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March 22, 2017

Caryn Cohen
Office of Science
Center for Tobacco Products
U.S. Food and Drug Administration
c/o Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: Tobacco Products Scientific Advisory Meeting Committee; Notice of Meeting (Docket No. FDA-2017-N-0001)

Dear Ms. Cohen:

On February 21, 2017, the United States Food and Drug Administration ("FDA") announced an upcoming meeting of the Tobacco Products Scientific Advisory Committee ("TPSAC") on April 6, 2017. *See* 82 Fed. Reg. 11226 (Feb. 21, 2017). The purpose of this meeting is to discuss FDA's premarket review of tobacco products. At the April 6 TPSAC meeting, "FDA will present information to the Committee on the processes used in review of tobacco product applications, including premarket tobacco, substantial equivalence, and modified risk tobacco product applications." *Id.* Topics to be discussed include the "statutory standards applicable to different types of applications" and "the scientific basis for review decisions." *Id.*

FDA invited interested persons from the public to comment, either orally or in writing, on these topics. *Id.* at 11227. As such, RAI Services Company ("RAIS"),[1] on its

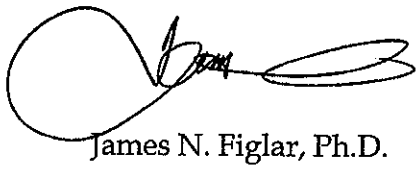
[1] RAIS bears primary responsibility for coordinating regulatory compliance for Reynolds American Inc.'s FDA-regulated tobacco operating companies, namely R.J. Reynolds Tobacco Company, American Snuff Company, LLC, Santa Fe Natural Tobacco Company, Inc. R.J. Reynolds Vapor Company and Kentucky Bioprocessing, Inc. References to RAIS in this letter refer to itself and its affiliated companies where applicable.

own behalf and on behalf of its affiliated companies, respectfully submits these comments.

RAIS looks forward to continuing to work with FDA to help implement the relevant statutory requirements, consistent with Congress's stated desire to permit the continued sale of tobacco products to adults, while ensuring that consumers are properly informed and that FDA has authority to address issues of particular concern to public health. RAIS thus welcomes this opportunity to submit these comments. RAIS is hopeful that FDA will work collaboratively with manufacturers in order to ensure a meaningful premarket review of new tobacco products, ensure that FDA is in a position to employ its limited resources efficiently and effectively, and further public health goals without unduly burdening manufacturers or consumers of tobacco products.

If you have any further questions or require additional information, please contact me at your earliest convenience.

Respectfully submitted,



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BACKGROUND

On June 22, 2009, the President signed the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act") (Public Law 111-31) into law. The Tobacco Control Act granted FDA the authority to regulate the manufacture, marketing, and distribution of cigarettes, cigarette tobacco, roll-your-own ("RYO") tobacco, and smokeless tobacco products to protect the public health and to reduce tobacco use by minors. The Tobacco Control Act also gave FDA the authority to issue a regulation deeming all other products that meet the statutory definition of a tobacco product to be subject to Chapter IX of the Federal Food, Drug, and Cosmetic Act ("FDCA"). On May 10, 2016, FDA issued that rule, extending FDA's tobacco product authority to all products that meet the statutory definition of "tobacco product." (81 Fed. Reg. 28,973).

Under section 910(a) of the FDCA, any product meeting the definition of a "new tobacco product" must undergo premarket review before manufacturers can legally introduce it for sale in interstate commerce. However, products already on the market as of February 15, 2007 are "grandfathered," and therefore exempt from the requirement for premarket review because they are not considered "new tobacco products." The Tobacco Control Act provides three (3) regulatory pathways by which manufacturers may obtain authorization to market new tobacco products:

1. by seeking an exemption for products that have had only minor modifications made to tobacco additives, *see* 21 U.S.C. § 387e(j)(3); or
2. by filing a report indicating, and obtaining an order from FDA confirming, that the new product is "substantially equivalent" to an existing tobacco product that is already marketed and sold to consumers, *see* 21 U.S.C. § 387j(a)(2)(A); or
3. by filing an extensive premarket tobacco application, with detailed evidentiary support, *see id.* § 387j(c)(2)(A); *id.* § 387j(b)(1)(A)-(C).

Congress intended the premarket review pathways to differ in the level of regulatory oversight and designed the statute to allow new products to enter the market in a timely manner. Only when a product has significantly different characteristics from an existing product and presents public health risks different from those presented by existing products, does the FDCA Act require that manufacturers submit a PMTA—a more extensive, data driven application—pursuant to section 910. Indeed, as Congress sought to "ensure that consumers are better informed," but also "to continue to permit the sale of tobacco products to adults," it intended to allow most tobacco products already on the market at the time the Tobacco Control Act was enacted to remain on the market. FSPTCA § 3. Accordingly, it developed a scheme that would allow already marketed products and products that are substantially similar (i.e., substantially equivalent) to remain on the market or proceed to market through a fairly simple premarket review process.

A new tobacco product is "substantially equivalent" to the predicate tobacco product if it:

1. has the ***same characteristics*** as the predicate tobacco product; or,
2. has ***different characteristics*** and the information submitted [in the SE report] contains information, including clinical data if deemed necessary by the Secretary, that demonstrates that it is not appropriate to regulate the product under [a PMTA] because the product does not raise different questions of public health.

21 U.S.C. § 387j(a)(3)(A)(i)-(ii)(emphasis added). This statutory scheme, established under sections 905 and 910 of the FD&C Act, mirrors that of the Medical Device regime established under the Medical Device Amendments of 1976.

On March 4, 2015, FDA issued a Final Guidance entitled, Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions ("SE FAQ Guidance"). The SE FAQ Guidance explained FDA's position that certain labeling changes that render a product distinct and changes in a product's quantity or portion size within a package, but which did not affect the underlying product, would render a product a new tobacco product subject to premarket review. In the SE FAQ Guidance, FDA established streamlined SE reports for these changes: a Same Characteristics SE Report for labeling changes, and a Product Quantity Change SE Report for quantity and portion size changes. A number of tobacco manufacturers, including RAIS's operating companies, challenged FDA's interpretation of the FDCA, as elaborated in the SE FAQ Guidance.

On September 8, 2015, FDA subsequently adopted an Interim Enforcement Policy with regard to the guidance and then issued a revised guidance, Guidance for Industry: Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions (Edition 2). Tobacco companies challenged the new guidance. In ruling on the case, the U.S. District Court of the District of Columbia invalidated part of the revised guidance concluding that "under the TCA, a modification to an existing product's label does not result in a 'new tobacco product' and therefore such a label change does not give rise to the Act's substantial equivalence review process." *Philip Morris USA Inc. v. FDA*, __ F.Supp.3d__ 2016 WL 4378970 (D.D.C.). In reaching this decision, the court took issue with FDA's narrow interpretation by defining "same characteristics" as identical characteristics, calling the conclusion illogical. *Id.* at 24. The court illustrated FDA's illogical interpretation by simply noting that the assumption cannot "be squared away with" other provisions of the Act, namely the SE exemption request provision. *Id.* at 33. The Court clearly pointed out that certain minor changes to a product should not require a SE report, but instead could fit squarely within the SE Exemption Pathway. Indeed, the Court found that "it is not reasonable to think that Congress intended to channel all non-exempt physical modifications through the 'different characteristic' prong. If it had wanted such a result, it would have said so expressly and not allow for SE exemptions.

However, it created a less burdensome 'same characteristic' prong that seemingly was intended for physical changes that were more than 'minor,' but yet not so significant so to require a showing, through clinical data if demanded, that 'the product does not raise different questions of public health.'" *Id.* at 34.

Indeed, it is in accordance with the U.S. District Court of the District of Columbia's *Philip Morris USA, Inc. v. FDA* opinion that FDA is compelled to revise its current views regarding the premarket review pathways, specifically (as discussed in more detail below), the SE exemption and SE pathways, as its current interpretation of these pathways fails to make the pathways meaningful and viable, and is contrary to Congress's expressed intent.

FDA'S CURRENT INTERPRETATION OF THE SE EXEMPTION AND SE PREMARKET REIVEW PATHWAYS FAILS CONGRESS'S INTENT AND IS NOT MEANINGFUL OR VIABLE

The Tobacco Control Act provides that FDA "shall issue regulations to implement" the exemption provision. Thus, the plain language of the statute obligates the FDA to promulgate regulations that implement the statutory requirements. While FDA issued a SE exemption regulation on July 5, 2011, FDA has not issued any guidance documents on the scope or manner of compliance with this pathway. Rather, FDA issued a regulation governing this pathway that simply parrots the language contained in the Tobacco Control Act without providing any granularity as to the type of changes that fall within this pathway or the type of evidence necessary to secure a clearance. 76 Fed. Reg. 38,961, 38,975 (July 2011)(describing 21 C.F.R. § 1107.1). The regulation did not define "minor," indicate when a substantial equivalence report is necessary, or provide factors that the agency might consider in determining whether an exemption is "appropriate." *Id.* at 38,962-64.

The lack of substantive guidance in the regulations makes the SE Exemption pathway onerous, burdensome, and uncertain. Indeed, the lack of substance in the current SE exemption regulation effectively nullifies the exemption pathway. To underscore this point, FDA has only cleared one SE exemption request in the nearly six years since the SE exemption regulation issued while refusing to accept 55 applications. By failing to elaborate on the statutory exemption provision, it remains uncertain as to the amount of evidence required to prove that a modification is "minor," that a substantial equivalence report is unnecessary, and that an exemption is otherwise "appropriate." Thus, manufacturers are burdened by having to provide a variety of information. While the preamble to the final regulations does provide that a manufacturer does not need to conduct studies to support a SE Exemption application and that a manufacturer can rely on literature reviews, previous studies, or other information to support a SE Exemption, the rule does not provide a standard or factors in which FDA will review the information. 76 Fed. Reg. at 38,965. Further, while FDA notes that it does "not expect that an exemption request will be as lengthy or detailed" as a SE report, FDA fails to specify what length or detail the report needs to be.

The confusion caused by the SE exemption regulation leads to a blending of the SE Pathway and the SE Exemption as manufacturers still need to submit a substantial amount of information in support of either pathway. The burdensome amount of information necessary to submit a SE Exemption application prevents the SE Exemption from providing a simpler, faster, and less burdensome alternative to the SE report, as Congress intended.

Further, FDA's current interpretation of the SE pathway has also proven to be impractical and unworkable. Inaction, delay, and uncertainty caused by FDA's current approach has effectively paralyzed the industry and left it without the clear guidance necessary to enable swift development and clearance of SE reports as Congress intended, particularly those products with the "same characteristics" as the predicate products.

The industry does not have sufficient guidance or regulation to define which minor modifications to a tobacco product are sufficiently large to warrant SE pathway review but do not warrant the Agency to determine whether different questions of public health exist. Indeed, while the Tobacco Control Act - like the Medical Device regime - clearly established two ways in which a new tobacco product can be considered "substantially equivalent," over the past five years, FDA has consistently interpreted the SE pathway as narrowly finding that the "same characteristics" prong of the SE pathway means identical characteristics. Thus, unless every characteristic of the new product is identical to the predicate product, the "same characteristics" prong cannot be used. Thus, FDA's view automatically requires a manufacturer to demonstrate that the new product does not raise different questions of public health from its predicate for every SE report. Under FDA's flawed interpretation, the first prong would be superfluous. That cannot be correct.

Further, to demonstrate the absurdity of the FDA's view of the SE pathway, FDA analyzes each characteristic, component, etc. of the product rather than the product as whole when determining whether the new tobacco product raises different questions of public health as the statute mandates. *See, e.g.*, 21 U.S.C. 387j(a)(3)(A) ("has different characteristics....but ***the product*** does not raise different questions of public health.") (emphasis added). FDA has placed undue and unreasonable importance on every individual change to a specific ingredient, material, or characteristic, no matter how minor or unrelated to public health, and without offering any explanation why these individual differences in characteristics could even possibly implicate different questions of public health. Moreover, it is only those changes in the new product that lead to an increase in an ingredient, material or constituent that drives FDA's review. Yet, in almost all circumstances, the new product also has decreases in the amounts of ingredients, materials and constituents as compared to the predicate but the agency places no importance in such reductions individually or in totality. FDA's refusal to consider the product as a whole, apart from being inconsistent with Congress's stated intent; overcomplicates what should be a rather streamlined process.

FDA MUST ISSUE REGULATIONS REGARDING THE SE PATHWAY THAT CLEARLY DELINEATE WHAT TYPE OF MODIFICATIONS FALL WITHIN THE PURVIEW OF EACH PRONG OF THE SE PATHWAY.

FDA must adopt regulations consistent with the court's decision in *Philip Morris USA, Inc. v. FDA* for the SE exemption pathway and SE pathway, and importantly, FDA must reject the notion that same means identical. Rather, the level of change reviewed under the "same characteristics" prong must exceed the level of change reviewed under the SE Exemption pathway so as to give meaning to Congressional intent. *See Philip Morris USA Inc. v. FDA*, __ F.Supp.3d__ 2016 WL 4378970 at *24 (D.D.C.) ("[t]his exemption for 'minor modifications' cannot be squared with...'same' characteristics as meaning 'identical' characteristics. Congress plainly meant to exclude from a substantial equivalence showing some new products that, although possessing different physical characteristics than their predicate product, did not raise sufficient health risks to warrant an FDA review.")

The SE exemption pathway must allow manufacturers to request an exemption under 905(j)(3) from filing a substantial equivalence report when the changes between the new product and the predicate product involve changes to the ingredient composition of the products. These types of changes include a change in the type or level of flavors, the type or level of filter or paper components, or combination of the above.

Then, with an understanding as to what changes do not give rise to a substantial equivalence filing, the focus shifts to those changes that must fit within the "same characteristics" prong under Section 910(a)(3). In keeping with the SE framework developed for devices, and on which Congress modeled the tobacco regime, FDA must borrow from the core SE principles established in the device context in interpreting the parameters of the term "substantially equivalent" with regard to tobacco products. Accordingly, FDA must interpret the "same characteristics" prong of the SE pathway to be less burdensome than the "different characteristic" prong and apply to products in which the new product differs from the predicate product in one or more design characteristics, but the types of components used to construct the new product and the predicate product and the intended use to which the new product and the predicate operate are the same. For example, the "same characteristics" prong should be used to evaluate a new cigarette product that – like the predicate product – incorporates a filter, tipping paper, and cigarette paper, but differs in ventilation and filter efficiency. Similar to the framework developed for devices, these two products are substantially similar and will be reviewed under the "same characteristic" prong. For such new products that are considered substantially similar to the predicate product, a manufacturer need only provide the following information for the new and predicate product: a listing of ingredients, materials, and characteristics and limited chemistry data. Using the cigarette example listed above, a manufacturer will meet its limited chemistry obligation by providing tar, nicotine, and carbon monoxide yield for the two

products. FDA will evaluate substantial equivalence by comparing the new product in its entirety and predicate product in its entirety.

Under the second prong, in those limited circumstances when a product does contain a materially different characteristic, FDA must determine the product is substantially equivalent if the chemistry demonstrates that the new product when viewed in its entirety does not raise different questions of public health, or when FDA cannot conclude that the differences scientifically demonstrate that the new product will substantially increase the risk of tobacco related diseases to a tobacco user of the predicate product. As discussed in *Philip Morris USA, Inc. v. FDA,* these differences may be fairly significant.

CONCLUSION

For the foregoing reasons, RAIS submits that FDA's current interpretation of the premarket review pathways is seriously flawed and should be substantially revised to faithfully implement the statute Congress passed and to take account of the realities of the manufacture of tobacco products. RAIS hopes these comments will help FDA to update its guidance and promulgate regulations that will satisfy the statutory requirements, allow FDA to employ its limited resources efficiently, and further public health goals without unduly burdening manufacturers or consumers of tobacco products.