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May 13, 2019

Dockets Management Staff (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 2061
Rockville, MD 20852

RE: Modified Risk Tobacco Product Applications: Applications for Six Camel Snus Smokeless Tobacco Products Submitted by R.J. Reynolds Tobacco Company, Docket No. FDA-2017-N-4678

The undersigned public health organizations submit these comments on the above-listed tobacco product modified risk applications submitted by R.J. Reynolds Tobacco Company (“Reynolds”) for six Camel snus products.¹ The subject applications should be denied for the reasons detailed in these comments.

I. SUMMARY OF REASONS THE CAMEL SNUS MODIFIED RISK APPLICATION SHOULD BE DENIED

In the subject modified risk applications for Reynolds’ Camel snus products, the company seeks an order permitting it to make various modified risk claims, including the claim: “Smokers who SWITCH COMPLETELY from cigarettes to Camel SNUS can greatly reduce their risk of lung cancer, oral cancer, respiratory disease and heart disease.” The applications should be denied for the following reasons:

- **FDA should not grant a modified risk application for a product that does not meet FDA’s own proposed product standard limiting the carcinogen NNN in smokeless tobacco. Instead, that rule should be made final without further delay and smokeless products like Camel snus should be taken off the market.**
- **Reynolds introduced insufficient evidence on the impact of the marketing of Camel snus with modified risk claims on the increased likelihood of tobacco use initiation by non-users, particularly youth.**
 - Given the history of youth usage of smokeless tobacco and the current crisis of e-cigarette usage, and the statutory requirement for FDA to make a determination about the impact of a marketing order on youth, it is essential for FDA to require evidence that the marketing of Camel snus

¹ See 82 Fed. Reg. 60206 (December 19, 2017).

with modified risk claims will not increase youth initiation of tobacco products.

- Without justification, Reynolds has failed to present evidence on youth perception of the Camel snus modified risk claims.
- **The evidence indicates that the marketing of Camel snus with modified risk claims will lead to greater dual use with cigarettes instead of leading substantial numbers of smoker to switch completely to Camel snus.**
 - The experience with smokeless tobacco in the U.S. suggests that Camel snus, even with modified risk claims, will not cause substantial numbers of smokers to quit smoking and switch exclusively to Camel snus.
 - The experience with smokeless tobacco in the U.S. suggests that the marketing of Camel snus with modified risk claims will lead to widespread dual use, particularly given the history of Camel snus marketing in the U.S.
 - In projecting population-wide benefits from allowing modified risk claims for Camel snus, Reynolds relies largely on the Swedish experience, which is not likely to be replicated in the U.S. even with modified risk claims.
- **TPSAC found that there is considerable doubt about the extent of the individual health benefits of switching from smoking cigarettes to using Camel snus and about the accuracy of some of the proposed modified risk claims.**

II. SUMMARY OF STATUTORY MODIFIED RISK STANDARDS

The Camel snus applications are governed by the standards set out in Section 911 of the Food, Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act of 2009 (Section 911). Section 911 was enacted as a response to the tragic history of false and misleading tobacco industry claims that certain tobacco products were less dangerous than other products that persuaded health-conscious smokers to switch to the “reduced risk” products instead of quitting altogether.

In enacting the Tobacco Control Act, Congress made specific findings about the potential harm to public health from modified risk claims that should guide FDA in its consideration of any modified risk product application. Congress found that “unless tobacco products that purport to reduce the risks to the public of tobacco use actually reduce such risks, those products can cause substantial harm to the public health. . . .” Sec. 2(37). Congress also found that “the dangers of products sold or distributed as modified risk tobacco products that do not in fact reduce risk are so high that there is a compelling governmental interest in ensuring that statements about modified

risk products are complete, accurate, and relate to the overall disease risk of the product.” Sec. 2(40). Congress determined that it is “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.” Sec. 2(36).

Under the Tobacco Control Act, a “modified risk tobacco product” is defined as a tobacco product that is sold or distributed for use to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products. A product is “sold or distributed” for such a use if, in relevant part,

(1) [its] label, labeling, or advertising, either implicitly or explicitly [represents] that

(i) the tobacco product presents a lower risk of tobacco-related disease or is less harmful than one or more other commercially marketed tobacco products;

(ii) the tobacco product or its smoke contains a reduced level of a substance or presents a reduced exposure to a substance; or

(iii) the tobacco product or its smoke does not contain or is free of a substance, or

(3) . . . the tobacco product manufacturer has taken any action directed to consumers through the media or otherwise, other than by means of the label, labeling, or advertising...that would be reasonably expected to result in consumers believing that the tobacco product or its smoke may present a lower risk of disease or is less harmful than one or more commercially marketed tobacco products, or presents a reduced exposure to, or does not contain or its free of, a substance or substances.

Thus, a modified risk product is defined in terms of the manufacturer’s claims of reduced risk or reduced exposure in marketing the product, as well as its actions that may suggest to consumers that a product reduces risk or exposure to hazardous substances.

Under §911(g)(1), the burden is on the applicant seeking an order allowing the marketing of the product with a modified risk claim 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.” (emphasis added).

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;
- (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 product is less hazardous to users than other tobacco products; in order for a modified risk application to be granted, the applicant is required to show that the benefits of risk reduction (considering the likelihood of smokers completely switching to the modified risk product) outweigh the risks of increased initiation or diminished cessation. In short, the statute requires FDA to make scientific judgments 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.

III. RELEVANT HISTORICAL BASIS FOR SECTION 911

FDA's application of the statutory standards set out in Section 911 must be mindful of the historical context that led Congress to enact those standards, particularly with respect to the Reynolds application for Camel snus.

The provisions of Section 911 were enacted in response to a massive evidentiary record of fraudulent health and "reduced risk" claims made by tobacco product manufacturers over the course of more than fifty years. Those claims caused millions of Americans to initiate cigarette smoking who otherwise would not have done so and caused millions of American smokers to continue smoking when they otherwise would have quit. In the absence of this massive industry fraud, literally millions of deaths, and untold suffering, would have been avoided.

The voluminous evidence of the industry's use of these false health-related claims was presented to the United States District Court for the District of Columbia in *United States v. Philip Morris, U.S.A., Inc.*² and furnished critical support for the court's conclusion that the defendant

² 449 F. Supp.2d 1 (D.D.C. 2006), *aff'd in relevant part*, 566 F.3d 1095 (D.C. Cir. 2009), *cert. denied*, 130 S.Ct. 3501 (2010).

tobacco companies, including Reynolds, had engaged in a conspiracy to defraud the American public so massive as to constitute racketeering under federal law. A central component of the fraud was the representation of “light” and “low-tar” cigarettes as safer than other cigarettes, when the companies knew, as actually used by smokers, such cigarettes were no less hazardous. The court found:

Even as they engaged in a campaign to market and promote filtered and low tar cigarettes as less harmful than conventional ones, Defendants either lacked evidence to substantiate their claims or knew them to be false. Indeed, internal industry documents reveal Defendants’ awareness by the late 1960s/early 1970s that, because low tar cigarettes do not actually deliver the low levels of tar and nicotine which are advertised, they are unlikely to provide any clear health benefit to human smokers, as opposed to the FTC smoking machine, when compared to regular, full flavor cigarettes.³

Thus, Reynolds and the other industry defendants were found by the court to have violated civil racketeering laws in perpetrating decades-long fraudulent conduct that included the “light” and “low-tar” fraud.

After finding that defendants’ fraudulent conduct was likely to continue into the future, the District Court required the defendants, including Reynolds, to publish corrective statements about the subject matters of the fraud to deter future false and misleading statements. The court ordered Reynolds and the other defendants to sponsor the corrective statements in newspapers, on television, on company websites and on package inserts, including this statement to remedy the “light” and “low-tar” fraud:

A federal court has ordered Altria, R.J. Reynolds Tobacco, Lorillard, and Philip Morris USA to make this statement about low tar and light cigarettes being as harmful as regular cigarettes.

- Many smokers switch to low tar and light cigarettes rather than quitting because they think low tar and light cigarettes are less harmful. They are **not**.
- “Low tar” and “light cigarette smokers inhale essentially the same amount of tar and nicotine as they would from regular cigarettes.
- **All** cigarettes cause cancer, lung disease, heart attacks, and premature death – lights, low tar, ultra lights, and naturals. There is no safe cigarette.

After years of litigation and other delaying tactics by the defendants, including Reynolds, these corrective statements have now appeared in newspapers and on television, as well as being

³ *Id.* at 430-31.

set forth in inserts on cigarette packs. They serve as reminders of the history of false claims of “reduced risk” products by the tobacco companies, including Reynolds. In light of that history, particularly the finding by a federal court that Reynolds and the other RICO defendants are likely to continue their fraudulent conduct, FDA should ensure that the statutory standards, enacted by Congress to prevent a similar public health disaster from ever repeating itself, are rigorously applied to Reynolds’ applications for Camel snus.

IV. THE APPLICATIONS SHOULD BE DENIED BECAUSE THE LEVEL OF NNN IN CAMEL SNUS EXCEEDS THE NNN LIMIT TO BE MANDATED BY THE FDA’S PROPOSED RULE ON SMOKELESS TOBACCO

On January 23, 2017, FDA published a proposed rule that would establish a limit of 1.0 microgram per gram of tobacco (on a dry weight basis) of N-nitrosornicotine (NNN), a potent carcinogen, in all finished smokeless tobacco products, which would include Camel snus.⁴ The pending application makes it clear that, at a range of 1.116-1.156 micrograms per gram of tobacco (as-is),⁵ the level of NNN in Camel snus exceeds the maximum level proposed as a product standard by FDA.⁶ Thus, in these applications, Reynolds seeks authorization to make modified risk claims for products that FDA has proposed to prohibit from the market because such a prohibition would be “appropriate for the protection of the public health.”

Should the proposed rule become final prior to FDA’s disposition of the pending MRTP applications for Camel snus, the applications would become moot because the Camel snus products would not conform to the new product standard. Should the proposed rule become final after an MRTP decision, the products would need to be withdrawn. Given the pendency of FDA’s proposal of an NNN product standard for all smokeless tobacco, it makes little sense for the agency to consider the modified risk applications for Camel snus before it makes a final decision on the proposed product standard.

FDA should issue a final rule establishing the NNN product standard without further delay. The proposed rule is amply supported by scientific evidence establishing that (1) NNN in smokeless tobacco is carcinogenic, (2) reducing the level of NNN in smokeless tobacco products marketed in the United States would substantially reduce the risk of oral cancers for users, and (3) conformance of smokeless tobacco to the proposed product standard is technically feasible as demonstrated by the presence on the U.S. market of Swedish snus products sold by Swedish

⁴ Proposed Rule for Tobacco Product Standard for NNN level in Finished Smokeless Tobacco Products, 82 Fed. Reg. 8004 (January 23, 2017) (Proposed NNN rule).

⁵ FDA Briefing Document for TPSAC meeting, Sept. 13-14, 2018 for MRTPAs by R.J. Reynolds Tobacco Co., Table 3, at 14 (FDA Briefing Document).

⁶ The NNN standard is for dry weight, but the FDA Briefing Document shows as-is, or wet-weight measurements. Based on the calculation included in the Proposed NNN Rule (at 49), the dry-weight measurement for NNN in Camel snus would be higher than the wet-weight measurement. Thus, the level of NNN in Camel snus must exceed the proposed dry weight product stand of 1.0 microgram per gram of tobacco.

Match that already meet the proposed standard.⁷ Indeed, FDA estimates that in the 20 years following implementation of the proposed product standard, approximately 12,700 new cases of oral cancer and approximately 2,200 oral cancer deaths would be prevented in the United States. During that 20-year period, approximately 15,200 life years would be gained were the standard to be put into effect.⁸

In light of the substantial benefit to public health FDA anticipates from adoption of its proposed NNN standard, the proposed rule should be made final, and the standard implemented as soon as possible. The proposed rule was issued well over two years ago and the public comment period has long been closed. There is simply no reason for FDA to further delay making the rule final. Once it does so, the pending MRTP applications for Camel snus will become moot. It makes little sense for FDA to grant these MRTP applications when it concerns products that, according to FDA's own scientific conclusions, should no longer be permitted on the market.⁹

V. THE APPLICATIONS SHOULD BE DENIED FOR INSUFFICIENT EVIDENCE ON THE IMPACT OF THE MARKETING OF CAMEL SNUS WITH MODIFIED RISK CLAIMS ON THE INCREASED LIKELIHOOD OF TOBACCO USE INITIATION BY NON-USERS, PARTICULARLY YOUTH

As noted above, in evaluating the Camel snus modified risk applications, FDA is required to determine whether granting the applications will lead to an "increased or decreased likelihood" that non-users of tobacco products will initiate use of Camel snus or some other tobacco product. Because initiation of tobacco products typically occurs when users are young, it is particularly important for FDA to assess the likelihood that the marketing of Camel snus with modified risk claims will lead to initiation by young people. Because Reynolds' applications offer no evidence of youth perception of the proposed modified risk claims, they should be denied on that ground alone.

- A. Given the history of youth usage of smokeless tobacco and the current crisis of e-cigarette usage, it is particularly important for FDA to require evidence that the marketing of Camel snus with modified risk claims will not increase youth initiation of tobacco products.

When Camel snus was first introduced, news reports indicated that it was popular among high school students because of its concealable nature. One news article from that time described a high school student admitting to using Camel snus during class, who said, "It's easy, it's super-discreet...and none of the teachers will ever know what I'm doing."¹⁰ Given that

⁷ See generally, Proposed NNN Rule, 82 Fed. Reg. at 8010-8026.

⁸ Proposed NNN Rule, 82 Fed Reg. at 8026.

⁹ Of course, once the proposed NNN rule becomes final and is implemented, Reynolds will be free to pursue a new MRTP for any of its products that conform to the new NNN standard.

¹⁰ Nelson, L, "If you think Snus is a safe alternative to smoking, think again," *Kansas City Star*, October 31, 2007.

smokeless tobacco rates among youth have not declined as rapidly as cigarette smoking,¹¹ it is important that FDA require Reynolds to produce data on the impact of expanding Camel snus marketing with a modified risk message on youth initiation, including a possible gateway effect to smoking and dual use. Data on youth perception is particularly important since nothing in Reynolds marketing plans for Camel snus as a modified risk product, which include print ads, provide assurance that youth will not be exposed to the modified risk claims.

Tobacco marketing plays an important role in attracting users – particularly youth. Tobacco companies have used a variety of strategies to entice youth to use smokeless tobacco: sweet and kid-friendly flavors, sponsorships of events popular with youth, advertisements with youth-oriented messages, and affordable prices.¹² The 2012 Surgeon General’s report, *Preventing Tobacco Use among Youth and Young Adults*, found that the “integration of product design with marketing helped to reverse the mid-twentieth century decline in smokeless tobacco use and spurred a rapid increase in smokeless tobacco use by adolescents and young adult males.”¹³

The importance of FDA requiring data bearing on the likelihood of increased youth initiation prior to releasing its order on these modified risk applications is underscored by the current crisis of e-cigarette usage among young people, which both the Commissioner of the FDA,¹⁴ and the Surgeon General of the United States,¹⁵ have declared to have reached “epidemic” proportions. Although there are obvious distinctions between e-cigarettes like JUUL and smokeless tobacco products like Camel snus, the fact that another kind of highly-addictive “reduced risk” product is proving so appealing to young people, in part because it can be used discreetly, should cause FDA to closely scrutinize the potential impact of modified risk claims for Camel snus on youth initiation.

During the discussion on FDA’s question about “the potential users of the proposed MRTPs,” at its meeting on the Camel snus applications, TPSAC “stressed the need for effective post-market surveillance if/when any claims are authorized.”¹⁶ However, by then it may be too late. As we have experienced with e-cigarettes and youth, not only have prevalence rates skyrocketed, but health professionals are struggling with treating more and more youth for nicotine addiction, to the point that FDA has scheduled two workshops on the issue.¹⁷ Post-

¹¹ U.S. Centers for Disease Control and Prevention (CDC), “Vital Signs: Tobacco Product Use Among Middle and High School Students — United States, 2011–2018,” *Morbidity and Mortality Weekly Report (MMWR)* 68(6):157–164, February 15, 2019, <https://www.cdc.gov/mmwr/volumes/68/wr/pdfs/mm6806e1-H.pdf>.

¹² Campaign for Tobacco-Free Kids factsheet, *Smokeless Tobacco and Kids*, <https://www.tobaccofreekids.org/assets/factsheets/0003.pdf>.

¹³ U.S. Department of Health and Human Services (HHS), *Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General*, 2012, at 539.

¹⁴ Statement from FDA Commissioner Scott Gottlieb, M.D., on the agency’s continued efforts to address growing epidemic of youth e-cigarette use, including potential new therapies to support cessation, November 2, 2018.

¹⁵ Surgeon General’s Advisory on E-Cigarette Use Among Youth, December 18, 2018 (SG Advisory).

¹⁶ Summary Minutes of TPSAC meeting, September 13-14, 2018 for MRTPAs by R.J. Reynolds Tobacco Company, Inc., at 6-7.

¹⁷ 83 Fed Reg 64752-57. 84 Fed Reg 12619-21.

market surveillance may be too little, too late. It cannot be considered an adequate substitute for requiring the necessary data as part of the premarket approval process.

B. Without justification, Reynolds has failed to present evidence on youth perception of the Camel snus modified risk claims

FDA should reject Reynolds' applications because they provide no data whatsoever on youth perceptions of Camel snus as a modified risk product and no evidence regarding the potential for adolescent use. No accurate assessment of the impact on the health of the population as a whole can be made without consideration of actual data derived from studies of the perceptions of those under age 18. The total absence of data on youth perception of Camel snus, with the proposed modified risk claims, should—standing alone—preclude granting Reynolds' applications. Indeed, the grant of these applications in the absence of that data would set the worst possible precedent and be wholly inconsistent with FDA's statutory mission to protect the public health.

As noted above, FDA's assessment of an MRTP application must consider the population-wide impact of the product on both users and non-users of tobacco products, which includes its impact on tobacco use initiation. Despite the fact that the effect of modified risk claims on underage users must be a central focus of FDA's evaluation of an MRTP application, Reynolds' MRTP applications provide no evidence whatsoever on the impact of the modified risk claims made for Camel snus on adolescent risk perception or adolescent use of tobacco products.

As FDA's Draft Guidance for the preparation of Modified Risk Tobacco Product Applications makes clear, FDA requires only that "all study subjects *receiving tobacco products* are current daily tobacco product users at least 21 years of age"¹⁸ (emphasis added). Not only is this limitation not applicable to studies of promotional material such as modified risk claims to determine the effect of such materials on adolescent risk perception or interest in using the product, but the 2012 Draft Guidance makes clear that inclusion of the effect on adolescent perception should be an essential feature of such studies. The Draft Guidance states:

To address the effect of the MRTP on tobacco use initiation, FDA recommends that applicants submit:

- Human studies that evaluate consumer perception of the product, including its labeling, marketing and advertising.

These studies should be designed to provide evidence regarding the likelihood of population benefit or harm from the proposed product, including...:

¹⁸ FDA, Draft Guidance, Modified Risk Tobacco Applications, March 2012, at 29 (FDA 2012 Draft Guidance).

- The likelihood that consumers who have never used tobacco products, *particularly youth and young adults*, will initiate use of the tobacco product;¹⁹ (emphasis added)

Moreover, the Draft Guidance instructs companies to “estimate the attributable risk of all of the various health effects for various types of individuals in the U.S. population, as well as the total number of individuals of each type.” The Draft Guidance goes on to state, “The types of individuals may include, but are not limited to, the following ... Non-users who initiate tobacco use with the proposed product, *such as youth*, never users, former users” (emphasis added).²⁰

Thus, far from prohibiting the testing of such messages on adolescents, the FDA Draft Guidance characterizes such testing as particularly important. In this light, Reynolds’ failure to provide any evidence of the effect of these messages on adolescent risk perception is an inexplicable omission that ignores FDA’s specific instruction to include that analysis.

Moreover, FDA’s Draft guidance describes how such youth consumer perception research should be done. Recognizing that research among non-smokers, and non-smoking youth in particular, requires care, FDA offered applicants an opportunity to work with the agency to determine the best way to conduct studies involving youth:

When designing consumer perception studies, applicants should take care that the studies themselves do not promote use of the product, particularly among vulnerable populations, such as youth, non-users of tobacco products, and pregnant women. FDA recommends that applicants meet with FDA to discuss research plans before embarking on research with vulnerable populations. Section IX.B of this guidance provides information on requesting a meeting with FDA.²¹

Reynolds’ failure to assess the impact of the marketing of Camel snus as a modified risk product on youth also contravenes recommendations made by the Institute of Medicine’s (IOM) 2012 report, *Scientific Standards for Studies on Modified Risk Tobacco*, which recommended that “FDA should require studies to include populations of special relevance, including (but are not limited to) ... adolescents”²² and included an assessment of the effects on youth as “an essential element in establishing the public health benefit of an MRTP.”²³ The report included research on adolescents in three of its “Evidence domains relevant to an MRTP application.”²⁴ The need to consider the effects of promotional statements on youth is vitally important in light of the industry’s documented history of marketing tobacco products in ways that attract

¹⁹ *Id.* at 20.

²⁰ *Id.* at 22.

²¹ *Id.* at 26.

²² Institute of Medicine, *Scientific Standards for Studies on Modified Risk Tobacco Products*, December 2011, at 14 (IOM report).

²³ IOM report, at 50.

²⁴ IOM report, at 7 (Summary).

adolescents and the role that youth initiation has played—and continues to play—in the recruitment of long-term adult smokers.²⁵

According to IOM, perceptions of and intentions to use a given MRTP are also likely to differ by age group. Thus, IOM noted that it is “critical that studies include participants in the following age groups: children (≤ 12 years old), adolescents (13–17 years old), young or emerging adults (18–25 years old), adults (≥ 25 years old).”²⁶ As noted by IOM, “adolescents’ perceptions of the risks and benefits of cigarette smoking play an important role in adolescents’ decisions to smoke. Given that adolescence is a period of heightened vulnerability for the initiation of tobacco use, it is important to evaluate whether adolescents accurately understand the purported benefits of an MRTP. Of particular importance are adolescents’ perceptions of the risks and benefits of using the product, and whether they intend to initiate tobacco use with the MRTP rather than a traditional tobacco product because they believe the former is a “safe” alternative.”²⁷

Similarly, the IOM report detailed ideas for how research on youth perceptions of risk of MRTPs can be conducted consistent with ethical standards of research.²⁸ For example, IOM suggests that such research could be appropriately done under the supervision of an independent third party.²⁹ Such a procedure would make it possible for an applicant to develop evidence regarding the effect of the marketing of a product on this population. IOM noted that, “Survey research or perception/messaging research among non-smokers is acceptable where the non-smokers are not being exposed to the product.”³⁰ Even in the case of studies that include exposure to a particular tobacco product among non-users (which is not critical in this case), IOM concluded, “Experimental research that exposes non-users to products is ethically problematic; but such research cannot completely be ruled out because it could provide critically valuable information. The ethics, risks, and benefits need to be determined on a case by case basis.”³¹

Despite the express instructions in FDA’s Draft Guidance on the preparation of modified risk applications and the extensive discussion in the IOM report on how research on youth risk perception could appropriately be conducted, Reynolds has submitted applications that ignore the effects of the proposed modified risk claims on youth. Applications that present no evidence on the effect of modified risk claims on youth initiation or perception of risk cannot possibly meet the public health standard.

²⁵ U.S. Department of Health and Human Services (HHS), *Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General*. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2012, at 530-41, 603-27 and sources cited therein (2012 Surgeon General’s Report); *U.S. v. Philip Morris*, 449 F. Supp. 2d, at 561-691.

²⁶ IOM report, at 174.

²⁷ IOM report, at 165.

²⁸ IOM report, at 10.

²⁹ IOM report, at 57.

³⁰ IOM report, at 52.

³¹ IOM report, at 52-53.

Reynolds' failure to assess, in any way, the impact of its proposed modified risk message on youth is a particularly significant omission, given data indicating that smokeless tobacco use could be associated with future smoking for youth and young adults. One small study found an association between snus use among non-smoking youth and young adults and increased likelihood of cigarette smoking initiation, current cigarette smoking, and more intense cigarette smoking two years later.³² Though the proportions from the study are small, those findings are supported by older studies linking smokeless tobacco use to later cigarette smoking.³³ More recently, a study using data from the Population Assessment of Tobacco and Health (PATH) study found that non-smoking youth (12-17 years old) using smokeless tobacco (including snus) at baseline had higher odds of cigarette smoking initiation and two times the odds of past 30-day cigarette smoking at follow-up a year later compared to non-users.³⁴ FDA's Briefing Document to TPSAC on the Camel snus modified risk applications also noted a "systematic review of multiple studies on smokeless tobacco use transitions (Tam et al., 2015)" finding "evidence of smokeless tobacco users moving to exclusive cigarette smoking (16.6% to 25.5% among adolescents)."³⁵

This pattern is not isolated to the U.S.: a study from Norway found that age may be a factor in transitioning from snus to cigarettes. It found that people who started using snus before 16 years old were much more likely to become adult smokers compared to those who started snus later.³⁶

Moreover, initial smokeless tobacco use is also associated with later multiple tobacco product use. A survey of adolescents and young adults who had ever used tobacco found that those who initiated any tobacco use with smokeless tobacco (or any other non-combustible

³² Soneji, S, et al., "Associations Between Initial Water Pipe Tobacco Smoking and Snus Use and Subsequent Cigarette Smoking Results from a Longitudinal Study of US Adolescents and Young Adults," *JAMA Pediatrics* 169(2):129-136, 2015.

³³ Tomar, SL, et al., "Is Smokeless Tobacco Use an Appropriate Public Health Strategy for Reducing Societal Harm?," *International Journal of Environmental Research and Public Health* 6:10-24, 2009, at 16. Severson, H, et al., "Use of smokeless tobacco is a risk factor for cigarette smoking," *Nicotine and Tobacco Research* 9(12):1331-1337, December 2007. Haddock, CK, et al., "Evidence that smokeless tobacco use is a gateway for smoking initiation in young adult males," *Preventive Medicine* 32:262-267, 2001. Tomar, S, "Snuff Use and Smoking in U.S. Men: Implications for Harm Reduction," *American Journal of Preventive Medicine* 23(3):143-149, October 2002. Tomar, S, "Is use of smokeless tobacco a risk factor for cigarette smoking? The U.S. experience," *Nicotine & Tobacco Research* 5(4):561-569, August 2003, <http://www.ncbi.nlm.nih.gov/pubmed/12959794>. See also, Tomar, SL, "Smokeless tobacco use is a significant predictor of smoking when appropriately modeled," *Nicotine & Tobacco Research* 5(4):571-573, August 2003, <http://www.ncbi.nlm.nih.gov/pubmed/12959795>.

³⁴ Watkins, SL, Glantz, SA, Chaffee, BW, "Association of Noncigarette Tobacco Product Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015," *JAMA Pediatrics* 172(2):181-187, 2018.

³⁵ FDA Briefing Document, at 61.

³⁶ Lund, I & Scheffels, J, "Smoking and Snus Use Onset: Exploring the Influence of Snus Debut Age on the Risk for Smoking Uptake With Cross-Sectional Survey Data," *Nicotine & Tobacco Research* 16(6):815-819, 2014.

product) had higher odds of using multiple tobacco products than those who initiated with a combustible product.³⁷

Therefore, Reynolds' failure to develop and submit any data whatsoever on youth perceptions of the proposed modified risk messages is sufficient, by itself, to support denial of the applications.

VI. THE APPLICATIONS SHOULD BE DENIED BECAUSE THE EVIDENCE INDICATES THAT THE MARKETING OF CAMEL SNUS WITH MODIFIED RISK CLAIMS WILL LEAD TO GREATER DUAL USE WITH CIGARETTES INSTEAD OF LEADING SUBSTANTIAL NUMBERS OF SMOKERS TO SWITCH COMPLETELY TO CAMEL SNUS

- A. The experience with smokeless tobacco in the U.S. suggests that Camel snus, even with modified risk claims, will not cause substantial numbers of smokers to quit smoking and switch exclusively to Camel snus.

Data related specifically to snus use in the United States are limited due to the very low use rate. Most of the relevant data in the U.S. assess consumer behavior with respect to the broad smokeless tobacco category that includes snus, dry and moist snuff and chewing tobacco, and of which moist snuff makes the largest portion. Camel snus currently has relatively low use rates in the U.S. compared to traditional smokeless tobacco products, and it is unlikely that a modified risk designation will increase its use by smokers who plan to switch completely, and more likely that those smokers will use Camel snus in addition to smoking cigarettes.

Current data, as provided by Reynolds and in studies evaluated by FDA, show that complete switching from cigarettes to smokeless tobacco is not common. In its briefing document to TPSAC, FDA noted, "Research submitted by the applicant and the published literature on smokeless tobacco provide limited evidence to suggest that current cigarette smokers, including those intending to quit, would switch completely to Camel Snus or other smokeless tobacco products."³⁸ Further, the FDA briefing document states, "Evidence from the broader peer-reviewed literature suggests that transitions from exclusive cigarette smoking to exclusive smokeless tobacco were rare (0%-1.4%), with transitions from exclusive cigarette smoking to dual use of cigarettes and smokeless tobacco being somewhat more common (0.1%-3.2%) (Tam et al., 2015)."³⁹

Despite the data from Sweden presented by Reynolds, there is not sufficient evidence in the U.S. on the impact of smokeless tobacco in helping smokers quit to support an inference that there would be a similar switching effect in the U.S. Swedish Match's original MRTTP

³⁷ Soneji, S, Sargent, J, & Tanski, S, "Multiple tobacco product use among US adolescents and young adults," *Tobacco Control*, 2014, [Epub ahead of print], <http://www.ncbi.nlm.nih.gov/pubmed/25361744>.

³⁸ FDA Briefing Document, at 61.

³⁹ FDA Briefing Document, at 61.

application for Swedish Snus demonstrates clearly that the historical and cultural background of tobacco use in Scandinavia is quite different from that in the United States. In Sweden, snus has been widely available and widely used for many years; by contrast, the product has had virtually no presence in the United States market. Swedish snus differs substantially from smokeless tobacco products that have been sold in the United States; it also differs substantially from the products advertised as “snus” that have been on the market in the United States. Other forms of smokeless tobacco popular in the United States have never been marketed in Sweden. Moreover, the entire market for tobacco products in Sweden differs from the United States market because Sweden permits no advertising of tobacco products—cigarettes or snus. Thus, advertising plays no role in the establishment of consumer preferences in Sweden. These differences may well account for differences in the way snus is used in Sweden as compared to how it would be used in the United States. Thus, from a scientific standpoint, the data on use from Sweden does not provide a basis for determining the impact of allowing Camel Snus to make a MRTP claim in the U.S.

The 2008 Update of the U.S. Public Health Service Clinical Practice Guidelines regarding tobacco cessation concluded, “the use of smokeless tobacco products is not a safe alternative to smoking, nor is there evidence to suggest that it is effective in helping smokers quit.”⁴⁰

U.S. smokers do not prefer to use smokeless tobacco, even snus, to quit smoking. One study showed that daily smokers were no more likely to stop smoking for seven days with Camel snus compared to with FDA-approved nicotine gum. The study authors stated, “Snus (with levels of nicotine similar to nicotine gum) was no better than nicotine gum in sustaining abstinence from smoking, but was significantly more toxic.”⁴¹ Older data on smokers’ attitudes about switching to smokeless tobacco confirm this finding.⁴² Among adult smokers given free Camel snus and who used the products beyond experimentation found them to be “poor substitute[s] for cigarettes.”⁴³ Even when smokers in a clinical setting were given free Camel

⁴⁰ Fiore, MC, et al., *Treating Tobacco Use and Dependence: 2008 Update*, U.S. Public Health Service Clinical Practice Guideline, May 2008, http://www.surgeongeneral.gov/tobacco/treating_tobacco_use08.pdf.

⁴¹ Berman, ML, et al., “Consortium on Methods Evaluating Tobacco: Research Tools to Inform FDA Regulation of Snus,” *Nicotine and Tobacco Research* [Epub ahead of print], doi: 10.1093/ntr/ntx228, October 4, 2017, <https://academic.oup.com/ntr/advance-article-abstract/doi/10.1093/ntr/ntx228/4331541>.

⁴² A 2009 study based on data from the California Tobacco Survey showed that the majority of daily smokers were not interested in switching their cigarettes for smokeless tobacco. In fact, 87 percent of smokers said they were “definitely not” or “probably not” open to the idea of replacing their cigarettes with smokeless tobacco, compared to only 12.7 percent of the smokers who reported that they “definitely” or “probably” would consider it. Timberlake, D, “Are smokers receptive to using smokeless tobacco as a substitute?” *Preventive Medicine* 49(2-3):229-32, 2009, <http://www.ncbi.nlm.nih.gov/pubmed/19631684>. A national cross-sectional study of current and former smokers found that just “7.8% of respondents reported that they tried to quit smoking by switching to chewing tobacco, snuff, or snus; an additional 5.8% considered it but never tried, and most never considered it.” Popova, L & Ling, PM, “Alternative Tobacco Product Use and Smoking Cessation: A National Study,” *American Journal of Public Health* 103(5):923-930, May 2013, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3661190/pdf/nihms456593.pdf>.

⁴³ Meier, E, et al., “Perceptions of Snus Among US Adult Smokers Given Free Product,” *Nicotine & Tobacco Research* 20(1):22-29, 2018.

snus, reminders not to smoke, and financial bonuses not to smoke, some continued to use some cigarettes while using snus, leading the authors of this study to conclude, “the uptake of this product and the success for complete switching may be low and therefore the public health benefit of snus as a modified risk product may be modest.”⁴⁴

FDA’s review of Reynolds’ clinical studies in its briefing document to TPSAC confirms this finding, stating, “The reduced abuse liability of Camel Snus may decrease the odds of the proposed MRTPs adequately substituting for cigarette smoking. In fact, evidence of cigarette smokers switching to exclusive Camel Snus use is limited, and dual use was common in the provided studies.”⁴⁵

The fact that U.S. smokers perceive snus as a temporary replacement, not a complete substitution for cigarettes⁴⁶ is not surprising given that many smokeless tobacco products have been marketed as a way to get a nicotine fix when smokers cannot smoke. Early marketing for Camel Snus used that precise message: One newspaper ad stated, “Snusing is allowed in the following places: In a **bar**, on a boat, or in your car. ... Pleasure for Wherever” (emphasis in original),⁴⁷ while a point-of-sale pamphlet stated, “Enjoy Snus: Anytime, Anywhere! It’s Limitless!”⁴⁸ Such marketing discourages smokers from taking the one step that is sure to protect their health, which is to quit smoking entirely. These types of messaging could undermine any modified risk statement about “switching completely.”

Instead, in the U.S., smokeless tobacco users were more likely to switch to cigarettes. One U.S. longitudinal study found that few male smokers stopped smoking and switched to smokeless tobacco (0.3 percent in one year) and few former smokers turned to smokeless tobacco (1.7 percent), and concluded that “smokeless tobacco is less useful for quitting smoking among U.S. smokers because in all likelihood they would quit smokeless tobacco before they quit cigarettes.”⁴⁹ Another longitudinal study of adolescent and young adult males who were smokers at baseline but did not use smokeless tobacco found that at four-year follow-up less than one percent (0.8 percent) switched to smokeless tobacco and 3.6 percent continued to smoke and became smokeless tobacco users as well.⁵⁰

⁴⁴ Meier, E, et al., “A Randomized Clinical Trial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure,” *Nicotine & Tobacco Research*, Advanced Access, April 11, 2019.

⁴⁵ FDA Briefing Document, at 56.

⁴⁶ Bahreinifar, S, Sheon, NM, & Ling, PM, “Is snus the same as dip? Smokers’ perceptions of new smokeless tobacco advertising,” *Tobacco Control* 22:84-90, 2013, <http://tobaccocontrol.bmj.com/content/22/2/84>.

⁴⁷ Camel snus ad in *The Austin Chronicle*, October 13, 2006, available at <http://www.trinketsandtrash.org/detail.php?artifactid=6792>.

⁴⁸ Camel snus point of sale pamphlet, 2008, available at <http://www.trinketsandtrash.org/detail.php?artifactid=5888>.

⁴⁹ Zhu, S-H, et al., “Quitting Cigarettes Completely or Switching to Smokeless: Do U.S. Data Replicate the Swedish Results?,” *Tobacco Control* 18:82-87, 2009, at 86.

⁵⁰ Tomar, S, “Is use of smokeless tobacco a risk factor for cigarette smoking? The U.S. experience,” *Nicotine & Tobacco Research* 5(4):561-569, August 2003, <http://www.ncbi.nlm.nih.gov/pubmed/12959794>.

In a study of smokers who did not intend to quit, among those who chose to use the provided snus product (Camel snus), more frequent and regular use were found to help prompt quit attempts and abstinence. However, this was a small minority of participants in the study. The researchers had provided some brief information about “why it [snus] might be considered safer than cigarettes” but did not provide instructions on how to use the products. The researchers indicated that providing snus without education about how to use the product could undermine quit attempts.⁵¹

Other evidence suggests that smokers in the U.S. prefer to use pharmaceutical nicotine products to quit over smokeless tobacco products. The previously mentioned study comparing preference for Camel snus to FDA-approved nicotine gum found that “When provided the option between snus and nicotine gum, current smokers appear to gravitate towards the less harmful nicotine gum as a preferred alternative to cigarettes.”⁵² Older studies of smokers have found similar preferences for nicotine replacement products over smokeless tobacco.⁵³

Another major consideration is that the popular smokeless tobacco products in the U.S. are traditional moist snuff, not snus. Even though Camel snus has the highest market share among snus products sold in the U.S., that overall snus market is quite low. Convenience store data show that spitless tobacco products, including snus, made up less than six percent of smokeless tobacco unit sales through 2018, and of the snus brands, Camel products were the most shipped brands.⁵⁴

While there may be some experimentation of snus, regular use of snus use is very low among adults and youth. In 2012, current snus use was 0.8 percent among middle school students and 2.5 percent among high school students.⁵⁵ A separate national survey of 2013-2014 data found 0.5 percent of youth (12-17 years old) were current snus users.⁵⁶ More recent youth surveys include snus within the smokeless category. Only 5.4 percent of U.S. adults had ever used snus in 2012-2013 and among current snus users, only 11.3 percent report using the product

⁵¹ Carpenter, MJ, et al., “Snus undermines quit attempts but not abstinence: a randomised clinical trial among US smokers,” *Tobacco Control* 26(2):202-209, 2017.

⁵² Berman, ML, et al., “Consortium on Methods Evaluating Tobacco: Research Tools to Inform FDA Regulation of Snus,” *Nicotine and Tobacco Research* [Epub ahead of print], doi: 10.1093/ntr/ntx228, October 4, 2017, <https://academic.oup.com/ntr/advance-article-abstract/doi/10.1093/ntr/ntx228/4331541>.

⁵³ O’Connor, RJ, et al., “US smokers’ reactions to a brief trial of oral nicotine products,” *Harm Reduction Journal* 8:1-10, 2011, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3032705/pdf/1477-7517-8-1.pdf>. Shiffman, S, et al., “Smokers’ Preferences for Medicinal Nicotine vs Smokeless Tobacco,” *American Journal of Health Behavior* 31(5):462-472, September/October 2007, <http://www.ncbi.nlm.nih.gov/pubmed/17555377>.

⁵⁴ “Tobacco: OTP,” *Convenience Store/Petroleum Category Management Handbook* 2019, https://www.qgdigitalpublishing.com/publication/?i=580380#%22issue_id%22:580380.%22page%22:46, at 45, 46.

⁵⁵ CDC, “Tobacco Product Use Among Middle and High School Students — United States, 2011 and 2012,” *MMWR* 62(45):893-897, November 15, 2013, <http://www.cdc.gov/mmwr/pdf/wk/mm6245.pdf>.

⁵⁶ Kasza, KA, et al., “Tobacco-Product Use by Adults and Youths in the United States in 2013 and 2014,” *New England Journal of Medicine* 376(4):342-353, 2017.

every day.⁵⁷ PATH data from 2013-2014 found that less than one percent of adults were current snus users.⁵⁸

Of the limited studies of Camel snus in the U.S. available, some show that smokers have little interest in Camel snus,⁵⁹ even with a modified risk message.⁶⁰ A modified risk message – which could be misinterpreted by non-smokers, especially youth – would likely have little impact on smokers, especially since Camel snus is no more effective in helping smokers completely switch than FDA-approved nicotine gum, yet exposes them to more toxicants.⁶¹ In addition, the popularity of e-cigarettes could have an impact on how consumers will react to the proposed modified risk messages for Camel snus.

- B. The experience with smokeless tobacco in the U.S. suggests that the marketing of Camel snus with modified claims will lead to widespread dual use, particularly given the history of Camel snus marketing in the U.S.

As indicated above, smokers may try snus for various reasons, including to reduce their smoking, but they more often end up using both products rather than switching completely.⁶² FDA’s briefing document to TPSAC stated, “In terms of patterns of use, cross-sectional data from the NTBM [RAI’s National Tobacco Behavior Monitor survey], Brand Tracker, and published data from the PATH [Population Assessment of Tobacco and Health] Study suggest that patterns of dual/poly tobacco use among current users of Camel Snus is high—with concurrent use of Camel Snus, other smokeless tobacco products, and cigarettes being the most common. Additionally, findings from Cheng and colleagues (2017) found that pouched snus users in the U.S. were more likely to report non-daily and poly tobacco use than other users of other types of smokeless products.”⁶³ Analysis of 2013-2014 PATH data show that 42.6 percent of adult cigarette smokers were snus users, compared to 27.7 percent of former smokers and 29.7 percent of never smokers who reported currently using snus.⁶⁴

⁵⁷ CDC, “Tobacco Product Use Among Adults — United States, 2012–2013,” *MMWR* 63(25):542-547, June 27, 2014, <http://www.cdc.gov/mmwr/pdf/wk/mm6325.pdf>.

⁵⁸ Cheng, Y, et al., “Patterns of Use of Smokeless Tobacco in US Adults, 2013–2014,” *American Journal of Public Health* 107(9):1508-1514, 2017. Kasza, KA, et al., “Tobacco-Product Use by Adults and Youths in the United States in 2013 and 2014,” *New England Journal of Medicine* 376(4):342-353, 2017.

⁵⁹ Carpenter, MJ, et al., “Snus undermines quit attempts but not abstinence: a randomised clinical trial among US smokers,” *Tobacco Control* 26(2):202-209, 2017. Biener L, et al., “Snus Use and Rejection in the United States,” *Tobacco Control* 25(4):386-392, 2016.

⁶⁰ Berman, ML, et al., “Consortium on Methods Evaluating Tobacco: Research Tools to Inform FDA Regulation of Snus,” *Nicotine and Tobacco Research* [Epub ahead of print], doi: 10.1093/ntr/ntx228, October 4, 2017.

⁶¹ Hatsukami, D, et al., “Randomised clinical trial of snus versus medicinal nicotine among smokers interested in product switching,” *Tobacco Control* 25:267-274, 2016.

⁶² Biener L, et al., “Snus Use and Rejection in the United States,” *Tobacco Control* 25(4):386-392, 2016, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4519419/pdf/nihms707341.pdf>.

⁶³ FDA Briefing Document, at 61.

⁶⁴ Cheng, Y, et al., “Patterns of Use of Smokeless Tobacco in US Adults, 2013–2014,” *American Journal of Public Health* 107(9):1508-1514, 2017, at 1513.

Reynolds acknowledges that dual use is the more common practice in its application: “the vast majority of users of Camel Snus, non-Camel snus, portioned moist snuff, loose leaf chew and loose moist snuff are dual/poly users of other combustible and/or non-combustible tobacco products.”⁶⁵ In referencing its own survey data and PATH data, Reynolds found that “Greater than 90% of Camel Snus users are dual/poly users of other combustible and/or non-combustible tobacco products.”⁶⁶

Studies from the years before e-cigarettes became popular show an increase in dual use of smokeless tobacco and cigarettes,⁶⁷ and Minnesota Adult Tobacco survey data show that the increase in smokeless tobacco use was largely due to current smokers using smokeless tobacco concurrently, not to smokers switching to smokeless tobacco.⁶⁸ Survey data show that multiple tobacco product use is common among youth and adult tobacco users,⁶⁹ and before e-cigarettes, dual use of smokeless tobacco and cigarettes was popular.⁷⁰

While *complete switching* to snus might “significantly” or “greatly” reduce smokers’ risk of certain smoking-related diseases, as Reynolds claims in its application, incomplete switching (dual use or merely cutting down smoking) keeps smokers’ risks of disease elevated. Reynolds downplays the health risks of dual use and cites two studies to claim that dual use of smokeless tobacco and cigarettes does not raise “unique health risks” separate from exclusive use of either product, and even that dual use shows “somewhat reduced risks.”⁷¹ It is important to note that one of the studies cited in the application was published by researchers working for Altria, and the other was funded by Altria and Swedish Match – companies that have a financial interest in increasing the use of smokeless tobacco, and, in the case of Altria, also maintaining the use of cigarettes. In 2009, Altria had marketed its own Marlboro Snus products in “convenient foilpack[s]” that “ride[s] perfectly alongside your smokes” because they were slim enough to fit

⁶⁵ Reynolds Executive Summary, at 168.

⁶⁶ Reynolds Executive Summary, at 109.

⁶⁷ Rath, JM, et al., “Patterns of Tobacco Use and Dual Use in US Young Adults: The Missing Link between Youth Prevention and Adult Cessation,” *Journal of Environmental and Public Health* 2012(679134):1-9, 2012, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3361253/pdf/JEPH2012-679134.pdf>. Boyle, R, et al., “Concurrent Use of Cigarettes and Smokeless Tobacco in Minnesota,” *Journal of Environmental and Public Health*, 2012.

⁶⁸ Boyle, R, et al., “Concurrent Use of Cigarettes and Smokeless Tobacco in Minnesota,” *Journal of Environmental and Public Health*, (2012).

⁶⁹ Kasza, KA, et al., “Tobacco-Product Use by Adults and Youths in the United States in 2013 and 2014,” *New England Journal of Medicine* 376(4):342-353, 2017.

⁷⁰ Substance Abuse and Mental Health Services Administration (SAMHSA), *The NSDUH Report: Smokeless Tobacco Use, Initiation, and Relationship to Cigarette Smoking: 2002 to 2007*, Rockville, MD: Office of Applied Studies, March 5, 2009, at 5. Tomar, SL, “Patterns of Dual Use of Cigarettes and Smokeless Tobacco among U.S. Males: Findings from National Surveys,” *Tobacco Control* 19:104-109, 2010, at 105. Rath, JM, et al., “Patterns of Tobacco Use and Dual Use in US Young Adults: The Missing Link between Youth Prevention and Adult Cessation,” *Journal of Environmental and Public Health* 2012(679134):1-9, 2012, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3361253/pdf/JEPH2012-679134.pdf>.

⁷¹ Reynolds Executive Summary, at 131.

inside cigarette packs.⁷² It remains in the company's best interest to publish studies that minimized health risks from dual use.

Dual or multiple product use is not a trivial concern. A substantial body of evidence supports the proposition that health benefits to an individual from quitting smoking occur only if the individual completely quits smoking. Merely reducing the number of cigarettes smoked or engaging in dual use of cigarettes and other tobacco products does not substantially reduce the health risk, as several U.S. Surgeon General's Reports and other studies have indicated that the risk of cardiovascular disease and other smoking-related diseases depends largely on the length of time a person smokes, not the number of cigarettes smoked.⁷³ According to the CDC, "If you only cut down the number of cigarettes you smoke by adding another tobacco product...you still face serious health risks. Smokers must quit smoking completely to fully protect their health – even a few cigarettes a day are dangerous."⁷⁴

Studies show that dual use can increase health risks because of continued smoking or perhaps added exposure from snus. Some smokers in a randomized control trial who were allowed to smoke and instructed to use Camel snus as they wished reduced their overall cigarettes smoked per day, but their biomarkers of exposure levels for several tobacco-related constituents did not change from before they began to dual use and were similar to the levels in exclusive smokers in the study. The researchers stated, "More importantly, smokers who used both cigarettes and snus...demonstrated increases in NNN in this study" which "[suggest] an overall increase in tobacco exposure from snus."⁷⁵

An older study concluded, "Because the health risks associated with cigarettes and ST are different in some respects, and because their effects may be additive if not synergistic, the concomitant use of cigarettes and ST may increase the risk of tobacco-attributable death and disease relative to use of either product alone."⁷⁶ A study from 2017 determined that reporting

⁷² Marlboro Snus website, screenshots taken April 16, 2009.

⁷³ U.S. Department of Health and Human Services (HHS), *How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease*, U.S. Centers for Disease Control and Prevention (CDC), Office of Smoking and Health (OSH), 2010, at 9. HHS, *Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General*, CDC, OSH, 2012, at 22, <http://www.surgeongeneral.gov/library/reports/preventing-youth-tobacco-use/index.html>. Schane, RE, Ling, PM, & Glantz, SA, "Health Effects of Light and Intermittent Smoking: A Review," *Circulation* 121(3):1518-1522, 2010. Tverdal, A & Bjartveit, K, "Health Consequences of Smoking 1-4 Cigarettes per Day," *Tobacco Control* 14(5), 2005. Hackshaw, A, et al., "Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports," *BMJ* 360:j5855, <http://doi.org/10.1136/bmj.j5855>, 2018.

⁷⁴ CDC, "Powerful new Tips from Former Smokers" ads focus on living with vision loss and colorectal cancer," CDC Press Release, March 26, 2015, <http://www.cdc.gov/media/releases/2015/p0326-tips.html>. See also: CDC, "Dual Use of Tobacco Products." <http://www.cdc.gov/tobacco/campaign/tips/diseases/dual-tobacco-use.html#ten>.

⁷⁵ Meier, E, et al., "A Randomized Clinical Trial of Snus Examining the Effect of Complete Versus Partial Cigarette Substitution on Smoking-Related Behaviors, and Biomarkers of Exposure," *Nicotine & Tobacco Research*, Advanced Access, April 11, 2019.

⁷⁶ Wetter, D, et al., "Concomitant Use of Cigarettes and Smokeless Tobacco: Prevalence, Correlates, and Predictors of Tobacco Cessation," *Preventive Medicine* 34:638-648, 2002.

health issues was more likely among people who used both smokeless tobacco and cigarettes compared to those who used only one product.⁷⁷

In addition to the potential additive health risks, dual use may keep smokers smoking longer, which also continues to elevate their health risks. Several studies have found that dual users have similar or lower likelihood of quitting or attempting to quit smoking compared to exclusive cigarette smokers.⁷⁸ One study has found that, while dual users were more likely to make a quit attempt compared to exclusive smokers, they tended to relapse more quickly compared to exclusive smokers, and had comparable 30-day abstinence levels to exclusive smokers.⁷⁹ Dual users of smokeless tobacco and cigarettes use smokeless tobacco to maintain their cigarette addiction, not to quit smoking,⁸⁰ and do not believe that smokeless products can help them quit smoking.⁸¹ One study found that smokeless users who used these products to cut down on smoking were no more likely to stop using cigarettes compared to those smokers who did not use smokeless tobacco,⁸² and another study found that smokers saw these products as temporary, rather than complete substitutes.⁸³

Because of the critical difference in health outcomes for those who completely quit smoking when they take up snus and those who use cigarettes and snus concurrently, it is essential that any modified risk claims for snus include clear and understandable statements to consumers advising them that any health benefits depend upon their switching entirely away from cigarettes. Moreover, because of the difference in the disease risk presented by Camel snus and that presented by other smokeless tobacco products, any such claims should make it clear that health benefits depend on consumers not using other smokeless products as well. Failure to

⁷⁷ Hernandez, SL, et al., “Relationships Among Chewing Tobacco, Cigarette Smoking, and Chronic Health Conditions in Males 18–44 Years of Age,” *Journal of Primary Prevention* 38(5):505-514, 2017.

⁷⁸ Schauer, GL, Pederson, LL, & Malarcher, AM, “Past Year Quit Attempts and Use of Cessation Resources Among Cigarette-Only Smokers and Cigarette Smokers Who Use Other Tobacco Products,” *Nicotine & Tobacco Research* 18(10):41-47, 2016. Klesges, RC, et al., “Tobacco Use Harm Reduction, Elimination, and Escalation in a Large Military Cohort,” *American Journal of Public Health* 100(12):2487-2492, December 2010, at 2490 (“Importantly, dual users were less likely to become tobacco abstinent than were smokers or smokeless tobacco users . . .”); Wetter, D, et al., “Concomitant Use of Cigarettes and Smokeless Tobacco: Prevalence, Correlates, and Predictors of Tobacco Cessation,” *Preventive Medicine* 34:638-648, 2002, (“Concomitant users were significantly less likely to quit using tobacco over the course of 4 years than were users of cigarettes or ST.”).

⁷⁹ Messer, K, et al., “Cigarette smoking cessation attempts among current US smokers who also use smokeless tobacco,” *Addictive Behaviors* 51:113-119, 2015.

⁸⁰ McClave-Regan, AK & Berkowitz, J, “Smokers who are also using smokeless tobacco products in the US: a national assessment of characteristics, behaviours and beliefs of ‘dual users’,” *Tobacco Control* 20:239-242, 2011, <http://www.ncbi.nlm.nih.gov/pubmed/21172853>.

⁸¹ McClave-Regan, AK & Berkowitz, J, “Smokers who are also using smokeless tobacco products in the US: a national assessment of characteristics, behaviours and beliefs of ‘dual users’,” *Tobacco Control* 20:239-242, 2011.

⁸² Kasza, KA, et al., “Cigarette Smokers’ Use of Unconventional Tobacco Products and Associations With Quitting Activity: Findings From the ITC-4 U.S. Cohort,” *Nicotine & Tobacco Research* 16(6):672-681, June 2014, <http://www.ncbi.nlm.nih.gov/pubmed/24376276>.

⁸³ O’Connor, RJ, et al., “US smokers’ reactions to a brief trial of oral nicotine products,” *Harm Reduction Journal* 8:1-10, 2011, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3032705/pdf/1477-7517-8-1.pdf>.

provide such information could mislead consumers into believing that dual use of snus and other tobacco products would confer a health benefit when in fact it would not.

Based on the evidence submitted by Reynolds, it is not at all clear that the proposed claim that switching completely from cigarettes to Camel snus will significantly reduce disease risk sufficiently conveys the key message that the health benefits from switching *depend* on complete switching from cigarettes and on exclusive use of Camel snus vs. use of other smokeless tobacco products.

- C. In projecting population-wide benefits from allowing modified risk claims for Camel snus, Reynolds relies largely on the Swedish experience, but no evidence has been presented to enable the FDA to conclude that the Swedish experience will be replicated in the U.S., even with modified risk claims.
 - i. Market differences in smokeless tobacco products available in Sweden and the U.S., including the way the products are regulated, may account for differences in snus use.

Because Swedish snus has been widely used in Sweden for many years, and because snus has constituted the vast majority of smokeless tobacco used in Sweden for many years, there exists a large data set for the evaluation of the health effects of Swedish snus in comparison with the health effects of cigarettes in Sweden. Snus has been available also in the United States and experience demonstrates that its availability has not led to widespread use. Thus, a reliance on the Swedish data is both arbitrary and inconsistent with the requirements of the statute.

It is important to note, however, that this experience exists only with respect to health outcomes in Scandinavia involving the use of Swedish snus itself. Because product standards that restrict levels of certain components in Swedish snus have been in place in Sweden for decades, the experience that Reynolds cites may not translate for use of U.S. smokeless tobacco products, including Camel snus and other snus products sold by other manufacturers in the United States. For instance, snus sold in Sweden must comply with maximum levels of certain toxicants and carcinogens, but no such standard currently exists in the U.S. As discussed earlier in these comments, the levels of NNN in snus products sold in Sweden are already below the maximum level proposed by FDA, while the levels of NNN in Camel snus currently exceed the proposed level.

The presence of other forms of smokeless tobacco that are more popular in the United States, but are not allowed in Sweden, could also affect how Camel snus modified risk messages are perceived and may make the Swedish experience inapplicable to the U.S. For example, given the variety of smokeless tobacco products that are more popular than snus in the U.S., Camel snus' modified risk message might be easily lost or ignored by smokers, or, even worse, non-tobacco users may mistakenly believe that the modified risk message approved for Camel

snus applies to other smokeless tobacco products and initiate use of these products, even though the risk profiles of such products are different.

Reynolds suggests - without proof - in its applications that, over time, exposure to the modified risk statements from Camel Snus will influence perceptions of relative risk among overall smokeless tobacco products compared to cigarettes, stating, “Indeed, education about relative risks of smokeless tobacco and snus versus smoking (in the form of Camel Snus modified risk advertising) has the potential to mitigate the prevailing misperceptions about relative risk of smokeless tobacco versus cigarettes.”⁸⁴ However, to the extent that the proposed Camel snus modified risk claims influence perceptions of risk for other smokeless tobacco products, this may lead, for example, to a greater risk of initiation of those other products.

For instance, Reynolds American also markets Grizzly moist snuff tobacco, which has the second highest market share in Nielsen-tracked channels⁸⁵ and in 2014 (the most recent available), it was most popular smokeless tobacco brand among 12-17 year olds.⁸⁶ Because the health risks associated with moist snuff products like Grizzly are greater than those from Camel snus, if the use of modified risk messages in Camel snus marketing increases the use of Grizzly or other smokeless tobacco products, particularly among youth and other vulnerable populations, such messages would have an adverse health impact on those populations.

- ii. Sweden’s restrictions on tobacco marketing may contribute to differences in snus use vs. the U.S.

It is also inaccurate to apply the Scandinavian experience to Camel snus when tobacco product marketing is prohibited in Sweden, while allowed in the U.S. This difference could affect the impact of the proposed modified risk messages on users and potential users; unlike in Sweden, where advertising plays no role in the establishment of consumer preferences.

Indeed, it is notable that Sweden has achieved high use rates for snus even without using the types of modified risk messages that Reynolds has proposed, because tobacco advertising in most media such as print advertisements and outdoor signage is not permitted in Sweden, though Internet and some point-of-sale advertising are allowed.⁸⁷ In the United States in 2017, the top five smokeless tobacco companies (including Reynolds American) spent \$718.3 million to advertise and market their products, nearly triple the 2005 expenditures (\$250.8 million), the year before Reynolds acquired a smokeless tobacco company and began marketing its own

⁸⁴ Reynolds Executive Summary, at 85.

⁸⁵ Wells Fargo Securities, *Nielsen: Tobacco All Channel Data Thru 3/23 - Cig Vols Decelerate Faster*, April 2, 2019.

⁸⁶ U.S. Department of Health and Human Services (HHS), SAMHSA Center for Behavioral Health Statistics and Quality, *National Survey on Drug Use and Health*, 2014. ICPSR36361-v1, Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], 2016-03-22, <http://doi.org/10.3886/ICPSR36361.v1>.

⁸⁷ 14-14b §§ Tobakslag [Tobacco Act] (Svensk författningssamling [SFS] 1993:581) (Swed.), available at <http://rkrattsbaser.gov.se/sfst?bet=1993:581>. English version available at <https://www.tobaccocontrolaws.org/files/live/Sweden/Sweden%20-%20SFS%202010727.pdf>.

smokeless tobacco products.⁸⁸ Tobacco companies also spent an additional \$8.6 billion to market cigarettes in 2017⁸⁹ – showing that these companies, including Reynolds American, are not ready to give up cigarette smokers to smokeless tobacco any time soon.

This difference may well account for distinctions in the way snus is used in Sweden as compared to how it would be used in the United States. In the United States, where spending on marketing cigarettes is far higher than that for smokeless tobacco and Reynolds has marketed its Camel snus products in ways that reinforce dual use rather than complete switching, it is not surprising that smokeless tobacco use patterns are different than in Sweden. The prevalence of dual use of smokeless tobacco and cigarettes has historically been higher in the U.S. than in Sweden,⁹⁰ as also mentioned in Reynolds' application.⁹¹ By contrast, most snus users in Sweden exclusively use snus.⁹²

- iii. Though TPSAC was not posed questions about the relevance of Swedish data in the Camel snus proceeding, TPSAC's conclusions about General snus in the Swedish Match proceeding provide no basis to believe the Swedish experience would be replicated in the U.S.

In considering the modified risk application filed by Swedish Match for its General snus products, TPSAC voted 6 votes “no,” one vote “yes,” and one abstention on this question: “Does the Committee believe that the epidemiological data from Sweden concerning tobacco use behavior provide relevant information on the likelihood that current tobacco users in the U.S. will switch to the use of these snus products?” Moreover, in the Swedish Match proceeding, TPSAC also cast 5 votes “no,” with 3 abstentions, on the question: “Does the Committee believe that the epidemiological data from Sweden concerning tobacco use behavior provide relevant

⁸⁸ U.S. Federal Trade Commission (FTC), *Smokeless Tobacco Report for 2017*, 2019, https://www.ftc.gov/system/files/documents/reports/federal-trade-commission-cigarette-report-2017-federal-trade-commission-smokeless-tobacco-report/ftc_smokeless_tobacco_report_2017.pdf. Data for top 5 manufacturers only: Altria Group, Inc.; North Atlantic Trading Company, Inc.; Reynolds American, Inc.; Swedish Match North America, Inc.; and Swisher International Group, Inc.

⁸⁹ FTC, *Cigarette Report for 2017*, 2019, https://www.ftc.gov/system/files/documents/reports/federal-trade-commission-cigarette-report-2017-federal-trade-commission-smokeless-tobacco-report/ftc_cigarette_report_2017.pdf [data for top 5 manufacturers only].

⁹⁰ Cheng, Y, et al., “Patterns of Use of Smokeless Tobacco in US Adults, 2013–2014,” *American Journal of Public Health* 107(9):1508-1514, 2017. Lund, KE, McNeill, A, & Scheffels, J, “The use of snus for quitting smoking compared with medicinal products,” *Nicotine & Tobacco Research* 12(8):817-22, August 2010, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2910876/pdf/ntq105.pdf>. Tomar, S, Alpert, HR, & Connolly, GN, “Patterns of Dual Use of Cigarettes and Smokeless Tobacco Among US Males: Findings from National Surveys,” *Tobacco Control* 19:104-109, 2010, <http://tobaccocontrol.bmj.com/content/19/2/104.full.pdf+html>. Agaku, IT, et al., “Use of Conventional and Novel Smokeless Tobacco Products Among US Adolescents,” *Pediatrics* 132(3):e578-86, September 2013, <http://pediatrics.aappublications.org/content/early/2013/07/31/peds.2013-0843.full.pdf>.

⁹¹ “[T]he vast majority of users of Camel Snus, non-Camel snus, portioned moist snuff, loose leaf chew and loose moist snuff are dual/poly users of other combustible and/or non-combustible tobacco products.” Reynolds Executive Summary, at 168.

⁹² Lund, KE & McNeill, A, “Patterns of Dual Use of Snus and Cigarettes in a Mature Snus Market,” *Nicotine & Tobacco Research* 15(3):678-684, 2013.

information on the likelihood that non-users of tobacco in the U.S. will initiate the use of these snus products?”

Finally, in its evaluation of the Swedish Match modified risk application, FDA found that the company had not demonstrated that “U.S. consumers would use Swedish snus in the same manner as consumers in Sweden and Norway (e.g. frequency or intensity of usage; exclusive use versus dual use with cigarettes); therefore, we cannot conclude that, as actually used by U.S. consumers, the products would substantially reduce the risk to smokers.”⁹³ Although the conclusions reached by TPSAC and FDA in the Swedish Match proceeding do not bind the agency in the Camel snus proceeding, they counsel great caution in assessing Reynolds’ claims based on the Swedish experience.

In order to evaluate the relevance of the behavior of individuals in different countries, it is necessary to take into account differences in culture, prior history, prior experience, laws and rules. There is no scientific basis for simply concluding that, because the population in one country responded to a product, or to how a particular product was marketed, in a particular way, that the population of another country will respond similarly. In light of the limitations noted by TPSAC and FDA on the use of Swedish data to predict the likely usage of snus modified risk products in the U.S., FDA’s decision in its recent PMTA order on IQOS, to rely exclusively on data from Japan and Italy in concluding that “the current evidence indicates low IQOS uptake by youth” in the U.S.⁹⁴ is, by any reasonable standard, arbitrary and impossible to defend from a scientific standpoint.

In fact, the FDA social science review of the IQOS application yielded “concerns with respect to: the lack of information about youth under age 18, as well as the lack of a discussion of submitted data’s applicability to youth and the lack of presentation of the data in stratified categories that would allow us to make inferences about youth”⁹⁵ Nevertheless, the Technical Project Lead disagreed with these concerns, relying entirely on data from Japan and Italy in predicting low youth IQOS uptake in the U.S., with no analysis of possible differences between the U.S. and those countries in their tobacco product markets, cultural factors, regulatory systems, etc. that could make invalid any prediction of the likelihood of youth uptake in the U.S. based on the experience in these other nations.⁹⁶ FDA granted the IQOS PMTA in reliance on the Japanese and Italian data. FDA should not make a similar mistake, rendering any such decision subject to judicial challenge, by relying on the Swedish experience with snus to grant the Camel snus MRTP.

⁹³ FDA, *Modified Risk Tobacco Product (MRTP) Application Technical Project Lead (TPL) Review*, <https://www.fda.gov/downloads/TobaccoProducts/Labeling/MarketingandAdvertising/UCM533233.pdf>, November 2, 2016, at 10-11.

⁹⁴ FDA, Technical Project Lead Review for PMI heated tobacco products, April 29, 2019, at 83.

⁹⁵ *Id.*

⁹⁶ *Id.*

VII. THE APPLICATIONS SHOULD BE DENIED BECAUSE TPSAC CONCLUDED THAT THERE IS CONSIDERABLE DOUBT ABOUT THE EXTENT OF THE INDIVIDUAL HEALTH BENEFITS OF SWITCHING FROM SMOKING CIGARETTES TO USING CAMEL SNUS AND ABOUT THE ACCURACY OF SOME OF THE PROPOSED MODIFIED RISK CLAIMS

Particularly as revealed in TPSAC's consideration of the Camel snus applications, there is considerable scientific uncertainty about the extent of the health benefits from switching completely from cigarettes to Camel snus and about the accuracy of certain of the modified risk claims proposed by Reynolds.

On the question of the extent to which the available scientific evidence substantiates the claims that smokers who switch completely from cigarettes to Camel snus can significantly reduce their risk of lung cancer and respiratory disease, TPSAC voted "yes" by 8-0. However, on the same question as to applied to oral cancer and heart disease, TPSAC was sharply divided, with 3 yes votes, 2 no votes and 2 abstentions.

Moreover, TPSAC was divided as to the scientific accuracy of some of the more general claims Reynolds' proposes to make:

- "...Camel snus contains less of the harmful chemicals than cigarette smoke." VOTE: 2 yes votes, 3 no votes, 3 abstentions
- "Smokers who use Camel snus instead of cigarettes can significantly reduce their health risks from smoking." VOTE: 1 yes vote, 5 no votes, 2 abstentions
- "Switching to snus means less risk for you." VOTE: 4 yes votes, 3 no votes, 1 abstention.
- "NO SMOKE=LESS RISK." VOTE: 6 yes votes, 1 no vote, 1 abstention.

As noted previously, under Section 911 a necessary obligation of the manufacturer is to demonstrate the accuracy of the modified risk claim being made; i.e., that the product will, in fact, "reduce harm and the risk of tobacco-related disease to individual tobacco users." Section 911(g)(4)(A) specifically requires FDA to consider "the relative health risks to individuals of the tobacco product that is the subject of the application." TPSAC's deliberations reveal considerable uncertainty about the relative health risks of Camel snus and the accuracy of some of the proposed modified risk claims.

Given Reynolds' failure to introduce meaningful data to allow an assessment of the risks of youth initiation, as well as the weakness of the evidence that marketing Camel snus as a modified risk product will actually cause smokers to switch completely rather than encourage

dual use, the uncertainty as to individual health benefits and the accuracy of the claims emerges as a further important factor counseling against the grant of these applications.

Respectfully submitted,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Heart Association

American Lung Association

Campaign for Tobacco-Free Kids