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Center for Tobacco Products
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

RE: Docket No. FDA-2013-N-0001, Tobacco Products Scientific Advisory Committee – Referrals of Modified Risk Applications to TPSAC

The Campaign for Tobacco-Free Kids submits these comments in connection with the April 30, 2013 meeting of the Tobacco Products Scientific Advisory Committee (TPSAC) concerning the process FDA will use to refer individual modified risk tobacco product applications to TPSAC.[1]

I. STATUTORY AND REGULATORY BACKGROUND

The Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act, or TCA) amended the Food, Drug and Cosmetic Act (FD &C Act) in part by adding Sec. 911 to strictly regulate modified risk tobacco products. Under Sec. 911(a) and (b), FDA must issue a premarket order before the introduction into commerce of any product "sold or distributed for use to reduce harm or the risk of tobacco-related disease . . . ." Such modified risk products include, for example, products for which the label or advertising of the product "represents . . . that the tobacco product presents a lower risk of tobacco-related disease or is less harmful" than other tobacco products.

Under Sec. 911(g)(1), the burden is on the applicant seeking an order allowing the marketing of a modified risk tobacco product to demonstrate that the product "as it is actually used by consumers will (A) significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and (B) benefit the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products."

Sec. 911(g)(4) further requires FDA to take into account the following specific empirical factors in determining whether the (g)(1) standard has been met:

(A) The relative health risks to individuals of the tobacco product that is the subject of the application;

[1] 78 Fed. Reg. 20927 (April 8, 2013).

(B) The increased or decreased likelihood that existing users of tobacco products who would otherwise stop using such products will switch to the tobacco product that is the subject of the application;

(C) The increased or decreased likelihood that persons who do not use tobacco products will start using the tobacco product that is the subject of the application;

(D) The risks and benefits to persons from the use of the tobacco product that is the subject of the application as compared to the use of products for smoking cessation approved under chapter V to treat nicotine dependence.

Thus, FDA must consider not only the effects of the asserted modified risk product on those who use it, but also its population-wide impact on tobacco use initiation, cessation and relapse, including an assessment of the likelihood that smokers would actually switch to the modified risk product. It is not enough for an applicant to show that the modified risk product is less hazardous to users than other tobacco products; if its availability and marketing would lead to greater initiation of tobacco use or diminished cessation of tobacco use, the applicant is required to show that the benefits of risk reduction to the individual (considering the likelihood of switching to the modified risk product) outweigh the broader population-wide effects on initiation and cessation. To make the required showing, the applicant would need to offer scientific evidence not only about the physical effect of the product's use, but also about the likely responses of potential consumers (both smokers and non-smokers) to the product's marketing as a modified risk product.

The language of Sec. 911 has its origins in the tobacco industry's dark history of making "reduced risk" and other health claims about its products, despite the industry's knowledge that the claims were false and despite its express recognition that these fraudulent health-related claims were likely to increase youth initiation of smoking and to discourage smokers from quitting. For example, in response to mounting evidence that cigarettes cause a wide range of fatal diseases, in the 1970s the industry began to promote cigarettes labeled as "light" or "low-tar" as a less harmful alternative, even though the manufacturers were well aware that such cigarettes, as actually used by smokers, were no less dangerous.[2] This massive fraud had direct consequences for public health, as countless smokers concerned about their health switched to these brands instead of quitting.[3] As a United States District Court found, in concluding that the defendant tobacco companies had engaged in an illegal conspiracy to defraud the American public:

> For several decades, Defendants have marketed and promoted their low tar brands as being less harmful than conventional cigarettes. This claim is false, as these Findings of Fact demonstrate. By making these false claims, Defendants have given smokers an acceptable alternative to quitting smoking, as well as an excuse for not quitting.[4]

In enacting the Tobacco Control Act, Congress made specific findings about the need to protect

[2] *See* National Cancer Institute, *Risks Associated with Smoking Cigarettes with Low Tar Machine-Measured Yields of Tar and Nicotine,* Smoking and Tobacco Control Monograph No. 13 (November 2001), at 69.
[3] *Id.* at 197.
[4] *United States v. Philip Morris, U.S.A., Inc.,* 449 F. Supp. 1, at 430 (D.D.C. 2006), *aff'd in relevant part,* 566 F.3d 1095 (D.C. Cir. 2009), *cert. denied,* 130 S.Ct. 3501 (2010).

the public from the harmful consequences of unsupported manufacturer claims of reduced harm. The congressional findings made specific reference to the "light" and "low-tar" fraud, noting the National Cancer Institute's finding that "mistaken beliefs about the health consequences of smoking 'low tar' and 'light' cigarettes can reduce the motivation to quit smoking entirely and thereby lead to disease and death."[5] Congress further found that "[t]hose who use products sold or distributed as modified risk products that do not in fact reduce risk, rather than quitting or reducing their use of tobacco products, have a substantially increased likelihood of suffering disability and premature death."[6] Congress thus found it "essential that manufacturers, prior to marketing such 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."[7] These Congressional findings gave rise to the rigorous standards for scientific proof in Sec. 911.

The statutory role of TPSAC in FDA's assessment of whether an applicant has met its burden under Sec. 911 demonstrates the decisive importance of science in that assessment. Unlike applications for drug approval, where the convening of an advisory committee is discretionary with FDA, the involvement of TPSAC in evaluating modified risk products is mandatory under the TCA. Sec. 911(f)(1) provides that FDA "shall refer" to TPSAC "any application" for a modified risk order. Sec. 911 (f)(2) in turn requires TPSAC to report "its recommendation on the application" to FDA within 60 days of the referral. Thus, no modified risk application can be approved, or disapproved, without FDA having received a recommendation from TPSAC, although the final decision on approval or disapproval rests with FDA. The central role of TPSAC in the scientific evaluation of modified risk applications underscores the importance of determining a process for referral that ensures TPSAC review that is both efficient and thorough.

II. THE NEED FOR CAREFUL FDA EVALUATION AND GUIDANCE PRIOR TO REFERRAL TO TPSAC

As noted above, Sec. 911 both requires every modified risk product application to be referred to TPSAC and requires TPSAC to report its "recommendations on the application" within 60 days of the referral. Because Sec. 911 contemplates a TPSAC recommendation on whether the application should be granted, the statute implies that TPSAC should consider the full range of scientific issues presented by the application, including evidence of the physical effects of the modified risk product on users and the population-wide impact on smoking initiation, smoking cessation and relapse.

In order that TPSAC's deliberations on each application be as thorough and efficient as possible, it is essential that FDA, prior to referral of the application to TPSAC, have done sufficient preliminary consideration of the application to give TPSAC substantial guidance as part of its referral. Thus, prior to referral, FDA should be in a position to frame the key scientific issues for TPSAC, highlighting those empirical questions on which TPSAC's investigation would be most critical to the ultimate disposition of the application. This is not to suggest that TPSAC's review should be limited to the specific issues highlighted by FDA; TPSAC has the authority under the statute to consider any scientific issue it determines to be material to the application. However, TPSAC will be able to function most effectively during the 60-day review period if it begins its consideration of the application with the benefit of a

[5] Tobacco Control Act, Pub.L. No. 111-31, §2(38).
[6] TCA, §2(37)
[7] TCA, §2(36).

careful preliminary analysis by FDA setting out FDA's view of the key scientific issues on which TPSAC's informed opinion would be most helpful.

Before FDA refers an application to TPSAC, it should require the applicant to provide all of the scientific and factual information necessary for FDA and for TPSAC to make a fully informed decision on every issue to be considered under Sec. 911. No referral should be made until FDA has made at least a preliminary review that it has been provided sufficient information to satisfy the statutory requirements. As part of its referral guidance to TPSAC, FDA should ensure that it has provided TPSAC all factual information and scientific data TPSAC will need for its deliberations. FDA's framing of the issues for TPSAC should also consistently reiterate that, under the statute, the issue is whether the applicant has met its burden on each of the scientific issues material to disposition of the application.

The importance of such a preliminary review by FDA suggests that, after FDA has accepted an application for a modified risk order, it allow a substantial amount of time prior to referral to TPSAC for its preliminary review and framing of the issues to occur. A referral to TPSAC shortly after the acceptance of the application would not lend itself to TPSAC's thorough and efficient evaluation of the scientific issues posed by claims of modified risk within the statutorily-mandated 60-day window.

If TPSAC concludes that it has not been provided sufficient information to complete a thorough review of the issues raised by the application within the 60-day period, TPSAC should be able within the 60 day period to return the application to FDA with instructions to obtain additional information, or request that FDA withdraw the referral until it can obtain the additional information. FDA could then make a new referral, with the additional information, which would trigger the running of a new 60-day period for TPSAC review. Alternatively, if TPSAC determines that it is lacking sufficient information to carry out its statutory duty, it should be entitled to report a recommendation (within the 60 day period) that the applicant has not met its burden and the application should be denied based on the information available to TPSAC.

III. THE IMPORTANCE OF PUBLIC PARTICIPATION THROUGHOUT THE FDA REVIEW OF MODIFIED RISK APPLICATIONS

The importance of public participation in the FDA modified risk review process is apparent from the text of Sec. 911. Section 911(e) requires FDA to make all modified risk applications available to the public (with exceptions for trade secrets and other confidential business information). It also requires FDA to "request comments by interested persons on the information contained in the application and on the label, labeling, and advertising accompanying such application." This is in contrast to applications for drug approval to FDA, which are not released to the public. The express provision of public notice and comment on specific applications recognizes that because Sec. 911 has its origins in the historic "reduced risk" fraud perpetrated on the public by the tobacco industry, the participation of the public in FDA's consideration of such industry claims in the future is especially justified.

FDA should make it clear that, once a modified risk product application is accepted, it will be made *immediately available* to the public. It should also provide for an opportunity for public comment on the application *well before* referral of the application to TPSAC. During the period of FDA's preliminary consideration of the application, during which FDA should identify the key scientific issues for TPSAC as recommended above, opportunity for public comment is essential. Public comment will be helpful to FDA as it does its initial analysis of the application and frames the issues for TPSAC; it will also

be valuable for TPSAC to have access to input from the public as it begins its review of the issues immediately following referral of the application from FDA.

FDA should also set out its interpretation of the statutory exceptions from disclosure for "trade secrets or otherwise confidential, commercial information" in a modified risk application. It should make it clear that public participation at the pre-referral stage also includes the right to challenge the designation of specific material as trade secrets or confidential business information. This right is especially important, given the tobacco industry's history of misusing such designations to hide evidence of its fraudulent conduct from courts and the public.

Of course, allowing public comment prior to referral to TPSAC must not adversely affect the right of the public to participate in the TPSAC proceedings themselves. That right is guaranteed by Sec. 10 of the Federal Advisory Committee Act, which provides that each advisory committee meeting be open to the public.[8] Sec. 10 also provides that "interested persons shall be permitted to attend, appear before, or file statements with an advisory committee, subject to such reasonable rules or regulations as the Administrator may provide."[9] FDA's regulations governing advisory committees implement the statutory right of public participation, by providing that "[e]very committee meeting includes an open portion, which constitutes a public hearing during which interested persons may present relevant information or views orally or in writing."[10] FDA should make it clear that interested persons have the right to present their views, both orally and in writing, in connection with TPSAC meetings on applications for modified risk products.[11]

IV. AS PART OF ITS GUIDANCE TO TPSAC, FDA SHOULD GENERALLY ADOPT THE INSTITUTE OF MEDICINE RECOMMENDATIONS FOR STANDARDS GOVERNING STUDIES ON MODIFIED RISK PRODUCTS

Section 911(l) requires that FDA develop regulations or guidance on the "scientific evidence required for assessment and ongoing review of modified risk tobacco products," and further requires that such regulations or guidance be developed "in consultation with the Institute of Medicine," along with the input of other appropriate scientific and medical experts, "on the design and conduct of such studies and surveillance." Pursuant to this provision, the Institute of Medicine (IOM) has issued a report, *Scientific Standards for Studies on Modified Risk Tobacco Products* (IOM report) setting forth twelve specific recommendations "designed to articulate the minimum standards for producing credible and reliable evidence to demonstrate that the marketing of [a modified risk tobacco product] is consistent with the protection of public health."[12] Following the issuance of the IOM report, FDA issued a Draft Guidance for Industry on modified risk applications.

The IOM report is a thorough and thoughtful discussion of the elements relevant to consideration of Sec. 911 applications. Whereas the FDA Draft Guidance addresses only the evidence to

[8] 5 U.S.C. App. §10(a)(1).
[9] 5 U.S.C. App. §10(a)(2).
[10] 21 C.F.R. §14.25.
[11] There is some question as to whether FDA's own regulations governing its advisory committees apply to TPSAC. The Tobacco Control Act 's amendments to the Food, Drug and Cosmetic Act are not referenced in the FDA regulations as among the FD&C Act provisions regarding advisory committees to which the regulations apply. *See* 21 C.F.R. §14.1(a). FDA should consider amending its advisory committee regulations to make clear their applicability to TPSAC.
[12] Institute of Medicine, *Scientific Standards for Studies on Modified Risk Tobacco Products* (2012), at 11.

be submitted by an applicant, the IOM report also addresses the criteria to be applied by FDA in evaluating such evidence. The IOM report therefore deals in considerably more detail with most of the statutory criteria. We suggest that FDA generally adopt the recommendations in the IOM report[13] and incorporate them, and the report itself, by reference, in its referrals of modified risk applications to TPSAC.

Respectfully submitted,

CAMPAIGN FOR TOBACCO-FREE KIDS

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[13] The only exception is IOM recommendation #10, which the Campaign for Tobacco-Free Kids opposes to the extent that it is intended to provide pre-approval to an independent third party entity to conduct research related to a specific Sec. 911 application. As we have stated elsewhere, "[t]he history and a large body of evidence supports the view that the tobacco industry will always find a way to undermine credible science and corrupt entities – even those entities whose integrity and mission seem incorruptible." Statement of Matthew L. Myers before the FDA Third Party Governance of Industry-Sponsored Tobacco Product Workshop, March 19, 2013. FDA should, however, adopt the other IOC recommendations, which are designed to establish rigorous scientific standards that all Sec. 911 applications should meet.