes, and did not consider the health effects of IQOS as compared to other tobacco products currently on the market; and (4) FDA did not adequately consider the health impacts of dual- or poly-use.

In contrast to the FDA's apparent *static* interpretation of the APPH standard based on the state of the market when the law passed, a *dynamic* interpretation of that standard that considers the state of the market when the PMTA is submitted is more appropriate.

The first step in deciding whether a new tobacco product is APPH is determining the specific toxicity of the product. As we discuss, Philip Morris's own clinical (human) studies demonstrate that IQOS may be no less toxic than cigarettes. Moreover, while *some* of the exposure and animal studies suggest reduced toxicity, others suggest more toxicity. But, specific toxicity is only the starting point and just one element of the overall assessment of impact on public health. Additionally, FDA is required to consider whether, taking into account actual use patterns of the proposed product (including dual- and poly-use), allowing the marketing of the product would decrease cessation and/or increase initiation of *any tobacco product available on the market* (including cigarettes, cigars, smokeless, e-cigarettes, other heated tobacco products, and/or other novel tobacco products). Reduced to its essence, FDA must conclude that allowing the introduction of the proposed product to the market as it exists at the time the application is assessed will lower the overall burden of tobacco product use on the population in order to authorize the new product for sale in the US.

If FDA applies the "no-more-dangerous-than-cigarettes" standard to the thousands of new tobacco product applications likely to come before it by September 2020,[13] it would lead to an absurd result by allowing virtually any new tobacco product on the market since it is unlikely that a manufacturer would seek to market a product that is as or more dangerous than cigarettes.

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