August 1, 2013

Caryn Cohen
Office of Science
Center for Tobacco Products
U.S Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

RE: Docket No. FDA-2013-N-0001-0056

Ms. Cohen:

The undersigned organizations submit the following comments to the above-referenced docket for consideration by the Tobacco Products Scientific Advisory Committee (TPSAC) as it considers possible approaches for evaluating information on the risk and potential benefits of a proposed modified risk tobacco product to the population as a whole, including at its public meeting on the topic on August 16, 2013.

Section 911 of the Food, Drug and Cosmetic Act, as added by the Family Smoking Prevention and Control Act of 2009 (Public Law 111-31) ("Tobacco Control Act"), requires submission of a Modified Risk Tobacco Product Application (MRTPA) before any product can be marketed as reducing harm, reducing exposure to a harmful constituent or reducing the risk of tobacco related disease. Section 911(g)(1) places the burden on the applicant to demonstrate that the product, as marketed and as actually used by consumers, will benefit the population as whole, taking into account not only the impact on the individual user but the impact on non-tobacco users (never and former) as well, including initiation, relapse, dual use, increased use, etc. The FDA has issued guidance for manufacturers on MRTPAs, on which the undersigned have submitted comments,[1] and the Institute of Medicine has issued a report advising FDA on its recommended approach.[2]

[1] As indicated in our comments, previously filed, FDA should adopt legally binding regulations consistent with its guidance document. See Comments of Campaign for Tobacco-Free Kids, et al. on Guidance for Industry on Modified Risk Tobacco Product Applications under Section 911, Docket FDA-2012-D-0071 (June 4, 2012).

The Tobacco Products Scientific Advisory Committee is seeking input on approaches for evaluating information on the impact of a modified risk tobacco product on the population as a whole. While the undersigned have identified key issues in the previously submitted comments referenced above (and we incorporate those comments into these comments), we believe there are a number of points that deserve special consideration as TPSAC addresses this critical issue.

In determining whether an MRTP offers benefit to the population as a whole, it must first be established that the product as marketed actually significantly reduces harm to the individual user. While this may seem obvious, there are some key considerations that must be taken into account, including:

- Whether the product significantly reduces harm to the user when used "as directed" and/or as intended.
- Whether the product increases the risk of some diseases even if it reduces the risk of others. This aspect requires solid scientific evidence related to the multiple risks posed.
- How the consumer actually uses the product. Any impact of the MRTP must be assessed based on how consumers actually use the product. For example, if the product causes the user to consume it more intensely, more frequently, or in some other fashion that affects exposure and impact of that exposure, a product that may appear to reduce harm may not in fact do so and could cause even more harm to the individual. Use by machines or in clinical or experimental settings does not meet the standard as we have learned from "Light" and "Low Tar" cigarettes.
- The abuse liability of the product. Can and will it be modified for use in ways that may cause more harm or lead to greater addiction or increased levels of use?
  Will the design change or the marketing claim(s) lead the individual tobacco user to alter the amount smoked or frequency of smoking or duration of tobacco use?

To evaluate these issues, evidence about more than the product's contents and design will be essential. Studies evaluating whether permitting the product to be marketed as a modified risk product will alter how a person smokes; how often a person smokes; a person's intention to quit and the likelihood of quitting are also essential.

The magnitude of the impact on the individual user must also be established in order to weigh it against any changes in use by the population as a whole – users and non-users.

Establishing the impact on the individual is of course one step in meeting the broader public health standard required by the Family Smoking Prevention and Tobacco Control Act – benefitting the population as a whole. Evaluating the impact on the population as a whole entails examination of a number of key issues and requires a variety of consumer testing approaches.

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[2] As indicated in our comments previously filed with TPSAC, FDA should adopt the IOM findings and recommendations contained in its report, "Scientific Standards for Studies on Modified Risk Products", with the exception of IOM recommendation #10 to the extent that it is intended to provide pre-approval to an independent third party entity to conduct research related to a specific MRTPA. See Comments of Campaign for Tobacco-Free Kids on Referrals of Modified Risk Applications to TPSAC, Docket FDA-2013-N-0001 (April 23, 2013).

The legislation sets a high bar precisely due to the history of the tobacco industry using claims of reduced harm to deter quitting and decrease the anxiety of smokers, potential smokers and former smokers about the health risks of smoking. Arguments that these high standards are somehow depriving consumers of less hazardous products are completely false. The ability to make a claim about a product is a totally separate decision from whether a product may be on the market. Section 910 governs what new products may enter the market. Section 911 governs when harm reduction claims may be made. Maintaining the intentionally rigorous standard in Section 911 does not deprive any consumer of access to the product, it just protects them and the public as a whole from claims that may reduce the number of people who quit or increase the number of people who start.

Evaluating the population impact requires rigorous pre-market testing AND post-market surveillance

The FDA's guidance document on MRTP applications and the IOM report make clear the importance of both pre-market testing and post-market surveillance. Still, this point cannot be emphasized strongly enough. While some may argue that the population impact can be gauged adequately with post-market surveillance, such surveillance is a complement to, not a substitute for, pre-market consumer research to ensure that modified risk products will benefit the population as a whole. Rigorous pre-market research is necessary to minimize the chance that the introduction of an MRTP will harm rather than benefit public health. Given the history of the disastrous impact of prior reduced harm claims, such as those for light and low tar cigarettes, on public health, it is absolutely essential that FDA know as much as possible about how consumers will react to these products, how they are marketed and claims permitted before an order is issued permitting an MRTP claim. FDA cannot and should not permit such claims in the absence of evidence regarding likely consumer response.

Pre-Market Testing Must Include the Product, Its Labeling, and Its Marketing

Those wishing to make a modified risk claim must show not only the impact of the product but also the impact of its labeling, packaging, and marketing on consumers. Thus, FDA should require submission of all advertising and promotional material relating to the product, both in advance of use and after the grant of a modified risk order. Because it is not only the availability of the product but the way it is marketed, packaged and labeled that will influence consumer behavior, all of these considerations must be the subject of consumer testing in advance with results submitted to the FDA.

The consumer testing must be conducted among smokers and non-smokers, including former smokers and those who have never smoked. Again, the public health debacle of light and low tar cigarettes is illustrative of how marketing convinced smokers that these products were less harmful and that they need not quit. Given the marketing resources and prowess of the tobacco companies, this is absolutely critical. Tobacco companies have spent as much as $15 billion per year marketing their products.[1] Because of the potential impact a claim of reduced harm can have on consumers, we must understand how consumers will react to it. Consumer testing must therefore involve repeated exposure to the proposed MRTP and its marketing to understand how consumers will perceive and process this information, react to it and alter their behavior in the real world.

Pre-Market Testing and Post Market Surveillance Must Include a Variety of Audiences

It is obvious that the public health standard requires evaluating the impact of an MRTP not only on tobacco users of different types but also on non-users – both former and never users – to determine if any gains to the individual user are offset by increases in use by users and non-users. Sub-audiences among these should also be addressed to ensure that the full impact of an MRTP and its marketing are understood. Key audiences include:

Tobacco Users: As noted throughout these and other comments, even the impact on the individual user involves consideration not only of the nature of the product for which a modified risk claim is proposed but also on how the user reacts to the product and its marketing. As noted above, testing must include actual use by consumers to understand how they use the product. It must also include an assessment of whether users might use more of the product, use it more frequently, switch to it completely, or use it in conjunction with other products (dual/poly use), etc. Such testing must also address the degree to which users who might otherwise have quit tobacco entirely use the MRTP instead of quitting. Because quitting smoking is so difficult, smokers may look for any justification for not doing so. Subgroups of concern include light and heavy smokers, groups based on intent to quit, degree of nicotine dependence, and those with disproportionately high tobacco use rates, such as those of lower income and education levels.

Never Users: It is critical to establish the degree to which those who would have never used tobacco products would be enticed to use them by a modified risk claim. Perception of risk, while not the sole factor, is related to use among young people.[2] Thus, changes in those perceptions could impact initiation and make users of those who otherwise would be tobacco-free. Even adult never-users could be impacted by the marketing of MRTPs. In addition to understanding how consumers might initiate with the new product, it will also be important to ascertain whether this experience leads them to use other products as well. New users could initiate with the less harmful product which might also serve as a gateway to more harmful ones. Youth and other users who are especially susceptible to tobacco use, often defined as "open to smoking" or tobacco use will be a key audience for this research. However, such research should not be limited to those "open" to smoking in general, as a modified risk claim could impact those not previously open.

Former Users: The availability and marketing of MRTPs may convince those who have successfully quit smoking or other tobacco use that they can resume use with little or no harm, thus leading to relapse. Again, even if the MRTP were minimally harmful, MRTP claims could draw former users back into nicotine addiction and lead them back to the products they were using before they quit. Former tobacco users are a large and very important audience. The health benefits of quitting smoking are well documented and many occur relatively quickly. To the degree that MRTPs and their marketing lead to relapse among smokers, any benefit of the new product could be largely offset in the broader population.

Consumer Testing (Pre and Post-Market) Must Go Well Beyond Risk Perception

Understanding how consumers react to an MRTP and its claims must include testing the understanding of any claims on the label, in advertising, etc., but it must also go well beyond that to understand how consumers act on those perceptions.

Even the testing of whether consumers understand any modified risk claim will be complicated and must be addressed in the context of their perceptions regarding the total health impact of the product and its claims. For example, if a product claims to reduce the risk of a specific disease (e.g., cancer) by a certain amount, consumers not only have to be able to translate that reduction to a real risk; they need to understand that any reduction in the risk for a single disease does not mean that same reduction in terms of overall risk. Consumers are much more aware of the impact of smoking on some diseases, especially cancer, than others.[3] To the degree that they think this is the primary risk, they may interpret a reduction in that disease as tantamount to total risk reduction. Given the large number of diseases caused by tobacco use, this concern is especially serious.

Even if consumers can understand a claim about modified risk and how it affects their chances of being harmed, many do not make decisions solely or even at all based on risk. Thus, while understanding how consumers understand risk, it is not sufficient to establish how they will react to an MRTP and its claims. Therefore, it is critically important to understand consumer intent that may be based on risk perceptions and any number of other factors influenced by the MRTP and its marketing. Many consumers who may understand risk do not apply it to themselves. Many smokers, particularly young ones, also overestimate their ability to quit and thus may believe the risks do not apply to them.[4] Tobacco company marketing has also been successful in fostering the impression that use of the product conveys benefits, real or imagined, that can outweigh any risk perceptions. The marketing of an MRTP could accentuate such misimpressions.

FDA Must Require Submission of All Research on the Proposed Product

While tobacco companies can obviously submit the data and analyses that they believe will meet the requirements set by FDA for a proposed MRTP, FDA should require the company to provide any and all research that it has conducted on the product. This includes basic science on the impact of the product as well as any consumer research the company has conducted on this specific MRTP or others that may inform the application to understand its appeal or other effects on consumers of all types. Typically, exhaustive market research studies will have been done before a company decides to market a product and close examination of such studies will be highly relevant in FDA's consideration of any MRTP application.

A Variety of Methods Must Be Used to Fully Understand Consumer Reaction and Population Impact

The issues outlined above will require the use of a variety of research methodologies with the spectrum of audiences pre- and post-market in order to enable FDA to fully understand both the individual and the population impact of the introduction of an MRTP. These include qualitative techniques, such as focus groups or one-on-one interviews, observational studies, product tests, large scale surveys, store simulations, virtual stores, and others. The FDA and the sponsor of an MRTP application must collaborate to identify the key questions to be answered based on the MRTP and proposed claims, the

studies required to answer these questions, and an analytic framework to assess the information that is produced. In the end, a synthesis of data from the individual impact studies, consumer testing, and other studies will be required to determine the population impact and the degree to which any benefits established for the individual are or are not offset by impacts on the population as a whole.

Issues Surrounding Research on Young People

While it is critical, as outlined above, to understand the impact of MRTPS and their marketing on fostering use (initiation or continued) among young people, steps must be taken to ensure that tobacco companies do not use the need for this research as a way to enhance their understanding of how to market their products to youth. The companies can use third parties to conduct this research, but there must also be a firewall and assurances that this research will not be shared with those responsible for marketing the product. While we support the use of third parties to conduct such research, we have taken the position in other submissions that these third parties not be pre-approved by FDA but that their research and its standards should be judged independently for any particular application.[5] Any third parties and the sponsoring companies should be required to submit assurances that none of the research will be used to market tobacco products to under-age youth and outline the steps taken to prevent that from happening.

Conclusion

The undersigned organizations appreciate the opportunity to provide input as TPSAC examines possible approaches for evaluating information on the risk and potential benefits of a proposed modified risk tobacco product to the population as a whole. Given the inherent danger posed by tobacco products and the experience with modified risk claims in the past (particularly with "Light" and "Low-Tar" cigarettes), determining whether an MRTP offers benefit to the population as a whole must be preceded by thorough and sound research. Indeed, the public health standard established in the Tobacco Control Act is a high standard for good reason. While the standard for research will be high, there are already commonly accepted research protocols for other products under FDA authority that can be built upon when formulating a set of standards to address the unique issues related to MRTP research. We look forward to providing additional comment when TPSAC addresses this issue at its public meeting on the topic on August 16, 2013.

Sincerely,

American Association for Cancer Research
American Cancer Society Cancer Action Network
American Heart Association
American Lung Association
American Public Health Association
Campaign for Tobacco-Free Kids
Tobacco Control Legal Consortium

[1] Federal Trade Commission (FTC). *Cigarette Report for 2011,* 2013, http://www.ftc.gov/os/2013/05/130521cigarettereport.pdf. See also, FTC, *Smokeless Tobacco Report for 2011,* 2013, http://www.ftc.gov/os/2013/05/130521smokelesstobaccoreport.pdf. Data for top 5 manufacturers only.]

[2] Jamieson, P., and D. Romer What do young people think they know about the risks of smoking. *In* Smoking: risk, perception & policy, edited by P. Slovic, Thousand Oaks, CA: Sage Publications, 2001; Romer, D., and P. Jamieson, " Do adolescents appreciate the risks of smoking? Evidence from a national survey," *Journal of Adolescent Health*, 29(1): 12-21, 2001.

[3] Weinstein, ND, et al., "Public Understanding of the Illnesses Caused by Cigarette Smoking," *Nicotine and Tobacco Research*, April 2004; Ayanian JZ, et al., "Perceived Risks of Heart Disease and Cancer Among Cigarette Smokers," *Journal of the American Medical Association*, March 17, 281(11):1019-21, 1999.

[4] Johnston, LD, et al., *National survey results on drug use from the Monitoring the Future study, 1975-1997, Volume I: Secondary school students*, National Institute on Drug Abuse, Rockville, MD, NIH Publication No. 98-4345, 1998; Slovic, P. (Ed.), Smoking: Risk, Perception and Public Policy, Thousand Oaks, CA, 2001.

[5] Statement of Matthew L. Myers, President of the Campaign for Tobacco-Free Kids, Before the FDA Third Party Governance of Industry Sponsored Research Tobacco product Workshop, March 19, 2013.