FOOD AND DRUG ADMINISTRATION (FDA)

Center for Tobacco Products (CTP)

Tobacco Products Scientific Advisory Committee (TPSAC) Meeting

January 22, 2026

TRANSCRIPT

This transcript has not been edited or corrected but appears as received from the commercial transcribing service.

Cristine Delnevo:
Good morning, everyone, and welcome to the January 26th meeting of the Tobacco Products Scientific Advisory Committee, or TPSAC. Thank you for joining us. I'm Cristine Delnevo, and the chair of the Tobacco Products Scientific Advisory Committee. Today, the committee will be discussing modified risk tobacco product applications submitted by Swedish Match USA for the products listed on the screen. Discussion will generally focus on evidence related to the relative health risks of the product, consumer understanding and perception of the applicant's proposed modified risk claim, and the potential public health impact of a modified risk marketing order. For the topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meetings will be a fair and open forum for discussion of these issues, and individuals can express their view on today's topic of discussion without interruption. Thus, as a reminder, individuals will be allowed to speak into the record only if recognized by the chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that their conversations about the topic at hand take place in an open form of the meeting. We are aware that members of the media are anxious to speak to the FDA about these proceedings. However, FDA will refrain from discussing the details of the meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topics during the break. And with that, I will turn the meeting over to Rachel Jang, the designated federal official to make administrative announcements, conduct roll call, and read the conflict of interest statement.

Rachel Jang:
Thank you, Dr. Delnevo. Good morning, everyone. I'm Rachel Jang, and it is my honor to serve as the designated federal officer for today's Tobacco Products Scientific Advisory Committee meeting. On behalf of the FDA, the Center for Tobacco Products, and the committee, I welcome everyone to today's virtual meeting. Next slide, please.

At this time, I would like to acknowledge the Office of Science and other individuals whose

contributions have been critical in preparing for today's meeting. The FDA staff in the Office of Science have put great effort into this meeting, including Dr. Benjamin Apelberg, the Deputy Director, Ms. Cristi Stark, the Associate Director, Dr. Cindy Chang, the Technical Project Lead for ZYN applications, Drs. Apoorva Rajan-Sharma and Amanda Fidalgo, Social Scientists, and Dr. Erin Ellis, the Modified Risk Tobacco Products Coordinator. You'll be hearing from some of them throughout the meeting.

I would also like to thank our advisors and consultant staff and supporting staff, including Ms. Jennifer Schmitz, the supervisor, Ms. Marcella Dolling, senior advisor, and Ms. Renee Wynter, lead program analyst and her team for their administrative support, as well as the Office of Ethics and Integrity for Managing Conflicts of Interest. And the Virtual White Oak Conference Center and our Office of Health Communication and Education for AV support.

Lastly, I would like to acknowledge our Office Director and Office of Center Director for their leadership and guidance. Dr. Matthew Farrelly, the Office of Science Director, Dr. Bret Koplow, the Acting Director of CTP, and Ms. Michele Mital, the Deputy Director of CTP. Next slide, please.

Please direct any press or media questions for today's meeting to HHS Press Room at 202-690-6343 or visit the website at the address displayed. This web address is also provided in the *Federal Register* Notice published on November 24th, 2025. The captioning and transcription services for today's meeting is provided by National Capitol Contracting.

Before we proceed with the roll call, I would like to mention a few housekeeping items related to today's virtual meeting format. For anyone joining us in the Zoom room, please keep yourself on mute, unless you're speaking. If you have your hand raised and are called upon to speak by the chairperson, please turn on your camera, unmute, state your name, and speak clearly so that your comments are accurately recorded for the captioning and transcription. Next slide, please.

We will now take a formal roll call of the committee members and temporary members. When it is your turn, please make sure your camera is on and you're unmuted. Then, state your name, organization, expertise, or role. When finished, you may turn off your camera so that we can proceed to the next person. Please see the member roster slide in which we will begin with the chairperson and the voting members. Dr. Delnevo, please go ahead and introduce yourself.

Cristine Delnevo:
Thank you, Rachel. Cristine Delnevo. I am the chair of TPSAC. I am from Rutgers University, and my area of expertise is population tobacco surveillance.

Rachel Jang:
Dr. Guy?

Mignonne Guy:
Can you see me right now? Okay, thank you. Good morning, I'm Mignonne Guy. I'm a professor in the Department of Family Medicine and Population Health at Virginia Commonwealth University, and my expertise is tobacco-related health disparities.

Rachel Jang:
Thank you. Dr. Jordt.

Sven-Eric Jordt:
Good morning. My name is Sven Jordt. I'm Professor of Anesthesiology, Pharmacology, and Cancer Biology at Duke University School of Medicine. I am also a member of the Cancer Prevention Program of the Duke Cancer Institute and a member of the Integrated Toxicology and Environmental Health Program at Duke. I'm a Vice Chair of the Tobacco Action Committee of the American Thoracic Society and a Fellow of the Society for Research on Nicotine and Tobacco. My expertise is in flavor chemicals in tobacco products and their effects on behavior and addiction.

Rachel Jang:
Dr. Popova.

Lyudmila Popova:
Good morning. My name is Lucy Popova. I'm a professor at the School of Public Health, Georgia State University. My expertise is in communication, marketing, and risk perceptions of various tobacco products.

Rachel Jang:
Dr. Rigotti.

Nancy Rigotti:
Hello, I'm Nancy Rigotti. I'm a professor of medicine at Harvard Medical School and director of the Tobacco Research and Treatment Center at Massachusetts General Hospital. My area of expertise is smoking behavior and changing that.

Rachel Jang:
Thank you. Dr. Robinson.

Risa Robinson:
Hello, can you see me? There we go. Hi, I'm Risa Robinson. I'm a professor of mechanical engineering at Rochester Institute of Technology. And my area of expertise is electronic cigarettes emissions and monitoring topography in the natural environment.

Rachel Jang:
Dr. Scout.

NFN Scout:
Morning, I'm Dr. Scout. My pronouns are they and he. I'm with the Cancer Network, and my area of expertise is with underserved populations, but I am the general population representative in this capacity.

Rachel Jang:
Thank you. Dr. Upson.

Dona Upson:
Good morning, I'm Dona Upson. I'm a professor of medicine at the University of New Mexico and a pulmonologist at the New Mexico Veterans Affairs Medical Center. I'm a member of the committee, and my expertise is in treatment of tobacco dependence. Thank you.

Rachel Jang:
Thank you, next we'll introduce the non-voting members on the committee. First, we'll go to our industry representatives. Dr. Bailey.

William Andy Bailey:
Thank you. My name is Andy Bailey, dark tobacco extension specialist with the University of Kentucky. My area of expertise is tobacco production at the farm level, and I serve as a tobacco grower representative on this committee. Thank you.

Rachel Jang:
Dr. Gogova.

Maria Gogova:
Good morning. I'm Maria Gogova. I am vice president and chief scientific officer at Altria, but today I'm serving in the role of industry representative for large tobacco manufacturers.

Rachel Jang:
Thank you. Dr. Madl.

Amy Madl:
Good morning, my name is Amy Madl. I'm president and senior principal health scientist with Valeo Sciences. My area expertise is toxicology, exposure assessment, and human health risk assessment. And I'm serving on this committee as a representative of small businesses.

Rachel Jang:
Thank you. We'll continue with the ex-officio members.

Alberta Becenti:
Good morning, my name is Alberta Becenti. I'm a public health advisor with Indian Health Service and my expertise is tobacco disparities among American Indian/Alaska Native population.

Rachel Jang:
Dr. Postow.

Lisa Postow:
Morning, everybody. My name is Lisa Postow. I am the chief of the Obstructive Lung Diseases Branch in the Division of Lung Diseases at NHLBI. And my expertise is tobacco-related lung diseases.

Rachel Jang:

Thank you. Finally, we'll introduce the expert consultants who are joining us today as temporary members. Dr. Benowitz.

Neal Benowitz:
I'm Neal Benowitz, Emeritus Professor of Medicine at the University of California, San Francisco. I'm a clinical pharmacologist and a cardiologist. My expertise has been the human pharmacology and toxicology of nicotine and nicotine products.

Rachel Jang:
Dr. Wackowski.

Olivia Wackowski:
Good morning, my name is Olivia Wackowski. I'm an associate professor at Rutgers University, and my areas of expertise are in tobacco product perceptions and communications.

Rachel Jang:
Thank you, Dr. Wachowski. Next slide, please. Thank you for your attention as I now proceed with reading the FDA Conflict of Interest Disclosure Statement for Public Record. We have 15 members participating in today's meeting. With the exception of the industry representatives, all standing and temporary voting members of the TPSAC are appointed as special government employees or regular government employees from other federal agencies and are subject to federal conflict of interest laws and regulations.

All committee members and consultants have been screened for potential financial conflict of interests, both personal and imputed, including those of their spouse, minor children, and for purposes of 18 U.S. Code 208, their employers. Interest reviewed include but are not limited to investments, consulting, expert witness testimony, contracts, grants, cooperative research and development agreements, teaching, speaking, writing, patents, royalties, and primary employment, current or under negotiation.

FDA has determined that all members of today's advisory committee meeting are in compliance with applicable ethics and conflict of interest requirements. Under 18 U.S. Code 208, FDA may grant waivers to SGEs or RGEs with financial conflicts of interest if the agency determines that the need for the individual's expertise outweighs the potential conflict or if the interest is not substantial enough to affect the integrity of the employee's service. For today's meeting, no waivers have been issued.

Committee members and consultants are reminded that if discussions extend to products or firms that are not listed on today's agenda and as FDA participants has a personal or imputed financial interest in such matters, that individual must recuse themselves. Any recusals will be noted for the record. For today's meeting, there were no recusals.

Finally, FDA encourages all participants to disclose any financial relationships with firms under discussion. This statement will be included in the official meeting transcript and made available for public review. This concludes the reading of the FDA Conflict of Interest Statement. Next slide, please. At this time, I would like to invite Dr. Bret Koplow for opening remarks.

Bret Koplow:
Thank you, Rachel. And thanks to all in attendance today for the Tobacco Products Scientific Advisory Committee, or TPSAC, meeting. I'm Bret Koplow, the Acting Director of the Center for Tobacco Products and it's a pleasure to welcome you all to today's meeting at which we will discuss the modified risk tobacco product, or MRTP, application submitted by Swedish Match for 20 of its ZYN nicotine pouch products.

While significant progress has been made in reducing cigarette smoking in the United States through comprehensive population-level strategies, more than 30 million adults in the U.S. still smoke cigarettes, and smoking remains the leading cause of premature death and disease nationwide. In fact, smoking causes about one in five deaths in the U.S. each year. That's a staggering statistic and one that we can and must reduce.

The MRTP pathway here at CTP helps the center achieve its public health goals by informing consumers of the relative harm of specific tobacco products, thereby helping people who use combustible products move down the continuum of risk. We know that many people who use tobacco products have misperceptions about the varying risks of tobacco products and those misperceptions—and those misperceptions may prevent them from switching to a lower risk alternative.

We also know that the concept of relative risk is complex. This complexity means it's important that adults who smoke have understandable and evidence-based information about the relative risk of different tobacco products, and that the information is delivered in a manner that minimizes any adverse impact on youth and other unintended audiences. The MRTPA pathway aims to do just that, ensuring information about relative risk is scientifically accurate, understandable, and will benefit the population as a whole.

TPSAC input is an important aspect of CTP's evaluation of MRTP applications. So, we appreciate everyone coming together today and continuing to implement this component of the process. I'd particularly like to thank the members of the public who are participating in today's meeting, either during the open public hearing or by providing written comments. Public participation in the regulatory process is an important part of the work FDA does. So, thank you to those who submitted comments and who will be speaking today.

The purpose of this committee is to provide valuable advice, information, and recommendations to the agency. CTP has put together some thoughtful and targeted questions to focus the committee's discussion today, and we have many staff here from the Office of Science who will be paying close attention to the discussions, which will be used to inform our evaluation.

Once again, many thanks to the committee members, our two additional guest consultants joining us today, the applicant, and the many CTP staff members who have worked for months to ensure a successful meeting. We look forward to a productive scientific discussion. Thank you.

Cristine Delnevo:
Thank you, Dr. Koplow. And with that, we're going to have our first presentation by the applicant. I'd like to introduce Ms. Keagan Lenihan, who is the vice president and chief external

affairs officer for Philip Morris USA. Ms. Lenihan, please proceed with your presentation and introduce the next presenter when finished.

Keagan Lenihan:
Good morning, everyone, and thank you to the FDA and members of the Tobacco Products Scientific Advisory Committee for the opportunity to discuss our modified risk tobacco product applications for ZYN nicotine pouches.

As mentioned, my name is Keagan Lenihan, Vice President and Chief External Affairs Officer for PMI U.S. Our team is here today on behalf of our U.S. affiliate and the applicant, Swedish Match USA. It's nice to see you all again. I have worked in public health and health care policy for more than 20 years, the majority in government settings, including at HHS and FDA. PMI's mission to improve public health by replacing combustible cigarettes with science-backed smoke-free products has led me here today. I truly understand and appreciate the need to accelerate the decline of cigarette smoking and the harm it causes. Together with your service on this advisory committee and with the FDA as the lead regulator, we can take an important step in achieving harm reduction.

It's important to remember why we have modified risk tobacco products and why we need to communicate to adults who smoke about these products. Cigarettes are still the number one cause of preventable death in America. Nearly 30 million adults smoke cigarettes, and each year smoking kills almost 500,000 Americans. Even though smoking may be less visible today, it's still the most common form of tobacco use. According to Nielsen data and other reports, combustible cigarettes represent roughly 70 percent of retail revenue from tobacco products. Accelerating the decline of cigarette smoking by encouraging switching to smoke-free products like FDA-authorized ZYN can dramatically benefit public health. But to do so, we must meet adults who smoke where they are and provide them with clear and accurate information.

While many adults want to quit smoking, and the best choice is total cessation, the fact is that more than 90 percent will continue smoking each year. We are here to change that statistic in line with the goals of Congress when it passed the Tobacco Control Act and established the MRTP process for developing less harmful products.

At PMI U.S., we are the leading innovator and manufacturer of FDA-authorized smoke-free products in the U.S. Since 2008, we've invested in developing, scientifically substantiating, and responsibly commercializing innovative smoke-free products for adults who would otherwise continue to smoke. Part of our commitment is reflected in the acquisition of Swedish Match in 2022. Swedish Match, like PMI U.S., is committed to a cigarette-free America. Their leading oral nicotine portfolio enables us to provide a broader range of smoke-free products for adults who smoke who would otherwise continue to smoke. We are committed to providing adults who smoke with access to FDA-authorized smoke-free products and more opportunities to switch completely away from cigarettes.

On January 16th, 2025, after nearly 5 years of review, the FDA authorized 20 ZYN products as appropriate for the protection of public health. FDA's scientific evaluation noted that due to substantial reduction in harmful constituents compared to cigarettes and most smokeless tobacco

products, ZYN poses a lower risk of cancer and other serious health conditions. Their evaluation also found that youth use of nicotine pouches remains low while sales of ZYN continue growing.

In addition to comprehensive product-specific data, the pre-market tobacco product applications included bridging evidence from Swedish Snus and in particular, General Snus, an FDA-authorized modified risk tobacco product to ZYN. FDA's decision included an assessment of the evidence for Swedish Snus, including the long-term health data, and applying it to ZYN nicotine pouches based on the following similarities: product format and use: consumers place the pouch between their lip and gum; chemical profile and toxicology: General Snus and ZYN have significant reduction in harmful and potentially harmful constituents compared to cigarettes; nicotine delivery: the nicotine absorption from General Snus and ZYN is similar to other smokeless tobacco products and nicotine replacement therapy; and use topography: consumers use a similar number of General Snus and ZYN pouches per day.

FDA determined in several areas of scientific review and overall that bridging from long-term data for Swedish Snus and General Snus to ZYN was appropriate to demonstrate the harm reduction potential of ZYN. Now we are seeking authorization of the following proposed modified risk claim for ZYN, which states: “Using ZYN instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” This claim will allow us to communicate directly to the millions of American adults who smoke about the potential health benefits of switching to ZYN.

The evidence and FDA's prior conclusions for ZYN show that the scientific evidence substantiates the proposed reduced risk claim. Due to the reductions in many harmful chemicals, switching from cigarettes to ZYN will lead to significant reductions in harm and the risk of tobacco-related diseases. Adults who smoke understand the proposed reduced-risk claim. The evidence shows that when exposed to the proposed claim, adults correctly understand the relative risk of ZYN compared to cigarettes. They also understand the risk associated with ZYN use. ZYN users switch from or significantly reduce their cigarette consumption. Marketing ZYN with the proposed claim will continue to encourage adults who smoke to completely switch. And, the proposed claim does not increase appeal to non-users. The evidence shows that marketing ZYN with a proposed claim does not increase intent among non-users.

Here is our agenda for today. First, I will provide a brief overview of ZYN and the MRTP statutory requirements. Second, my colleague, Dr. Tryggve Ljung, Global Medical Head of Oral Products, will review the clinical and non-clinical scientific assessment that substantiates the accuracy of the proposed claim. Third, Dr. Jessica Seifert, Head of Regulatory Insights for the U.S., will review the consumer understanding, perceptions, and behavior research demonstrating appropriate comprehension of the modified risk claim. She will also provide a brief overview of U.S. surveys monitoring underage use of tobacco products and nicotine pouches in particular. Fourth, I will review our responsible marketing practices, including how we propose to communicate the claim to consumers. And lastly, I'll conclude our presentation and be available for any questions you may have.

Let's begin with a short overview of ZYN pouches, including the product design, history, and key FDA findings when it authorized ZYN as appropriate for the protection of public health. I

will also review the statutory requirements for modified risk tobacco products. In the early 2010s, our commitment to innovation led us to create the next generation of smoke-free products building upon the proven harm reduction power of General Snus. We wanted to provide the exact same experience in nicotine delivery with even greater harm reduction potential for adults who smoke. ZYN nicotine pouches are made with plant cellulose fibers and contain pharmaceutical-grade nicotine derived from real tobacco leaves, fillers to provide the appropriate mouthfeel, stabilizers to maintain the proper moisture and pH balance, and sweeteners and flavorings to ensure adult consumers find a product that encourages complete switching from other, more harmful tobacco products. ZYN pouches are placed between the upper lip and gum where nicotine is absorbed orally. They are used much like General Snus, but importantly, are tobacco leaf-free.

ZYN was first marketed in the United States in 2014 in one state. Today, ZYN is available in all 50 states and over 40 countries globally. Our pre-market tobacco product application for ZYN were filed on March 4th of 2020. As previously mentioned, on January 16th of 2025, FDA issued their marketing authorizations for 20 ZYN pouches. FDA authorization included several important conclusions. First, switching from cigarettes to other smokeless tobacco products to ZYN is expected to lead to substantial declines in health risk. Second, ZYN was associated with meaningful levels of complete switching from other tobacco products. And third, the risk of initiating with ZYN, including initiation among youth, is low.

As FDA recently acknowledged, authorizations of scientifically substantiated products are an important moment for public health and something that should be celebrated. We agree. These authorizations represent a real opportunity for harm reduction for adults who smoke. To meaningfully address tobacco-related disease and death, the Tobacco Control Act recognizes three key complementary pillars: prevention, cessation, and harm reduction. Harm reduction is embedded in the statute, primarily through section 911, the Modified Risk Tobacco Products. This pathway was specifically designed to encourage and oversee industry efforts to develop and introduce modified risk products that can move adults who smoke away from cigarettes and down the continuum of risk.

The specific section of the statute we are focused on today is 911(g)(1). The statute gives FDA the authority to embrace harm reduction and the continuum of risk by verifying that products which claim to reduce harm and risk actually do so, by ensuring that adults are accurately informed about the product, and by making these products available to adult consumers. The standard requires that a modified risk tobacco product as actually used by consumers must significantly reduce harm and risk of tobacco-related diseases and benefit the health of the population as a whole, taking into account people who use tobacco products today and people who don't currently use them.

Starting with part A of the statute, the science in our application is a comprehensive package of both clinical and non-clinical data. As FDA concluded when it first authorized ZYN, due to the significant reductions in harmful chemicals, smokers who completely switched to ZYN reduced their risk of several tobacco-related diseases. And Part B of the statute requires that modified-risk tobacco products benefit the population overall. This requires us to assess the intended use of ZYN by both adults who smoke and who would otherwise continue to use cigarettes, as well

as the unintended use, meaning those who do not currently smoke or use tobacco or nicotine products today.

As we will discuss in further detail, our U.S. data shows that when given accurate product information, adult consumers understand the proposed claim. And at the same time, evidence shows that interest in ZYN from unintended individuals, whether that's non-users and in particularly youth, remains low.

On April 5th, 2024, we submitted our application seeking authorization for ZYN as a modified risk tobacco product with the reduced risk claim. Our application includes the following proposed claim that clearly communicates the result of our scientific assessment. “Using ZYN instead of cigarettes puts you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.”

To be absolutely clear, ZYN is not risk-free. It does contain nicotine, which is addictive. The best choice for any adult who smokes is to quit altogether. But for millions of American adults who smoke, the evidence shows that ZYN is a better choice than continuing to smoke cigarettes. During our presentation, we'll demonstrate how ZYN can lead to significant harm reductions and risk of tobacco-related diseases for adults who smoke.

I will now pass the podium to Dr. Ljung to review the scientific evidence that substantiates the proposed claim. Thank you. Dr. Ljung.

Tryggve Ljung:
Thank you, and good morning. I am Dr. Tryggve Ljung, Global Medical Head of Oral Products, and I will present the scientific evidence that supports granting the MRGO for ZYN nicotine pouches. As previously mentioned, the standard requires an evaluation of data demonstrating that these products present a lower risk of tobacco-related disease than combustible cigarettes. The FDA completed scientific evaluation of these ZYN products through the PMTA pathway last January and determined that they were appropriate for the protection of public health. I will present the chemical, toxicological, and epidemiological evidence demonstrating the potential health effects from switching to ZYN.

While nicotine pouch category is relatively new, long-term health effects can be predicted based on Swedish Snus data as long as some fundamental assumptions are met. For example, that nicotine patches contain the same or less amount of harmful and potentially harmful constituents or HPHCs, or that no additional harmful or potentially harmful constituents are present. Or that users are not exposed to higher levels of nicotine and that the product is used in the same way. After these assumptions, all of these assumptions have been met for ZYN, allowing the FDA to conclude that bridging the health effects from the extensive epidemiology data on Swedish Snus is reasonable.

As a reminder, in 2019, eight General Snus products were granted an MRTP. That authorization was then renewed in 2024 based upon scientific evidence of reduced levels of HPHCs and decades of Swedish epidemiology data demonstrating a decline in tobacco-related diseases over time. Altogether, this is known as the Swedish experience. The ZYN products we are discussing

today have a similar format and use topography as the General Snus products.

The main difference between the two is that General Snus is tobacco-based while ZYN is tobacco leaf-free. This is why the FDA emphasized that comparisons between ZYN and General Snus are appropriate in their PMTA review of ZYN. In fact, the appropriateness of bridging the potential health effects of ZYN from Snus, of General Snus products, was emphasized by the FDA in their previous evaluation. And here is the specific language of their conclusion. From a chemical and toxicological perspective, "comparisons between General Snus and ZYN are appropriate" and can be informative when evaluating the new product's impact on public health.

When assessing the potential risk associated with a tobacco or nicotine product, the chemical profile, specifically the levels of HPHCs, is a critical piece of scientific evidence. This graph compares HPHC reductions of both authorized General Snus in dark blue and seen in light blue, relative to a traditional reference smokeless tobacco product. While the Snus reductions in HPHCs are very substantial, the reductions with ZYN are even more pronounced. This data suggests that General Snus, which has already received and renewed its authorization, serves as a reasonable comparator for ZYN.

Furthermore, ZYN nicotine pouches contain considerably lower levels of HPHCs than the majority of tobacco nicotine products currently available on the market. I have included a comment from the FDA's TPL review on this slide, where they noted that, "The test data demonstrates that the new products contain reliably lower levels of the majority of HPHCs, including nicotine, free nicotine NNN, and NNK than Swedish Match General Snus products."

Now, the proposed claim will inform consumers that switching to ZYN from cigarettes will reduce the risk of many tobacco-related diseases. So while it's difficult to compare HPHC profiles across different routes of administration, in this case oral versus inhaled, you can see from the data that there is an average 99-percent reduction in the top nine HPHCs in ZYN compared to smoke from a reference cigarette.

After a thorough review of the HPHC data in the literature and in our application, the FDA's toxicological assessment reached an important conclusion. The toxicology review concludes that adults who smoke and switch completely to the new products are expected to experience reduced risk of cancer, respiratory toxicity, and cardiovascular toxicity. This finding strongly supports the proposed modified risk claim. In addition to this chemical analysis, we conducted a real-world study to look at biomarkers of exposure and potential harm. This study was a non-randomized design evaluating biomarkers among four groups: current daily users of nicotine pouches, tobacco-based Snus, and combustible cigarettes, and non-users of tobacco nicotine products. A total of 198 subjects participated. Those in the three nicotine user groups continued using their regular products ad libitum throughout the 14-day study period with assessments as shown here.

All oral products included in the study were manufactured by Swedish Match under consistent quality standards. The average nicotine content in the study’s pouches was slightly higher than ZYN. However, product components, manufacturing standards, and HPHC levels were all comparable. Let's start by looking at the plasma levels of three carcinogens found in cigarette smoke, the tobacco-specific nitrosamines NNAL and NNN, as well as 3-hydroxybenzo(a)pyrene,

following ad libitum use of nicotine pouches, snus, and cigarettes compared to nonusers.

There were no significant differences in NNAL or NNN levels between nicotine-pouch users and non-users. You can see this by comparing the NP bar with the no TNP bar in the two charts. Nicotine pouch users and nonusers had significantly lower NNAL and NNN levels compared to both snus users and cigarette smokers. There were no differences in biomarkers for BAP between nicotine pouch users, snus users, and non-users. And all three of these had markedly lower levels than cigarette smokers.

To summarize, as used by consumers under real-world conditions, users of nicotine pouches such as ZYN demonstrate significantly lower exposure to harmful and potentially harmful constituents compared to users of other tobacco products. As you know, successful switching requires adequate nicotine delivery. After 14 days of ad libitum product use, there were no significant differences in plasma nicotine levels among users of nicotine pouches, snus, or combusted cigarettes. This real-world study demonstrates that users of nicotine pouches experience enough nicotine support switching and similar exposure compared to snus users.

We also conducted a comparative PK study to assess abuse liability of ZYN. Both the three and six milligram ZYN products were associated with nicotine exposure, comparable or lower than the authorized General Snus products, as well as the market-leading moist snuff pouch. Although I won't go into that data here, the FDA concluded that, "Based on the information provided in the PMTAs, the abuse liability of the new products is lower than combusted cigarettes and is similar to smokeless tobacco products."

Now, I would like to spend a few minutes on the appropriateness of bridging from Swedish Snus data to ZYN. The FDA conducted an epidemiology review and concluded that bridging the published literature on the long-term health effects of Swedish Snus to these newer products based on similarity in user topography was appropriate. This means that the extensive evidence on Swedish Snus, which spans many decades of real-world use, health outcomes, and risk reduction can be applied to ZYN. And let me remind the panel of some key elements of the Swedish experience.

The reduced-risk claim for General Snus was reported by over 30 years of Swedish epidemiology data showing decreased cigarette consumption with the uptake of snus. This transition was associated with decreasing rates of tobacco-related disease in Sweden. While longitudinal data like this is not available for ZYN today, the product’s similar design, use patterns, and user populations makes the Swedish experience relevant.

ZYN has an improved toxicological profile to General Snus, so ZYN users face comparable or lower health risks than those using General Snus, and of course, significantly lower risks than cigarette smokers. The Swedish experience demonstrates the potential public health impact that can occur when a reduced-risk product is substituted for cigarette smoking. Let's stop to remember that Sweden has the lowest smoking rate in the European Union among males shown on the far left of this graph. And that has led to a real public health benefit as the country also has the lowest number of deaths attributable to tobacco across the European Union, again, shown by the blue bar on the left.

Let's also look at specific smoking-related diseases that are mentioned in our proposed claim. These are listed in the left-hand column in this forest plot. The vertical line represents the risk estimate for nonusers of nicotine and tobacco product set to one. Dark blue points represent risk estimate for Swedish Snus. Most data show no increased risk for mouth cancer, cardiovascular disease, or respiratory disease with only a few studies indicating small increases compared to nonusers. Gray points represent cigarette use.

Here, the contrast is very clear. Users of snus products, including the recently reauthorized General Snus, face substantially lower risk of cancer, cardiovascular disease, and respiratory disease compared to smokers. Given that ZYN products have even lower levels of HPHCs than General Snus, it is reasonable to conclude that ZYN poses even lower health risks. In fact, the FDA has considered this as well and concluded that "the new products have similar user topography but lower HPHC levels compared to Swedish Snus. The health effect of Swedish Snus represent an upper limit on the likely long-term health effects of the new products."

In conclusion, epidemiological evidence demonstrate that Swedish Snus carries significantly lower risk of cancer, cardiovascular disease, and respiratory disease compared to cigarette smoking. Chemistry and toxicology studies show that ZYN has an even lower risk profile than General Snus and far below that of cigarettes. Further, FDA's pharmacological evaluation found that ZYN abuse liability is lower than cigarettes and comparable to other smokeless tobacco products such as General Snus.

Importantly, FDA concluded that the health effects of Swedish Snus represent an upper limit on the likely long-term health effects of ZYN. Taken together, the scientific data, along with FDA's rigorous pre-market review, confirms that the claim, "Using snus instead of cigarettes, put you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis" is scientifically valid.

With that foundation established, I am pleased to introduce my colleague Dr. Seifert, who will present our Consumer Perception and Behavioral Studies.

Jessica Seifert:
Thank you, Dr. Ljung, and thank you to the committee for your time and attention this morning. My name is Dr. Jessica Seifert, and I am the Head of Regulatory Insights for PMI U.S. I will present the consumer understanding, perceptions, and behavior research as it relates to ZYN and the proposed modified risk claim.

As mentioned previously, the U.S. Food and Drug Administration authorized the commercialization of the proposed MRTP in January 2025. The agency made their determination based on evidence provided by Swedish Match, including the findings shared by my colleague, Dr. Ljung, showing that switching from cigarettes to ZYN will lead to significant reductions in harm and risk of tobacco-related diseases. Swedish Match also presented evidence demonstrating the potential benefit to adults who smoke or use smokeless tobacco, including that adults understand the modified risk claim; that most adults who smoke and then start using ZYN either switch to ZYN and stop smoking completely or reduce their cigarette use; and that the proposed claim does not increase appeal to nonusers and that ZYN use among youth remains low.

Today, I will review the evidence for these conclusions by leveraging data provided in the MRTPA and requisite amendments, as well as from data generated by independent scientists. I would like to first provide context around nicotine pouch use among adults in the U.S. In a secondary analysis of 2022 and 2023 data from the Tobacco Use Supplement to the Current Population Survey, Delnevo and colleagues generated the first prevalence estimates of daily nicotine-pouch use in the U.S. The 2022 current nicotine pouch use estimate from this secondary analysis is summarized here along with current smoking prevalence estimates from the same year. The current smoking statistics were generated by Stone and colleagues in a secondary analysis of 30 years of tobacco use supplement data.

In 2022, only 0.3 percent of adults, depicted by the blue bar, were using nicotine pouches every day or some days. However, 9.4 percent of adults were smoking cigarettes every day or some days. In other words, 31 times more adults in the U.S. were smoking cigarettes compared to using nicotine pouches in 2022.

But the national numbers may not tell the whole story. The five states here, as shown here, Maine, West Virginia, Iowa, Oklahoma, and Mississippi have the highest prevalence of current smoking across all 50 states, with prevalence ranging from 16.4 in Maine to 14.3 in Mississippi. While state-level estimates for current nicotine pouch use are not available, and variation is expected both within and between states, with nationwide nicotine-pouch use at 0.3 percent, we can expect that state-level prevalences are low, and, in some cases, likely not reliably detectable. This illustrates that the difference between nicotine pouch use and cigarette smoking observed at the national level likely masks even larger disparities observed at the state level.

I want to highlight two key takeaways from these data. One, among adults in the U.S., cigarette smoking, one of the leading causes of preventable morbidity and mortality, remains high, with some states across the U.S. experiencing increased burden relative to the nation as a whole. And two, there is a huge contrast between the prevalence of cigarette smoking and nicotine pouch use. This disparity highlights the persistence of cigarette smoking, but also the massive public health opportunity and need to communicate to adults who do not quit smoking that scientifically demonstrated lower-risk alternatives are available. So, we know that nicotine-pouch use among adults is low, but it is important to consider how people are coming to these products.

In the analysis of the 2022–2023 Tobacco Use Supplement data, Delnevo and colleagues found that nicotine pouch use was virtually nonexistent among tobacco-naive adults. To illustrate this finding, let's take a look at the unweighted percent of those who were tobacco naive across the ever use, current use, and daily use nicotine pouch use patterns. For reference, the authors define tobacco naive as those responding no to ever using cigarettes, e-cigarettes, cigars, smokeless tobacco, hookah, pipe, or heated tobacco.

On the left, we see that among those reporting having ever used nicotine pouches even once, nearly all at 98.2 percent had used a tobacco product previously. In contrast, 1.8 percent or 59 out of the 3,199 adults who reported ever nicotine pouch use were tobacco naive. Among the 484 adults reporting current nicotine pouch use, 95.9 percent had used a tobacco product previously, with 4.1 percent or 20 out of the 844 being naive to tobacco.

And lastly, among the 229 adults reporting daily nicotine pouch use, 94.8 percent had used a tobacco product previously, with 5.2 percent or 12 individuals out of the 299 being tobacco naive. When looking at daily use specifically, the authors found that the highest prevalence of nicotine pouch use was among those who had ever used smokeless tobacco, followed by those who had quit smoking cigarettes since nicotine pouches first became widely available in 2019.

These findings from a nationally representative, U.S.-based surveillance system, align with our internal research on adults who use ZYN, including the ZYN User Profile Study. The ZYN User Profile Study was a cross-sectional study among past 30-day ZYN users with the purpose of trying to characterize ZYN users and better understand how they were using the product following national market expansion. The study recruited 1,305 ZYN users who had a registered account in the ZYN Consumer Database, had opted in to receive communications from Swedish Match, and had used ZYN at least once a week in the past 30 days, irrespective of other tobacco or nicotine product use.

One of the measures captured in the ZYN User Profile Study was the first tobacco or nicotine product participants had used prior to using ZYN, which is summarized here. As you can see, nearly all ZYN users, 97 percent, had used a tobacco or nicotine product prior to using ZYN, with the majority, nearly 80 percent, reporting either cigarettes or smokeless tobacco as the product they first used prior to using ZYN. The remaining 17 percent have reported either other combustible tobacco products, a different nicotine pouch brand, or e-cigarettes, as the first type of tobacco or nicotine product they had used prior to ZYN.

The ZYN User Profile Study also investigated changes in cigarette consumption among those who reported smoking cigarettes at the time they first started using ZYN. Of the 1,305 total ZYN users in the study, 400 reported smoking cigarettes at the time they first started using ZYN. This figure summarizes the change in cigarette consumption among those 400 from when they first started using ZYN to the time of survey.

At the time of the study, of the 400 ZYN users who were smoking when they first started using ZYN, over half or 53.3 percent, had not smoked cigarettes during the past 30 days, depicted in the green. In addition, 26.8 percent reported having decreased their consumption by more than 50 percent, depicted in the dark blue, and 11 percent reported decreasing by 50 percent or less, depicted in the lighter blue below.

Now, let's take a closer look at those ZYN users who continued to smoke after starting ZYN. I've broken this group out into their own figure presented on the right. Of the 400 ZYN users who were smoking when they first started ZYN, 187 or 46.8 percent were still smoking at the time of survey. It is important to note that more than 80 percent had managed to decrease their cigarette consumption, with 23.5 percent decreasing by up to 50 percent, depicted in light blue, and 57.2 percent decreasing their consumption by over 50 percent, depicted in dark blue.

Next, I'm going to walk you through an additional analysis of changes in cigarette consumption by daily ZYN use intensity. When we looked at the 187 ZYN users who continued to smoke by their daily ZYN use, we observed that a higher percentage reported substantial reductions in their cigarette consumption if they also reported higher daily ZYN use. For reference, the bar on the

left is the same figure from the previous slide, Changes in Cigarette Consumption Among All ZYN Users Who Continue to Smoke After Starting ZYN. The bar to the right summarizes changes among ZYN users who reported using more than 10 pouches per day. Over three-quarters of these ZYN users reported reducing their cigarette consumption by more than 50 percent since they first started ZYN, and an additional 10.5 percent reported reductions up to 50 percent.

Next, let's take a look at the group reporting four to nine pouches a day. We see that 61.4 percent reduced their cigarette consumption by over 50 percent, with an additional 21.4 percent reporting reductions up to 50 percent. While the majority still reported substantial reductions in cigarette smoking, there were considerably fewer reporting reductions compared to the 10 pouch per day group.

Lastly, let's compare those reporting one to three ZYN pouches per day. Thirty-five percent of those who used one to three ZYN nicotine pouches per day reduced their cigarette consumption by over 50 percent after starting ZYN. This is a dramatic difference from the higher use groups. Taken together, we see that most ZYN users who continue to smoke after starting ZYN reduce their cigarette consumption, regardless of daily ZYN use intensity, and that higher daily ZYN use appears to promote greater reductions among these dual users.

At this point, we've seen that ZYN is used almost exclusively by those with a history of other tobacco or nicotine product use, predominantly among those who previously used either smokeless tobacco or combustible cigarettes. We've also seen that when ZYN is used by actual adults who smoke cigarettes, most switch completely, and those that do not reduce their cigarette consumption.

Now, let's take a look at their understanding of the claim. As noted previously, given the similarities in the products and the lower risk profile, the proposed modified risk claim for ZYN is the same as what was granted for General Snus. When presented with the evidence in the original General Snus MRTPA, the FDA stated, "the proposed claim did not lead smokers to believe that partial substitution would reduce their disease risk."

"The proposed claim enabled consumers to understand that dual use of General Snus with cigarettes is more harmful than exclusively using General Snus." So, consumers and adults who smoke understood the claim pre-market, but what about post-market?

To refresh our memories a bit, here are findings from the post-market General Snus Patterns of Use Study presented to this committee during the General Snus renewal meeting back in June 2024. When participants were asked how many cigarettes can be smoked in addition to using General Snus to maintain a lower risk of diseases, over 80 percent of General Snus users selected zero cigarettes, and they did so consistently across the 24-month follow-up period, as shown by the green bars. This demonstrates that consumers continue to understand that to maintain a lower risk of disease when using the modified-risk tobacco product, they must not smoke any cigarettes.

Okay. So consumers, when exposed to the claim, understand what to do to obtain the reduction

in risk when using a modified risk product, but how might the claim impact adults' perceptions of and intentions to use the product? In 2024, PMI, on behalf of Swedish Match, conducted the ZYN Perceptions and Likelihood of Use Study to evaluate the impact of the modified risk claim. The study recruited a total of 3,450 adults belonging to five tobacco or nicotine product use groups: current established smokers, former established smokers, and other tobacco or nicotine product users not using cigarettes or smokeless tobacco, current established smokeless tobacco users, as well as two separate groups of adults who had never established tobacco or nicotine product use, a general sample of adults ages 21 years and older, and an oversample of young adults ages 21 to 24 years old.

Participants were assigned to either the control group, where they were exposed to a ZYN nicotine pouch product concept, similar to a point of sale display—depicted on the left-hand side of the slide—or the test group, where they exposed to a similar but different version of the product concept where the claim language was included. The dotted line box on the control version shows where the claims was added for the test condition.

Participants were presented with health conditions related to the claim and asked, what impact do you believe using ZYN on a daily basis would have on your risk of getting the following, sometime during your lifetime, because you used ZYN? For each health condition, participants could select 1, no risk, to 5, very high risk. The figure on this slide summarizes the average perceived risk scores for each claim-related health condition among those assigned to the test condition.

Starting with the never-established tobacco or nicotine product users on the left-hand side, we see that both groups perceived that if they were to use ZYN on a daily basis, they would have a moderate to high risk of developing emphysema, chronic bronchitis, lung cancer, stroke, heart disease, or mouth cancer.

Looking next at the former established smoking and other tobacco or nicotine use group exposed to the claim, added to the right-hand side, we see like the never established use group, they also associated daily ZYN use with risk of developing any of the six health conditions included in the claim.

Finally, while current established smokers and current established smokeless tobacco users, the last two groups added on the right, reported lower perceived risk scores compared to the other groups, it is important that they did not perceive that daily use of ZYN would completely remove their risk of developing any of claim-related health conditions.

So, regardless of current or historical tobacco or nicotine product use, adults exposed to the claim understood that using ZYN is not risk-free. In addition to perceived risk of using ZYN, the study also evaluated the impact of the claim on intention to use ZYN across all five study groups. Intention to use was measured with the Juster scale, which provides estimates of the probability that a population will perform a certain behavior by a future time. Prior to exposure, participants were presented with a list of tobacco or nicotine product categories, including nicotine pouches, and were asked how likely or unlikely are you, yourself, to use each of the following products on a regular or ongoing basis? For each product, they could then indicate their likelihood on a scale

of 0 to 10, with 0 being no chance, almost none, and 10 being certain, practically certain.

Pre-exposure scores for each test condition in the three nonuser groups, general and young adult never established tobacco or nicotine product use groups, and the former established cigarette smokers and other product use group are shown in the light blue bars. Participants were asked the same question after exposure to the claim, with ZYN added to the product list. These scores are shown in the dark blue bars, neither of the two never use groups on the left-hand side of the chart reported current intention to use pouches or future intention to ZYN, regardless of exposure to the claim. The former established smoker and other product use group on the right were similar, although participants in this group reported a very slight possibility in the future that they would use ZYN, but this was irrespective of exposure to the claim.

The findings from this study demonstrate that nonusers have negligible to no intention to use ZYN regardless of exposure to the modified risk claim. The only groups demonstrating any intention to use nicotine pouches or ZYN were the current established smokers and current established smokeless users. While there was limited impact following a single exposure to the claim on intention to use ZYN, demonstrated by no differences between the test or control conditions in either group, there does appear to be a potential effect of exposure to ZYN product information. This is shown by the increase between the current likelihood estimate captured prior to exposure, the light blue bars, and the future likelihood estimate captured after exposure to the stimuli, the dark blue bars.

Finally, let's take a look at nicotine pouch use among youth in the U.S. Data from the National Youth Tobacco Survey has shown that since 2014, youth tobacco use of any kind has declined 67 percent, with 24.6 percent in 2014 to 8.1 percent in 2024. Further, combustible cigarette use has declined by approximately 85 percent, with 9.2 percent in 2014 to 1.4 percent in 2024. These declines can almost certainly be attributed to the tremendous public health efforts over the last decade, including Tobacco 21, enacted in December 2019, which raised the minimum purchasing age for tobacco and nicotine products to 21 years.

Nicotine pouches, launched in 2014, were first included in the NYTS in 2021. And observations since have shown low use uptake with prevalence of past 30-day use among middle and high school students at less than 2 percent. Monitoring the Future shows similarly low prevalence of nicotine pouch use across grades. Further, the survey also captures data on frequency of use, which provides helpful context to the past 30 day nicotine-pouch use observed.

While 2025 use occasion data are not yet available, in 2024 we see that among high school seniors, most, 96.5 percent, reported no nicotine pouch use occasions in the past 30 days. A slim minority reported any past 30 day nicotine pouch use, and less than 1 percent reported using nicotine pouches on 10 or more occasions in the past 30 days. Importantly, the most frequently reported use occasions, 1.8 percent of high school seniors, were 1 to 2 nicotine-pouch use occasions in the last 30 days.

Taking all of this evidence together, we see that adults understand the modified risk claim. They understand that adults who smoke need to completely switch and that ZYN use is not without risk. Further, ZYN is being used by adults with a history of tobacco use, predominantly by those

with a story of smoking cigarettes or using smokeless tobacco. We also see that most adults who smoke cigarettes and start using ZYN either stop smoking completely or decrease their cigarette consumption. And, ZYN has low appeal among nonusers, including adults who do not use tobacco products and youth.

With that, I will now hand the podium back over to Ms. Lenihan, who will review our responsible marketing practices and conclude the presentation.

Keagan Lenihan:
Thank you, Dr. Seifert. Now let's turn to how we responsibly market to legal-age adults who smoke and encourage complete switching from cigarettes to ZYN. First, it is important to understand why we market our smoke-free products. Cigarettes are still the leading cause of preventable death in America. They cause nearly 500,000 deaths a year, which is over 1,300 a day. At the same time, misperceptions about nicotine, harm reduction, the continuum of risk, and the availability of FDA-authorized smoke-free products persist. These misperception prevent many adults who smoke from making a change.

As we've seen from FDA's assessment and the evidence presented by my colleagues, ZYN presents a significant opportunity for harm reduction for adults who smoke. Standing in the way of this opportunity is the fact that awareness of these products among adult smokers remains very low. To see real harm reduction realized in the U.S., we must inform adults who smoke, and to inform adults to smoke, we must meet them where they are, in the real world.

PMI U.S. is committed to communicating accurate information about smoke-free products to adults who smoke, and we do this in a way that responsibly encourages and empowers them to leave cigarettes behind. Our commitment to responsibility is grounded in robust safeguards designed to help prevent underage exposure and align with regulatory requirements. Only adults age 21 and older should have access to tobacco and nicotine products. Our under 21 access prevention efforts rely on these key pillars. First, responsible marketing practices. We direct our marketing and advertising to current nicotine consumers age 21 years and older. Second, responsible retail support. We work with retailers, regulators, and other partner organizations to promote responsible retail practices and prevent underage access to age-restricted products. And third, real-world monitoring and engagement. We regularly engage with regulators and legislators, and we monitor social media, traditional media, scientific developments, illicit trade, and other government resources to ensure our practices stay informed and up to date.

Our products are intended for the 45 million existing nicotine consumers age 21 and older in the U.S., including the nearly 30 million adults who continue to smoke combustible cigarettes. Our commitment to responsibility is reflected in the following marketing guidelines. We direct our marketing of all products to those age 21 and over. We limit our social media presence to platforms that enable age-restricted controls. We require that our advertising features only individuals age 35 years and older. We do not pay social media influencers to endorse our products. We enforce rigorous online age verification for our branded websites. And we require ID checks at the door for all of our own events to confirm that all guests are 21 and older, as well as any one-on-one product discussions or trials at all events.

ZYN has been on the market since 2014, providing FDA with over a decade of real-world visibility into our marketing practices. FDA's 2025 authorization of ZYN as appropriate for the protection of public health included reviewing and assessing our submitted marketing materials, labels, and all the channels used, as well as assessing how they will impact tobacco use behavior on the population as a whole. FDA's authorization of ZYN noted that our marketing plans were directed towards our target audience and that our marketing plans included measures designed to limit youth exposure.

In addition to our own responsible marketing practices, we comply with FDA's comprehensive post-market reporting requirements. This includes providing FDA with a final full-color advertising, marketing, and/or promotional materials; a summary of all formative consumer research studies related to new labeling, advertising, marketing, and promotional materials; a summary of the products labeling, advertising, and marketing, and promotional materials; a description of all advertising and marketing plans; and an analysis of the actual delivery of those advertising impressions.

These requirements include reporting of digital media, such as owned digital properties, shared digital media, and paid digital media. This collaborative process and ongoing oversights helped ensure ZYN continues to meet the APPH standard. Now let's look at how we plan to communicate the ZYN claim to our intended audience.

We will use these five channels to communicate the proposed claim. And we will use the same safeguards that we employ in our marketing to limit youth exposure. These channels include the ZYN.com website, which includes independent age verification, with third party systems to identify, confirm the age of every visitor, point of sale materials at retail, email and direct mail communication to age 21-plus age-verified consumers, print and digital advertising where 85 percent or more of the audience is 21-plus and through digital platforms such as social media and digital marketing where we can use age restricting capabilities to communicate to 21-plus consumers. The FDA is aware of all of these channels and has ongoing oversight of our use of these channels. And as a part of our MRGO, we will continue to comply with FDA's requirement for all marketing materials and the use of the proposed claim.

The proposed claim speaks directly to adults who smoke and informs them about the potential benefits of switching to ZYN as a modified risk tobacco product. The proposed claim states that “Using ZYN instead of cigarettes puts you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” This is the same modified risk claim that was authorized for General Snus in 2019. It was largely based on decades of epidemiology and was renewed in 2024. FDA's scientific review confirming ZYN’s even lower risk profile and the appropriateness of bridging ZYN to General Snus suggests that the proposed claim is applicable to ZYN.

As FDA recently acknowledged, adults who smoke need accurate information about different tobacco products and the relative risks associated with them to make informed decisions that can impact their health. We agree. We need to provide adults who smoke with accurate science-based information about ZYN's reduced risk profile and empower them to make informed decisions. The reduced risk claim is a critical lever for encouraging adults who continue smoking

today to switch to ZYN, a product with significantly less risk of cancer and other smoking-related diseases.

I want to close by highlighting a few key takeaways from our presentation today. As you have heard, the FDA has already authorized ZYN as appropriate for the protection of public health. Today's meeting is about the standard Congress set in 2009 for modified risk tobacco products and the importance of information and harm reduction for adults who smoke. Based on the FDA's comprehensive review of the evidence presented today, we think the conclusions are clear. The scientific evidence substantiates the proposed reduced risk claim because ZYN significantly reduces exposure to harmful and potentially harmful constituents, switching to ZYN from cigarettes will substantially reduce health risks, including cancer, respiratory toxicity, and cardiovascular toxicity.

Adults who smoke understand the reduced risk claim. They understand the health risk of using ZYN. They understand that risks associated with ZYN are lower compared to smoking, and they understand the importance of fully switching from cigarettes. ZYN users completely switch from or reduce their cigarette consumption, and marketing ZYN with a proposed reduced risk claim will continue to encourage adults who smoke to completely switch. And that the evidence shows that marketing of ZYN, with the proposed reduced risk claim, does not increase appeal to nonusers. Since ZYN was first launched in 2014, our responsible marketing practices help ensure that ZYN is used by our intended audience, adults age 21 years and older who smoke.

The scientific evidence presented today demonstrates the substantial harm reduction potential of ZYN with the reduced risk claim. And it supports the conclusion that the modified risk application should be granted. Adults who smoke have the power and the ability to make decisions regarding their tobacco product use and experience a meaningful impact to their health, but only if they have accurate and reliable information on the relative risks of tobacco products—tobacco and nicotine products.

For years, stigma and shame have been relied upon to change adults who smoke, and the results are clear. Nearly 30 million adults still smoke cigarettes in the United States. We can change this statistic in years to come by informing and empowering adults who smoke to make a change and reduce their risk. The MRTP pathway is critical to ensuring these adults have the information they need to make informed decisions.

In closing, I'd like to thank the committee, the FDA, members of the public, and our team for the collaborative effort behind the innovation and scientific evidence that supports these important MRTP applications, and what that effort could mean for adults who smoke. We look forward to continuing the discussion, and I'm now happy to answer any questions that you may have. Thank you.

Cristine Delnevo:
Thank you. We're going to move into a period of clarifying questions, and I'd like to start with one. So the marketplace does look quite different than it did even 1 or 2 years ago, with increased sales for nicotine pouches across a variety of brands and the NYTS data is a little outdated in terms of what's available and so, I'm wondering, especially given that there have

been disruptions to national surveillance systems to have that data come out, what other data might PMI use to kind of monitor youth uptake, potential youth uptake of their product?

Keagan Lenihan:
We continue to rely on national surveys. We'd love to see NYTS be released for the 2025 data. We've looked at the preliminary data around Monitoring the Future. Everything that we've seen so far that's come out still suggests that youth use is low. We haven't seen an uptick on youth numbers across the board, but we continue to monitor.

Cristine Delnevo:
Thank you. Dr. Jordt.

Sven-Eric Jordt:
Thank you. I have a question about the products included in the MRTP application. I recently came across these new ZYN products. These are holiday-themed products that, in terms of their flavors, mojito, espresso, and lime, et cetera, strongly appeal, in my opinion, to children and young adults. I would like to know how ZYN can really differentiate these. These products are not included in the MRTP. They don't have a PMTA. How can ZYN make sure consumers really understand that these products do not have an MRTP if these are granted and others do? And will ZYN market similar products in the future based on seasonal themes?

The other products I recently saw are these. And these are in a footnote in the MRTP application. These are ZYN Chill and Classic, I believe. Can you clarify why you want to market ZYN Chill as ZYN Classic? Is this to bypass state regulations on flavors? Please clarify that. The product strategy is really confusing. And I'm not sure if customers will really understand what the MRTP is for and if all products or not are covered by MRTP. Thank you.

Keagan Lenihan:
Thank you for the question. Just to clarify, any ZYN product on the market today does have an MGO. All of the SKUs that we have on the shelves in retail stores today are ZYN FDA-authorized products. Each and every ZYN offering appearing there has a marketing granted order. Not every adult smoker is the same. They have different needs, understanding, and motivation of preferences. Any types of limited-time offers or promotions are just designed to raise awareness of 21-plus consumers and reach adults who smoke. We try to take every opportunity we can for harm reduction and give adults more access. We view Smooth and Chill as unfavored varieties, and they're marketed that way.

Sven-Eric Jordt:
Thank you. I think this is really confusing, but thanks.

Cristine Delnevo:
Dr. Popova.

Lyudmila Popova:
Thank you. The presentation talked about Swedish experience, which is in general, there's a lot of talk how it shouldn't be used, but we have an American experience with General Snus. So

since it's been marketed with MRTP, with modified risk claim, which was authorized in 2019, have the smokers in the U.S. been informed and empowered and made correct decisions to switch? And if not, why not?

Keagan Lenihan:
Thank you for the question. As you recall from the renewal MRTP discussion in 2024, there was a very limited availability to see the claim of General Snus when it was first authorized in 2019. It was hidden, kind of, in the basement of the website. Since the renewal, we have been given the opportunity to expand the use of that claim outside of where it was originally designated in 2019, which we believe will provide much better visibility to the adult consumer around the General Snus claim, but it's still a little early to see any data to suggest how that claim is being used and if it's having any effect to have change. The claim that we're going after today with ZYN, I think will give us a much broader way to reach the adult consumer and move them down the continuum of risk.

Cristine Delnevo:
Dr. Scout.

NFN Scout:
Good morning. So a few questions. First of all, considering the Tobacco Control Act requires that there's product-specific analysis, I'm just curious as to why it is we were only provided with dual-use information deriving from Snus and not from ZYN itself. And I'll go through all my questions first and then you can answer them all.

Second of all, I just want to confirm that in the specific ZYN study, there was no breakout of ZYN use. It was simply other tobacco products. I'm curious as to why that was not something that was considered. And then also I understand in that study that the young adult oversample was simply for nonusers. I'm particularly concerned about other tobacco product users in that young adult category. So I'm curious as to why that was a deleted sample. And then, well, it's rolled into all users, but it's not something that was oversampled.

And then last, I think probably the biggest issue here is as we see from, like, the *New York Times* story about the wild explosive growth in marketing to young adults through a lot of these social channels. I haven't yet heard you talk about counters to that, except that you're saying like it's only for adults, but if there is an existing social campaign that is very aggressively hitting young adults, I would really like to hear what kind of counters could take that campaign away or neutralize it in some manner.

Keagan Lenihan:
So let me start with a couple of your questions, and I might yield to Dr. Seifert to come up and talk a little bit about the breakout of the ZYN use and the young adult study specific to your question. But first around the kind of the dual use and the bridging data. I do think that—if you can pull up slide one. There's a lot more epidemiology data when it comes to General Snus because it's been on the market for 30, 40 years versus ZYN. We only started marketing in 2014 in a limited capacity. I think the FDA recognized that this was reasonable to make that bridge. This is something FDA does across all product centers, bridging. So that's why we've used that.

And then when it comes to marketing to young adults, you know, there's user-generated content is one thing. We don't control that. It's not something, as I mentioned before, we don't use social media influencers. We continue to monitor these types of behaviors and try to take down when we can, when there's misuse or abuse of the product. But this is a conversation I think needs to be much broader than just PMI. I think FDA plays a role here, policymakers play a role here, the legislature plays a role here, and clearly youth are being exposed to products outside of nicotine that are also not good for them. So there's something I think broader conversation that needs to happen there. But we will continue to monitor that and do takedowns that we can. And now I'm going to turn it over to Dr. Seifert to talk a little bit about your other questions. Thank you.

Jessica Seifert:
Hello, thank you, yes. So regarding, I believe you're speaking to the Perceptions and Intentions to Use Study. This study was designed to evaluate the impact on the claim on key populations. So those being those who we would like to see the claim, so current adult smokers, current smokeless users, and those we would like to, if they see the claim, not want to use it. So that would be those folks who were formerly smoking, those who are using other tobacco or nicotine products, those who are never established tobacco users, as well as, you know, specifically those who are younger, so the 21- to 24-year-old category. So, the determinations of those groups was wholly based on the purpose of the study to evaluate the impact of the claim on intentions to use perceptions, et cetera.

NFN Scout:
So that means there's no information on young adults who are currently using other tobacco products from that study, correct?

Keagan Lenihan:
Sorry. Do you mind repeating your question one more time?

NFN Scout:
So that means you can see no information from that study on young adults who are currently using something like ZYN. So in other words, young adults have a comparison of ZYN with modified risk, ZYN without modified risk. Is there any information that can be gleaned from that study as far as their intention to use?

Jessica Seifert:
Thank you. The purpose of the study was designed specifically to evaluate the impact of the claim on key populations. So those who are using ZYN, we would hope that they would have seen the claim. And obviously from our data that we've showed, they understand it. So, the point would be to evaluate the impact of the claim on those key populations: current smokers, former smokers, never tobacco users.

Cristine Delnevo:
I'm just going to piggyback on Scout's question. So could you, though, for example, do a subgroup analysis of young adults who are e-cigarette users? We are seeing in the data that a lot of nicotine pouch users not only have a history of cigarette smoking, some of them also have a story of e-cigs. And cigarette smoking is very, very low in young adults generally. And so would

it even be possible to do a subgroup analysis of that with the data you have?

Keagan Lenihan:
That's certainly something we can explore in the future, and if we're awarded the availability of the claim, then we're happy to work with FDA on providing that data in the future.

Cristine Delnevo:
Thank you. Dr. Wackowski.

Olvia Wackowski:
Hi, so I had two clarifying questions. So, one is pertaining to the marketing plans. If you could clarify whether the claims would be on the product packaging, and if you could say a little bit more about the plans to market at the point of sale. I think of the channels you showed, that's the one that isn't generally age-gated. And then the second question area that I had was about the perception studies. So, you had designed this perception study for this application, collecting new data about ZYN, except for the outcome about comprehension about the need to switch. And only seemingly that important outcome was relied on the General Snus study. And I was just wondering why not, in the context of the study, you were doing for this application also ask about the switching comprehension issue. And if I recall from the General Snus application that stimuli with a video was a bit different than kind of this sort of static ad, and so comprehension might be a little bit different. Thank you.

Keagan Lenihan:
I'm going to try to address all three of your questions. If I don't, just let me know and I'll jump back in. So starting with market plans, at this time, we do not plan on putting the claim on the can, just in advertising promotions and then also at point of sale and some of the other—maybe pull up slide one—using the existing channels that we already use today in marketing the—when it comes to plans around retail and using the claim, obviously it is, the claim itself is specifically targeted to smokers, right? So we're saying if you switch from ZYN from cigarette smoking, you can reduce your cause of cancer, respiratory and cardiovascular disease. So you're speaking to the smoker community that's walking into retail there.

And then when it comes to the perception study in the application, remember this is—these in the study, these folks were only—they only got to view the claim one time. So changing behavior is never going to happen when you see this one time, it's going to have to take a repeated access and exposure to the claim, which is why we'd like to use all of the additional channels in marketing to ensure that adult consumers of cigarettes continue to see that they could markedly reduce their risk of any of those diseases that I mentioned earlier, if they switch to a product like ZYN. So that's where we hope to use the claim.

Cristine Delnevo:
You good, Olivia?

Olvia Wackowski:
I mean, I don't think it really answered the last question about why not ask about switching comprehension in the perception study that was conducted for ZYN versus relying on the

previous General Snus.

Keagan Lenihan:
Okay, well, I'm happy to ask Dr. Seifert here to come up and ask if there's any additional evidence to support.

Jessica Seifert:
Hello, thank you so much. I appreciate the question. So with the specific comprehension piece, so do adults who are exposed to the claim understand that in order to get the reduction risk, they have to stop smoking completely? So, this was evaluated twice. So, first in the General Snus premarket application and results from that demonstrated that adults, when they were exposed to the claim, they understood what they needed to do to get the reduction in risk. The second piece, this was evaluated again in post-market. Again, results demonstrated that adults when exposed to the claim understood what they need to do to get the reduction in risk. And then thirdly, there's an entire body of research and evidence, scientific literature that demonstrates that exposure, including repeated exposure to the claim, specifically about ZYN, when adults are repeated exposure to the claim, they understand what they need to do to get a reduction in risk. So with that, the purpose of our study was to really focus on the impact on the claim on perceptions and intentions to use among those key populations.

Cristine Delnevo:
Thank you. In the interest of time, we have—I'm going to ask on Dr. Benowitz, and then we are going to move to a break. Neal.

Neal Benowitz:
Yes, one quick question. Just to follow up on the chair's comment, smoking prevalence among younger people is quite low and dropping quickly. The big target populations are really older smokers, 35, 50 and older and they're the people at greatest risk. Have you developed any marketing that should go to those high-risk groups who need to quit smoking or stop as soon as possible? It seems to me that that's where the marketing should be focused. Are you planning anything like that?

Keagan Lenihan:
I think once we're given the authority to use the claim, absolutely. We see the same disparities that you mentioned. So certainly, I think, one, our focus is all adults that smoke, but where there is over-indexed populations, I think there is an opportunity to speak to those populations more generally.

Neal Benowitz:
Thank you.

Cristine Delnevo:
Thank you. With that, we're going to take a 10-minute break and we will resume at 10:45.

Keagan Lenihan:
Thank you.

[break]

Cristine Delnevo:
Welcome back, everyone. I would like to now introduce Dr. Cindy Chang, who's going to be presenting and leading us into FDA's presentation. Dr. Chang.

Cindy Chang:
Thank you, Dr. Delnevo. Good morning, everyone. My name is Dr. Cindy Chang, and I'm the Chief of Epidemiology Branch 1 in CTP's Office of Science. I'm going to present an overview of Swedish Match USA's modified risk—oh, sorry. Next slide, please.

So, I'll be presenting an overview of Swedish Match USA's modified risk tobacco product applications, or MRTPAs, for their ZYN products. This application is currently under review. This presentation provides an overview of the ZYN MRTPA, and then focuses on the evidence that FDA intends to discuss with the committee. The next slide is going to present a disclaimer about this presentation. Next slide, please. I'll just pause here for everyone to read the disclaimer. Next slide, please.

Today, we will summarize the current MRTPAs under review. This will include details about the summary of the scientific evidence submitted in support of a risk modification order. I will first present an overview of the individual health risk data submitted. Then, I will turn the presentation over to our social science reviewers, Dr. Apoorva Rajan-Sharma, who will present on the impact of the proposed claim on consumer understanding and perceptions, followed by Dr. Amanda Fidalgo, who will present on the likelihood of use and impacts to the population. I will then provide an overall summary, and we will then leave some time for clarifying questions. Next slide, please.

The 20 products subject to the MRTPAs that are under review are ZYN nicotine pouches. These products received marketing authorizations through the PMTA pathway on January 16th, 2025. For today, we are focused on the MRTPAs and the marketing of the products with the applicant's proposed modified risk claim. The applicant describes the ZYN products as 400-milligram sealed pouches containing tobacco-derived nicotine in a type of salt formulation with nicotine concentrations of 3 or 6 milligrams, in a variety of flavors, and without any whole, cut, or ground tobacco leaf.

The applicant states ZYN has the same intended use as smokeless tobacco products such as General Snus products. Which are authorized MRTPs. The ZYN product is held between the lip and gum for a period of use and then discarded. Next slide, please.

As a reminder, here is an overview of the timeline. As I mentioned earlier, in January of 2025, FDA issued PMTA marketing authorization to Swedish Match USA for 20 of its ZYN nicotine pouch products. The MRTPAs were accepted in February of 2025 and filed in June of 2025, which is also when a public comment docket was opened. And today we are convening the Tobacco Products Scientific Advisory Committee, or TPSAC, for a meeting. Next slide, please.

Again, the company is seeking orders under Section 911(g)(1) of the Federal Food Drug and

Cosmetic Act or FD&C Act to market the 20 previously authorized ZYN products with the following modified risk claim: “Using ZYN instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” Next slide, please.

These are the requirements for a 911(g)(1) risk modification order. FDA evaluates all information and statements on the proposed label, labeling, and advertising submitted by the applicant as part of the agency's scientific review. In addition to determining if the proposed modified risk claim is scientifically accurate, FDA assesses whether the applicant has demonstrated that the proposed MRTPAs as actually used by consumers will significantly reduce harm and risk of tobacco-related disease to individual users of the tobacco product and benefit the population as a whole, taking into account both tobacco users and persons who do not use tobacco.

FDA also assesses whether the advertising and labeling for the proposed MRTPs enable the public to understand the information concerning modified risk and the relative significance of the information in the context of total health and in relation to all of the diseases and health-related conditions associated with the use of tobacco products. Next slide, please.

For the relative health risks of using ZYN, I'll be presenting on the constituent profile of the product followed by clinical and epidemiological evidence of potential health risks associated with use of the product. Next slide.

Starting with a little bit of background, in 2012, FDA published a preliminary list of harmful and potentially harmful constituents, or HPHCs. These are chemicals or chemical compounds in tobacco products or tobacco smoke or emissions that cause or could cause harm to people who use tobacco products and people who do not use tobacco products. As presented in the ZYN PMTA, which the applicant cross-referenced, the applicant tested for 42 HPHCs in the ZYN products. Testing results for ZYN showed that levels of 36 of the 42 HPHCs are below the level of quantification. The chemistry review of the PMTAs concluded that all testing methods used to measure HPHC were validated and fit for purpose.

Among the HPHCs that were quantifiable in at least one of the products, the levels were actually below those expected to pose a risk to health. Levels of nearly all HPHCs except nicotine were lower in ZYN than in the comparison products, which include General Snus, again, which are products that have been previously received an MRTP authorization with the same modified risk claim as that proposed to be used with ZYN.

Notably, General Snus products contain quantifiable levels of NNN and NNK while ZYN does not. The applicant did not provide a direct HPHC comparison between ZYN and any compared or combusted cigarette product. Thus, FDA made this direct comparison and found that HPHCs were lower in ZYN compared with the mainstream smoke of a reference combusted cigarette generated under both the ISO non-intense and ISO intense smoking regimens. Next, I will describe the new biomarker study submitted by the applicant as part of these MRTPAs. Next slide, please.

Generally, biomarkers of exposure are used to assess the level of human exposure to chemicals as a result of using tobacco products, while biomarkers of potential harm are measurements of biological changes in humans due to such an exposure that may indicate long-term disease risk. The applicant submitted a biomarker study as part of the MRTPAs. This was a non-randomized, cross-sectional, multi-center study conducted in Sweden from January to March of 2023.

The study enrolled a total of almost 200 healthy adult volunteers who were considered eligible if they belonged to one of the following use groups: exclusive daily use of one brand of Swedish Match nicotine pouch products; exclusive daily use of Swedish tobacco-based snus; exclusive daily use of combusted cigarettes; or less than 100 lifetime tobacco uses and no use in the past year. Participants in the tobacco use groups use their product of choice exclusively as desired over the study period of 14 days. Additionally, blood and urine were collected to analyze biomarkers. Next slide, please.

The study found biomarker profiles of adults who use nicotine pouches were generally similar to those of adults who do not use tobacco and lower than those of those adults who smoke combusted cigarettes. The applicant reported the following. Biomarkers of HPHCs, such as TSNAs, were lower in adults using nicotine-pouch products compared to adults who use snus and adults who smoke combusted cigarettes. Inflammatory and oxidative stress biomarkers were generally lower in adults using nicotine pouch products compared to adults using combusted cigarettes. Adults who used nicotine pouches had similar nicotine biomarker concentrations to adults who used snus, but higher than adults who use combusted cigarettes.

FDA identified a number of limitations in the submitted biomarker study. First, the study used a cross-sectional design, which means that the exposure levels and outcomes were assessed at one time point. Therefore, we can't establish a causal relationship. Additionally, there were no adjustments or sociodemographic or behavioral variables which may have further explained differences among the groups. Participants were asked to use only one product exclusively for 14 days, which may not necessarily reflect real-world behavior. And finally, the study was not product specific. Although 65 percent reported using ZYN, some participants using ZYN used different flavors and nicotine concentrations different from the authorized products in these MRTPAs. Next slide, please.

Nicotine pouch products are generally considered relatively new to the market, thus long-term health data specific to these products are still being collected. The applicant did not submit any observational or clinical studies directly evaluating health outcomes associated with ZYN. As summarized in the 2025 PMTA decision summary, the applicant referenced data pertaining to Swedish Snus. The applicant's justification for the applicability of the published literature on the long-term health effects of Swedish Snus to ZYN was based on similarities in use topography and systemic nicotine exposure.

The applicant points out the following similarities. In terms of product characteristics, both products are pouched, manufactured by the applicant and under similar quality management systems. They have similar types of flavors and comparable nicotine content, pH, route of exposure, and exposure levels. Both are non-combusted and used by placing them in the oral cavity where nicotine dissolves in saliva and is absorbed through the mucous membrane of the

mouth. Both have similar use patterns, such as how often, for how long, and what amount is used. Both have similar consumer characteristics, and that many people who used ZYN previously used moist snuff.

In the 2025 ZYN PMTA decision summary, FDA reviewers concluded that the Swedish Snus epidemiological studies were applicable to the health risks of ZYN based on these similarities. In the next slides, I present a summary of the Swedish Snus literature by disease outcome that was submitted by the applicant to substantiate the proposed claim. This is the same body of evidence used in the cross-reference 2014 MRTPA for General Snus. Next slide, please.

Based on a pooled analysis of applicant-submitted studies, snus use is not clearly associated with risk of oral cancer compared to smoking combusted cigarettes, which is actually reported to increase the risk of oral cancer by 5 to 11 times. Next slide, please.

A cohort study of almost 280,000 Swedish construction workers observed no association between snus use and incidence of lung cancer, whereas smoking increases risk of dying from lung cancer by 25 times. Next slide, please.

A meta-analysis found no association between current snus use and heart disease, while a pooled analysis observed a small increased risk of death from cardiovascular disease. However, the risk is much higher for smoking combusted cigarettes. We want to note here that the cardiovascular effects of nicotine would not be expected to be different for snus compared to other nicotine-containing products. Combusted cigarette smoke, however, has other cardiovascular toxins not found in snus. Next slide, please.

A meta-analysis observed no increased risk of stroke incidents among people who use snus and never smoked compared to people who did not use snus and never smoked. This is in contrast to a slightly increased risk among people who used traditional smokeless tobacco. Additionally, the risk of dying of stroke is still higher for smoking. Next slide, please.

Given no inhalation of smoke, we don't expect to see an increased risk of chronic respiratory disease with Swedish Snus. In comparison, smoking is associated with 22 to 25 times greater risk of dying from diseases such as COPD. Next slide, please.

As a reminder, the applicant is proposing the following modified risk claim: “Using ZYN instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” For each of these outcomes, the Swedish Snus epidemiological literature shows lower to no risk associated with snus use, whereas the risks associated with combusted cigarette smoking are all higher.

FDA's review of the ZYN PMTA concluded that completely switching from combusted cigarettes to snus reduces risk of smoking-related diseases. ZYN products are similar to snus with regard to use patterns, but HPHCs are lower compared to snus. Therefore, the health effects of ZYN are expected to be lower than that of snus use. Thus, using ZYN instead of cigarettes, as instructed by the proposed claim, is expected to reduce disease risks. Next slide, please.

The HPHC and biomarker data suggest that exposures to toxicants is lower in people who use nicotine pouches as compared with those who use combusted cigarettes, but also lower compared to those who used snus. As for the long-term epidemiological data based on Swedish Snus use, FDA previously concluded that snus use is associated with lower risk as compared to combusted cigarette smoking for mouth cancer, heart disease, stroke, lung cancer, emphysema, and chronic bronchitis.

Taken together, FDA's preliminary evaluation of the evidence suggests the proposed modified risk claim—"Using ZYN instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer stroke, emphysema, and chronic bronchitis"—is scientifically accurate.

Thank you for listening. I now turn the presentation over to Dr. Apoorva Rajan-Sharma.

Apoorva Rajan-Sharma:
Good morning, everyone. My name is Dr. Apoorva Rajan-Sharma. I'm a social scientist in CTP's Office of Science. I will present information on the impact of the proposed claim and consumer understanding and perceptions. Next slide, please.

I will begin this presentation by presenting one potential way of breaking down and thinking about consumer understanding of MRTPs. As a reminder, section 911(h)(1) says that labels, labeling, and advertising materials or LLA concerning modified risk products must enable the public to comprehend the modified risk information and understand its relative significance in the context of total health and in relation to all diseases and health-related conditions associated with the use of tobacco products.

This slide reflects a framework that CTP has used in the past for evaluating applications under this provision. It breaks consumer understanding into three components or buckets. First, understanding the specific risk reduction or exposure risk reduction that the LLA describes. Second, understanding that the proposed MRTP does confer health risks or harm, and is more harmful than nonuse of tobacco products, and understanding the risks relative to cessation with or without the use of FDA-approved cessation therapies. And third, understanding how to use the proposed MRTP to reduce one's risk or exposure. Next slide, please.

To begin, let's dive into the information submitted by the applicant. The applicant submitted a Consumer Perceptions and Likelihood of Use study, which was an online pre-test, post-test quasi-experimental study that used non-random assignment. The study was conducted from February to March 2024. The study assessed absolute and relative risk perceptions of ZYN and label comprehension exclusive of the claim, which we will discuss now. Other measures such as intentions to use tobacco products, including intentions to use ZYN and intentions to quit smoking will be discussed later by my colleague, Dr. Amanda Fidalgo.

The study sample was recruited from consumer panels and stratified by current and past tobacco use status. Respondents were assigned to either the test or the control condition, based on which condition was least filled, resulting in non-random assignment. Respondents in the test group viewed a product concept with a proposed claim and respondents in the control group viewed the concept without the proposed claim. Next slide, please.

Here are the stimuli for the study. They were designed to resemble a counter mat point of sale display with a picture of the product, details about the different varieties, strengths and flavors of ZYN, and the required nicotine warning. The test group viewed the stimulus on the left, which included the proposed claim. The control group viewed the stimulus in the right, which excluded the proposed claims. On the next few slides, I will discuss key findings from the study. Next slide please.

First, let's review study findings regarding consumer understanding of the risk reduction described in the claim. The applicant provided risk perceptions of ZYN relative to combusted cigarettes for all six health conditions mentioned in the claim. Given that the pattern of findings was similar across health conditions, I will present the findings of two health conditions as examples.

First, I want to talk about the difference between the test group that saw the claim and the control group that did not see the claim. The figure on this slide shows lung and mouth cancer risk perceptions of ZYN relative to combusted cigarettes among test and control group adults who use combusted cigarettes, reflecting the group that stands to benefit most from a lower risk alternative to combusted cigarettes. The first two bars represent lung cancer relative risk perceptions among the test and the control group. The second two bars represent mouth cancer relative risk perceptions among the test and control groups.

Although the applicant did not report any tests of statistical significance, we see that point estimates moved in the expected direction for both health conditions, though differences appear small. Click for animation, please.

As you can see here, compared to 47.9 percent of people in the test group, 43.6 percent of those in the control group correctly perceives ZYN to confer lower lung cancer risk than combusted cigarettes. Click for animation, please.

Similarly, compared to 38.8 percent of people in the test group, 35.1 percent of those in the control group correctly perceive ZYN to confer lower mouth cancer risk than combusted cigarettes. However, between 35.5 percent and 55.1 percent of consumers using combusted cigarettes perceive ZYN to pose an equally or higher risk than combusted cigarettes. This risk overestimation is consistent with previous research cited here on the slide, showing that consumers tend to overestimate the risk of other tobacco products relative to combusted cigarettes.

In contrast, between 5.9 percent and 13.7 percent of consumers using combusted cigarettes underestimate the risk of using ZYN relative to combusted cigarettes. Next slide, please.

The figure on this slide depicts relative risk perceptions of lung and mouth cancer among young adults who never regularly use tobacco, a group defined as those ages 21 through 24 who have smoked fewer than 100 combusted cigarettes in their lifetime and do not currently use a tobacco product. Thus, this group would not benefit from the use of a comparatively lower risk alternative to combusted cigarettes.

As in the previous slide, although the applicant did not report any tests of statistical significance, we see that point estimates moved in the expected direction for both health conditions. Similar to adults who use combusted cigarettes, differences also appear to be modest for young adults who never regularly use tobacco. When compared to the findings among adults who smoke on the previous slide, these young adults who never regularly use tobacco generally had higher perceived relative risk of ZYN, larger percentages report that ZYN has the same or higher risk relative to combusted cigarettes, sorry, and smaller percentages report lower or no risk compared to adults who smoke combusted cigarette.

For example, here, 42 percent to 67.8 percent of young adults reported ZYN had the same or greater risk as combusted cigarettes, which is higher than the 35.5 percent to 45.1 percent of adults who perceived ZYN to have the same amount or higher risk than combusted cigarettes. This finding is what we would expect and is consistent with existing literature showing that young adults, especially those who do not use tobacco, attribute greater risks to tobacco products than adults who use tobacco. Next slide, please.

Next, let's review study findings regarding whether consumers understand that the proposed MRTP still confers health risk. Overall, the Consumer Perceptions and Likelihood of Use study found that consumers understood ZYN still confers health risk relative to nonuse and cessation and is not risk-free. Mean absolute risk scores range from 2.6 to 3.9 on a five-point scale where 1 indicated no risk and 5 indicated very high risk.

Particularly, we know that participants in the test group who viewed the proposed modified risk claim and attributed lower risk to ZYN relative to combusted cigarettes also understood that ZYN is not risk-free. Across both the test and control group, 82 percent of adults who are using combusted cigarettes and 92 percent of young adults who never regularly use tobacco perceived ZYN to confer a health risk. Next slide, please.

Third, let's review study findings regarding whether consumers understand how ZYN must be used to confer lower risk. To demonstrate this, the applicant cited their Perceptions and Behavioral Intentions, or PBI, study included in the General Snus MRTPA. The PBI study tested a reduced risk claim that is currently in use as a General Snus modified risk claim and is identical to the proposed claim except for the product name. For reference, the slide shows the proposed claim for ZYN and the authorized claim for General Snus. Next slide, please.

As you can see in the figure shown on this slide, PBI study findings demonstrated that consumers understood that when using General Snus, they would need to use zero combusted cigarettes to confer lower risk. Fifty-six percent of young adults who were smoking combusted cigarettes who saw the claim understood that they would to use zero combusted cigarettes to confer low risk compared to 45 percent of young adults who did not see the claim.

Forty-four percent of adults who were smoking combusted cigarettes who saw the claim understood that they would need to smoke zero combusted cigarettes to confer lower risk compared to 34 percent of adults who did not see the claim. Importantly, as we saw on the prior slides reporting the effects of claim exposure on risk perceptions, adding the claim did not increase the proportions of those smoking combusted cigarettes who selected the response

options consistent with partial substitution. This suggests that the proposed claim did not lead those smoking combusted cigarettes to believe that partial substitution would reduce their disease risk. Next slide, please.

All right, so to summarize, here are the main consumer understanding findings I would like to emphasize. First, FDA's preliminary evaluation of the evidence suggests consumers correctly understood the risk reduction described in the claim. Specifically, consumers understood that relative to combusted cigarettes, ZYN confers lower risk of the diseases mentioned in the proposed claim. Consumers also correctly understood that although ZYN confers lower risk relative to combusted cigarettes, ZYN is not risk-free and confers at least some health risk.

Additionally, FDA's preliminary evaluation suggests consumers correctly understood how to use the product in the proposed claim to confer lower risk. We note that the Consumer Perceptions and Likelihood of Use study had some limitations, including non-random assignment to experimental conditions and lack of statistical testing. Findings indicate, however, that regardless of claim exposure, many consumers still appear to overestimate health risks associated with ZYN. Therefore, misunderstanding of the claim was not in the direction of underestimating the risks associated with ZYN and may be a result of preexisting beliefs.

As I mentioned previously, these findings are in line with existing research. Now that we have covered consumer understanding, my colleague, Dr. Amanda Fidalgo, will present on likelihood of use and FDA's preliminary evaluation of the impacts to the population. Thank you.

Amanda Fidalgo:
Thank you, Dr. Rajan-Sharma. And hello, my name is Dr. Amanda Fidalgo and I'm a social scientist at CTP's Office of Science. I will discuss the potential impacts of marketing ZYN with the proposed claim on the likelihood that people who use and do not use tobacco products will begin using ZYN nicotine pouches and the impact of the proposed claim on the population as a whole. To discuss these topics, I will first present findings from national surveys and applicant-submitted evidence from their PMTA that examine patterns of ZYN use. Of note, this evidence pertains to the use of ZYN absent to any marketing of the product with the proposed modified risk claim. I will then present evidence from applicant-submitted data about intentions to use ZYN after exposure to the proposed claim. Next slide, please.

I will begin by discussing the prevalence of nicotine pouch use among adults. The Tobacco Use Supplement to the Current Population Survey, or TUS-CPS, is a survey of tobacco use in the United States among adults 18 and older. TUS-CPS is nationally representative and uses a probability sample, which is a robust design that allows for more precise estimates. The most recent data from this study show that 0.4 percent of adults reported currently using nicotine pouches. Among that group, about 25 percent reported currently smoking combusted cigarettes, almost 34 percent reported formerly smoking combusted cigarettes, and 41 percent reported never smoking.

Among adults who had ever used nicotine pouches, relatively few, 1.8 percent, had never used tobacco before. Thus, the currently available data suggest that ZYN may not be a product of initiation among adults. Daily nicotine pouch use was most common among adults who recently

quit using other tobacco products, particularly smokeless tobacco products and combusted cigarettes. While the TUS-CPS does not include brand preference information, sales data shows that ZYN was the most popular brand of nicotine pouches at the time of the survey. Nicotine pouch sales continue to rise, with Nielsen data showing that monthly pouch sales more than tripled from 2021 to 2024. Next slide, please.

Next, we can turn to the applicant's submitted evidence. In their MRTPA, the applicant cross-referenced their patterns of use study, which was originally submitted in their PMTA for these ZYN products. This observational study included two phases, a retrospective study followed by a prospective study, neither of which included use of the proposed claim. The cross-sectional retrospective study had a sample of 1,266 respondents who were using ZYN with or without other tobacco products, and 733 respondents who were using other tobacco products only. It asked about past 30-day tobacco use, reasons for using ZYN, and intentions to quit various tobacco products.

Participants from the cross-sectional study were then invited to participate in a 10-week prospective study, which evaluated patterns of use among those using ZYN and among those only using other tobacco products. By week 10, the final sample included 346 participants using ZYN and 196 participants using other tobacco products only. Over the course of the 10 weeks, among those using ZYN, the proportion who also used combusted cigarettes declined from 15.9 percent to 8.1 percent. This decline suggests that approximately half of those who would dual-use ZYN and combusted cigarettes at baseline completely switched to ZYN by the end of the 10 week follow-up.

Additionally, close to a quarter of those using ZYN completely switched to ZYN from a broader group of tobacco products, including combusted cigarettes, moist snuff, snus, e-cigarettes, cigars, or cigarillos. Of note, the pattern of use study experienced significant loss to follow-up. Participants who completed the study may have been those most committed to using ZYN, and in a real-world scenario, rates of complete switching from combusted cigarette to ZYN may be lower. Next slide, please.

Moving to youth use of nicotine pouches and ZYN, estimates from national survey data indicate that prevalence of nicotine pouch use is relatively low. The National Youth Tobacco Survey, or NYTS, is a nationally representative annual survey of middle and high school students in the United States. The 2024 NYTS data showed that 1 percent of middle school students and 2.4 percent of high school students reported currently using nicotine pouches. ZYN was the most commonly used nicotine pouch brand among youth. Among middle school students who reported currently using nicotine pouches, 35 percent reported that ZYN was their usual brand. Among high school students who reported currently using nicotine pouches, 72 percent reported that ZYN was their usual brand.

While the 2024 NYTS did not reveal a significant increase in youth past 30-day pouch use overall, the 2024 Monitoring the Future study showed that among a combined sample of 10th and 12th graders, nicotine pouch use increased from 2023 to 2024. The Monitoring the Future study is another nationally representative survey of youth in the United States, and it indicated that nicotine pouch use prevalence increased for lifetime use from 3 percent to 5.4 percent, for

past 12-month use from 2.4 percent to 4.6 percent, and for past 30-day use from 1.3 percent to 2.6 percent. Next slide, please.

On the four previous slides, I presented data on the prevalence of nicotine pouch use among adults and youth without exposure to the proposed modified risk claim. Now, I will focus on the applicant's Consumer Perceptions and Likelihood of Use study, which was previously described by Dr. Rajan-Sharma. This study assessed the effect of the proposed claim on respondents' intentions to use ZYN and the intentions of those who currently smoke to quit smoking. The figure on this slide presents the mean intentions to use ZYN after exposure to the stimuli with or without the proposed modified risk claim. Of note, we focus on the post-exposure intention scores here because the applicant measured intentions to used nicotine pouches rather than intentions to ZYN prior to exposure to the proposed modified risk claim.

Intentions were measured on an 11-point scale in which those who selected 0 report no or almost no chance that they will use ZYN on a regular ongoing basis. And those who selected 10 report that they are certain or practically certain to use ZYN on a regular ongoing basis. The orange bars present the means for respondents exposed to the proposed claim and the striped blue bars present the mean for those not exposed to proposed claim. Intentions to use ZYN were low to moderate among people who use tobacco products with mean intention scores slightly higher among those that use smokeless tobacco.

Overall, this study found that among adults who currently use tobacco products, viewing the stimuli with the claim did not impact intentions to use ZYN, compared to viewing the stimuli without the claim. Of note for this study, nearly 20 percent of respondents who currently use combusted cigarettes and over half of those who currently use smokeless tobacco reported using nicotine pouches every day or some days. Respondents who reported using nicotine pouches were still asked whether they intend to use ZYN in the future, which may have limited the ability of the study to detect any impact of the proposed claim, because those who are using nicotine pouches were likely to report a higher intention to use ZYN regardless of whether they viewed the proposed claim.

While not shown on this figure, the Consumer Perceptions and Likelihood of Use study also tested the impact of the proposed claim on quit intentions among respondents who currently use combusted cigarettes. There was no difference in quit intentions between respondents who viewed the stimuli with the claim and those who viewed stimuli without the claim. Next slide, please.

I will now turn to the findings for people who were not using combusted cigarettes or smokeless tobacco products at the time of reporting. This included three groups: young adults ages 21 to 24 who had never regularly used tobacco products, adults ages 21 and over who had regularly used tobacco products, and adults who formerly used cigarettes and/or adults who currently use tobacco products other than combusted cigarettes and smokeless tobacco products. Overall, intentions to use ZYN were low among all three groups, with mean post-exposure intention scores ranging from 0.5 to 1.3 on the same 0 to 10 scale described on the last slide. Viewing the stimuli with the proposed claim did not increase intentions to use ZYN among any of these groups compared to viewing the stimuli without the claim. Next slide, please.

To summarize, data from nationally representative surveys suggest that adult and youth use of nicotine pouches is currently relatively low based on the most recently available data. However, nicotine pouch sales are on the rise with Nielsen data showing monthly patch sales more than tripled from 2021 to 2024. The vast majority of adults who use nicotine pouches have a history of tobacco product use and nicotine pouch use is most common among adults who recently quit other tobacco products.

The applicant's cross-reference Patterns of Use study found that some participants who used ZYN without the proposed claim switched completely from other tobacco products to ZYN at the end of the 10-week prospective study. Study findings add to the body of evidence that some people who use ZYN use the product to help them quit other tobacco products, including combusted cigarettes. The applicant's Consumer Perceptions and Likelihood of Use study found that viewing the proposed claim did not impact intentions to use ZYN among participants who were currently using tobacco products, nor did it impact intentions to quit smoking among respondents who are currently using combusted cigarettes.

Based on the currently available information, intentions to use ZYN were relatively low among those who were not using tobacco products, including young adults, and viewing the proposed claim did not increase these intentions. Next slide, please.

Thank you and I will now turn it back over to Dr. Chang for the overall summary.

Cindy Chang:
Thank you, Dr. Fidalgo. Next slide, please. FDA's preliminary evaluation of the evidence suggests the proposed modified risk claim is scientifically accurate. Levels of nearly all HPHCs in ZYN are lower than in Swedish Snus, and ZYN has similar use topography, but lower HPHC levels. Thus, compared to Swedish Snus, the health effects of ZYN are anticipated to be lower than those of snus.

As for the long-term epidemiological data based on Swedish Snus use, FDA previously concluded that snus use confers lower risk than combusted cigarette smoking for mouth cancer, heart disease, stroke, lung cancer, emphysema, and chronic bronchitis. Next slide, please.

Additionally, FDA's preliminary evaluation of the evidence suggests consumers correctly understood that ZYN confers lower risk than combusted cigarettes. At the same time, they understood that while lower risk than combusted cigarettes, ZYN still confers health risks. Consumers also understand how they need to use ZYN in order to confer lower risk. In other words, they understood they must completely switch from combusted cigarettes to ZYN to lower risk to their health.

Additionally, any misunderstanding of the claim was not in the direction of underestimating risks associated with using ZYN. Many consumers overestimate risks associated with ZYN regardless of claim exposure. Next slide, please.

With regard to the impact to the population, among those using tobacco products, the majority of adults who use nicotine pouches have a history of tobacco product use, with nicotine pouch use

being most common among adults who recently quit other tobacco products. The applicant observed in their Patterns of Use study that 24 percent of participants who use ZYN completely switched from other tobacco products to ZYN by the end of the study, though the study did not include the proposed modified risk claim. In the Consumer Perceptions and Likelihood of Use study, viewing the proposed claim did not impact intentions to use ZYN. Among those who do not use tobacco products, based on the currently available information, the prevalence of nicotine pouch use among youth is currently relatively low. Among young adults who do not currently use tobacco, viewing the proposed claim did not increase intentions to use ZYN. Next slide, please.

Well, thank you for your time. We're happy to answer—address any brief, clarifying questions. And just as a reminder, we also have time for more questions during the in-depth discussion this afternoon.

Cristine Delnevo:
Thank you, Dr. Chang. I'd like to open it up to the committee for any clarifying questions. Dr. Popova.

Lyudmila Popova:
Thank you, Dr. Chang. Just really quickly, when the FDA saying there was an overestimation of risk of using ZYN, are you using the comparative risk measurements and saying that there was a large proportion of participants saying they're equally harmful as cigarettes? Have you looked at the absolute risk perceptions that are also in the application, which show when you look at the mean of risk perceptions, ZYN is much, much lower than cigarettes?

Cindy Chang:
Thank you for the question. I'd like to direct that question to Dr. Apoorva Rajan-Sharma, please.

Apoorva Rajan-Sharma:
Hi, Dr. Popova. Yeah, we looked at the relative risk perceptions of ZYN and how those are overestimated for people.

Lyudmila Popova:
Thank you.

Cristine Delnevo:
Dr. Upson.

Dona Upson:
Thank you. You reviewed a lot of the evidence from the industry studies. I'm wondering if FDA looked at independent studies or conducted your own studies to confirm the data that you presented. I know it's been a short time since it was submitted. Thank you.

Cindy Chang:
Hi, I can speak to the biomarker study. We did look at just a few biomarker studies that have been published around nicotine pouch use. And there was some consistency with the literature.

So I will defer to my social science colleagues to address the published literature around your studies.

Amanda Fidalgo:
Hi Dr. Chang, I can address that and just note that we did—while we didn't necessarily conduct any of our own studies, our review focus is on the applicant-submitted evidence and the literature. So we did do a thorough literature search as part of our review.

Cristine Delnevo:
Do we have anyone else that has additional questions for FDA? Dr. Jordt.

Sven-Eric Jordt:
Thank you. It seems that FDA has simply followed the documentation by the applicant and just focused on the health indications that basically they listed. But I mean, there are a lot of other health effects that nicotine and oral tobacco products have. And I mean recent studies have shown consistently that nicotine pouches cause oral, like, lesions, inflammation, leukoplakia. These are precursors of potentially cancerous lesions. There have been reports of people, especially women, using larger numbers of nicotine pouches having reduced fertility. So why have you restricted your analysis on these fairly standard indications that are usually associated with combusted use and not necessarily indications related to nicotine use?

Cindy Chang:
Yeah, that's a great point. We, first of all, focused on the health outcomes that were outlined in the proposed modified risk claim. We certainly would be concerned about all health effects and certainly the use of the ZYN products is not without risk. So yeah, we certainly take those into consideration. I will say that, you know, we don't anticipate there being any higher risk of the ZYN, using the ZYN products, compared with other smokeless tobacco products that already are out there, including Swedish Snus. But I would love to take this opportunity to have Dr. Benowitz maybe speak to some of the other health effects of potential health risks of ZYN.

Neal Benowitz:
Sure. Can you see me? Hear me? I think Dr. Jordt is certainly right that it can cause oral lesions, but certainly the Swedish experience, in terms of oral cancer, shows that the risk is relatively low. And so it's lower risk than that, I think. There clearly are concerns about pregnancy, and that the pregnancy risks not only fertility, but also risk of things like preeclampsia can be different compared to nonsmokers. But again, the risks seem to be lower than that of cigarette smoking.

For cardiovascular disease, there are some concerns in people who already have cardiovascular disease, but it doesn't seem to accelerate atherosclerosis or cause cardiovascular disease per se. It can aggravate it, but doesn't seems to be a primary cause of it. So, I think that like Dr. Chang said, there clearly are these risks, but I don't think any of them come up to what the risk of cigarette smoking are. I think the main concern from my perspective is the addictive potential, because many people who use snus products, use them all day long and have great difficulty quitting if they try. So that's a quick summary of my perspective.

Cristine Delnevo:
Thank you, Neal. Do any other committee members have any additional clarifying questions? Dr. Wackowski.

Olivia Wackowski:
Yes, so we saw some data about the relative risk perception outcomes comparing ZYN versus cigarettes on lung cancer and mouth cancer as some of the specific health outcomes mentioned in the claim. But there was also a similar measure that was asked in that set of questions that just ask about, sort of in general, the perceived risk of ZYN versus cigarettes. And I'm wondering if there was results for that comparison between the test and control groups as that might've kind of captured sort of a response to the gist of the claim versus, you know, we don't know to what extent they recall every single disease that was mentioned in the claim. So, just wondering if there was results for that general outcome measure. Can you hear me?

Apoorva Rajan-Sharma:
Oh, sorry about that. Hi, Dr. Wackowski. Thanks for the question. There was that measure in general, the pattern was similar across the overarching relative risk perceptions and then the one that's focused on the specific health conditions. And we saw similar pattern in terms of what the distribution looked like. And we also saw that depending on the population, there was an overestimation of relative risk perceptions.

Olivia Wackowski:
Thanks.

Cristine Delnevo:
Any additional questions from the committee for FDA? All right. With that, we're actually going to go to break early, lunch early. I'm going to ask the committee to return and be logged in by 12:50. We are going to start the open public hearing promptly at 12:55 and with the 20 presenters, I think people's attention to time will be greatly appreciated. So see you all back here. We are going to be resuming at 12:55.

Cristine Delnevo:
Welcome back everyone, and welcome to the open public hearing session. Please note that for both the FDA and the public believe in a transparent process for information gathering and decision-making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the committee of any financial relationship that you may have with the sponsor, its products, and if known, its direct competitors. For example, this financial information may include the sponsors' payment of expenses in connection with your participation in this meeting.

Likewise, FDA encourages you at the beginning of your statement to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking. We have

21 open public hearing speakers today. So that we may move through the agenda as scheduled, please remember that you are allotted 3 minutes only for your presentation. The timer will start after the yellow flash. And I would like to now invite our first speaker. Next slide. Open public hearing speaker number 1, please turn on your camera and unmute to speak.

Male Speaker:
Madam Chair, committee members, and FDA staff, thank you for the opportunity to provide public comment. I do not have any financial conflicts of interest in making this presentation. I'm a professor emeritus at the University of Louisville. From 1994 until last month, I conducted and published research on tobacco harm reduction. The TPSAC decision today, of course, is do ZYN nicotine pouches meet the statutory criteria for MRTP authorization?

First, ZYN products contain substantially fewer and lower levels of harmful constituents than combustible cigarettes, and ZYN eliminates the smoke. ZYN delivers nicotine through oral absorption. Although it's addictive, it is not entirely without risk. Nicotine is not the principal driver of smoking-related diseases. Second, an important MRTP precedent exists for ZYN. In 2019 and 2024, FDA issued MRTP orders for General Snus products, and in '23 for Copenhagen Moist Snuff. These decisions were based in part on published research documenting the use of traditional smokeless products like snus and Moist Snuff confer very small health risks.

ZYN represents a logical extension of this approach because ZYN pouches contain only nicotine and flavors. I followed the ZYN story with great interest and conducted research on ZYN use. In 2020, my colleagues and I published the first study about ZYN in the American Journal of Addictions assessing its use, appeal, and interest among adults. Following draft guidance from the FDA, Swedish Match collected and provided us with data on surveys of adults who had no previous exposure to use or use of ZYN and adult current ZYN users.

We found that 90 percent of never and former users did not find ZYN to be appealing, while one-third of current smokers, more than half of current ST users, and two-thirds of dual users did. Our results were compatible with the much more complete study by Delnevo et al. in 2025. MRTP authorization for ZYN will have a separate advantage of correcting misinformation that nicotine causes diseases. This misperception among American public and even physicians contributes to the high persistent death toll from smoking.

As I noted, the question in front of the TPSAC is whether ZYN, compared to cigarettes, meaningfully reduces harm and can contribute to improve public health outcomes. I respectively submit that ZYN warrants MRTP authorization. Thank you for your time and consideration.

Cristine Delnevo:
Thank you. Speaker two.

Lauren Lempert:
Hello. My name is Lauren Lempert, and I'm affiliated with the University of California San Francisco. We submitted three comments that provide significant scientific evidence showing why the applicant failed to meet a statutory burden to provide the necessary evidence specific to ZYN pouches that is actually used by consumers. These products will benefit the public health,

including youth and other nonusers. I urge you to read these comments as together, they contain citations to more than 100 published peer-reviewed papers, most of which were not addressed by the applicant with relevant scientific evidence.

Our submission leaves no doubt that the answer to all four discussion questions presented to this committee is no. FDA should not authorize marketing ZYN with THE proposed MRTP claim because, one, the proposed claim is not accurate. Two, ZYN use among youth is skyrocketing and is harmful. Three, consumers do not understand the proposed claim. And four, it's likely that smokers will not switch completely, but instead will dual use ZYN and other products.

Now I'll discuss two of these four issues. First, the proposed modified risk claim is not accurate. The applicant failed to provide long-term safety data supporting their claim that using ZYN significantly reduces the risk of tobacco-related disease and fails to address evidence of oral health risks and other harms such as cardiovascular disease. The fact that ZYN pouches contain lower amounts of some HPHCs does not demonstrate that the products lower disease risk. ZYNs also expose users to other harmful constituents not included on that outdated HPHC list.

ZYN nicotine products are not snus. So, reliance on FDA authorization of General Snus is insufficient to support ZYN's applications. And the Swedish experience of snus does not apply to the American experience of ZYN. Next, of particular concern, the premise underlying question four is wildly wrong. Our comment provides data showing skyrocketing sales of nic pouches with more than a billion pouches sold per month in 2024 and increasing rapidly. We provide substantial evidence of soaring nicotine pouch use among young people, which more than doubled among high school kids from 2021 to 2024. And 2024 NYTS data show they were the second most prevalent product after e-cigs.

Our comment details the aggressive marketing tactics used to sell ZYN that target youth, including using youth-appealing flavors, high nicotine strengths, colorful tins that look like candy, and Instagram posts explicitly stating FDA-approved ZYN with health benefits. These factors increase the likelihood that youth and other nonusers will initiate with ZYN because they believe they are risk free. To conclude, FDA should not authorize marketing ZYN with the proposed MRTP claim. Thank you.

Cristine Delnevo:
Thank you. Speaker three.

Alex Weatherall:
Thank you. My name is Alex Weatherall and I own a convenience store in Sherborn, Massachusetts. It's a small town within commuting distance of Boston. My wife and I have been part of the community for 15 years. And during that time, we've seen choices around nicotine consumption change dramatically for the better. Cigar usage has practically disappeared and cigarette consumption has plummeted.

Ten years ago, smokers bought 53 packs a day in our store. In 2025, they bought 27 and a half. That's a 48-percent reduction, a compound rate of decline of 6.3 percent per year over 10 years. What's more impressive, the decline is accelerating very quickly. Last year, so 2025, smokers

bought 12.4-percent fewer packs from us than they had in 2024. We carry cigarettes because a slice of our customer base wants them. That's what a retailer does. But it's not a good business for us. Cigarette manufacturers raise their prices four times a year. And that means we're spending almost as much to stock the category today as we spent 10 years ago, and we're selling half as many.

So, where are nicotine users going since it's obvious they're giving up smoking? In our store, a sizable number of them are moving to nicotine pouches. We see it every day. Men in their late 20s to late 50s, tradesmen, attorneys, truckers, grad students, dads. They're replacing combustible tobacco with products like ZYN. I'll share one example. Our assistant manager is a bit of a rascal, smart, anti-authoritarian. He's in his late 20s, doing great work for us while he figures out what to do with his life. We've enrolled him in accounting classes, hoping he sticks around for a while.

But he switched to ZYN. He feels better, doesn't smell like smoke, isn't damaging his lungs. It's the kind of change that my wife and I are proud to encourage. Smokers and vapers in particular, but nicotine users in general, need science-based information about the health effects of what they're using. I see it as a broad continuum, with cigarettes and contraband vapes on one extreme and PMTA-blessed pouches on the other. Most people don't know the difference and their confusion risks pushing them to bad decisions, including illegal products.

To me as a C store owner, FDA authorization of whatever kind provides assurance I'm selling products lawfully. It validates the efforts of compliant retailers, while strengthening responsible adult access. So, authorizing ZYN's MRTP application would give adults the facts they need to make good choices, pouches versus cigarettes, for instance. And based on what my wife and I have witnessed, it accelerate the move toward a smoke-free future. Thank you very much for the time.

Cristine Delnevo:
Thank you. Speaker four.

Lindsey Stroud:
Yes. Can you guys hear me? Hello. Okay. Chairwoman, members of the committee, thank you for your time today. My name is Lindsey Stroud. And right now, I'm representing Independent Women, where I serve as a visiting fellow focused on tobacco harm reduction. Independent Women is a national women's organization dedicated to celebrating women's accomplishments and expanding women's options and opportunities. As far as their financials go, I'm not privy to that. But I also want to thank the committee and FDA CTP for helping me fill in for the original speaker.

Public health discussion around tobacco harm reduction often focus disproportionately on youth use. Far less attention is paid to adult women who smoke despite facing unique barriers to quitting. Independent Women supports accelerating PMTA marketing authorizations and expanding the use of the modified risk tobacco product or MRTP orders. These pathways are especially important for women who struggle more with smoking cessation. Research shows women have greater difficulty quitting smoking than men. Studies indicate nicotine can interfere

with enzymes involved with estrogen regulation. Women also report greater concerns about weight gain and mood changes, stronger withdrawal symptoms, higher relapse rates during stress or anxiety, and are actually more likely to relapse into smoking.

Emerging evidence suggests smokeless harm reduction products, including oral nicotine pouches, can help close these gender gaps. A 2025 report examining Sweden's tobacco landscape had a specific focus on women. Historically, women quit smoking at lower rates than men. From 2009 to 2015, smoking rates among Swedish women declined only by 16 percent compared to a 27 percent reduction among men. After oral nicotine pouches entered the market, this trend reversed. From 2016 to 2024, smoking among women declined 49 percent and this surpassed the decline among men.

Survey data also indicated that these women were using nicotine pouches to quit smoking. In a Swedish national survey, nicotine pouches ranked as the most effective cessation tool among all the adults who were smoking—or quit smoking, yet women rated pouches three times more effective than vaping products. And flavors are really important to this as well. Sixty percent of women cited flavors as a top reason for use, compared to 55 percent of men. This report also highlighted that these products may have design features that resonate with women, including this gender-neutral design, discretion and cleanliness, compatibility with daily life, and an alignment with social norms.

I also want to emphasize that Independent Women strongly does support robust regulation to prevent youth access to age-restricted products. Importantly, youth use of nicotine pouches still remains low. According to the 2024 National Youth Tobacco Survey, only 1.8 percent of U.S. middle and high school students were reported currently using nicotine pouches and just 0.9 percent of female students.

Independent Women supports efforts to make America healthy again. Expanding adult women's access to reduced risk products and allowing accurate communications about their relative risk is part of that goal. We encourage the FDA to continue authorizing MRTP orders and accelerate PMTA marketing orders so adult smokers, especially women, have access to effective harm reduction options. Thank you for your time.

Cristine Delnevo:
Thank you. Speaker five.

Ed Lopez-Reyes:
Thank you for the opportunity. My name is Ed Lopez-Reyes, vice president of 60 Plus. And the latest 2024 National Youth Tobacco Survey revealed that the rate of youth tobacco use dropped to its lowest level since the survey began 25 years ago. Adult cigarette smoking is also at historic lows. But there are still 30 million adult smokers in the United States, and smoking still remains a leading cause of preventable disease and death. These declines in smoking rates have unfortunately been uneven, with groups such as older Americans, veterans, those with low educational attainment, and those with mental health conditions falling behind.

According to studies, the prevalence of smoking habits decreased in every age bracket except

one, the 65 and up crowd. They also showed that while the prevalence of regular smokers dropped to 15.2 percent down from 21.2 percent, a little over a decade for middle age group, older adults saw an increase from 8.7 percent to 9.4 percent in the same time frame.

In terms of the economic burden of adult smoking, the costs are quite substantial. Cigarette smoking costs the United States more than 600 billion, including more than 240 billion in health care spending and approximately 185 billion in lost productivity from smoking-related illnesses and health conditions. That is a significant number, but we're not doing enough about it.

Smoking cessation tools are not always accessible or successful. And beyond that, better communication about the relative risk of different tobacco products is needed to help older smokers make informed choices about their health. And add that to the fact that there are often misperceptions of risk when it comes to lower risk smoke-free tobacco products and a lack of understanding that these innovative products can pose fewer health risks than traditional cigarettes.

Pouches contain nicotine which is highly addictive, but nicotine itself is not a carcinogen. For adults who smoke, switching completely from cigarettes to nicotine pouches may reduce exposure to many harmful chemicals found in cigarettes. FDA needs to provide comprehensive support to move people away from smoking combustible cigarettes. For those who are not able yet to quit nicotine, moving away to safer alternatives such as nicotine pouches would be a better option. Existing efforts to discourage people from smoking should continue, but supplementing these measures of the tobacco harm reduction approach can accelerate a decline in smoking.

The FDA Center for Tobacco Products is the primary regulatory body for products in the U.S. and therefore has a responsibility and the authority to protect the public health from everyone, old and young. The fact is that we have older Americans who smoke cigarettes, and with the FDA's focus only on youth prevention, such as through FDA’s a Real Cost campaign, we missed opportunities to provide much-needed information, education, and care to meet the needs of adult smokers.

There needs to be better balance. We are eager to see FDA doing its part to educate the public on the relative risks tobacco products across a continuum of risk, to rebuild trust through patient-centered communication, and in doing so, empower medical professionals and adult smokers with clear evidence-based tools to make impactful harm reduction decisions. Thank you very much.

Cristine Delnevo:
Thank you. Speaker six.

Guy Bentley:
Good afternoon, Chair. Good afternoon, committee members. My name is Guy Bentley and I'm director of consumer freedom at the Reason Foundation, a nonprofit public policy think tank which also publishes Reason Magazine. I'm here to support Swedish Match's modified risk tobacco product application for ZYN nicotine pouches. The MRTP pathway exists for exactly this purpose, to provide adult smokers with accurate, scientifically validated information about

products that are significantly less harmful than cigarettes.

ZYN clearly meets that standard. When FDA authorized these products for sale last year, the agency found that they do benefit adults who completely switch from cigarettes or smokeless tobacco. The data, as we've heard, continues to show low youth use of these products with just 1.8 percent of nicotine pouch past-month use among students in 2024. But after PMTA authorization, now comes the critical next step. Allowing accurate communication about relative risk to those who need it most.

A majority of Americans, including smokers themselves, incorrectly believe that many safer nicotine alternatives are just as or more dangerous than cigarettes. While there is a wealth of literature documenting consumer misperceptions of the relative risks of e-cigarettes, there is a small but growing body of evidence demonstrating—albeit to a slightly lesser extent—the misperceptions of the relative risks of nicotine pouches among smokers.

Without accurate information, smokers who would switch to dramatically safer products continue smoking instead. We saw this after the EVALI outbreak in 2019 when misinformation about e-cigarettes caused demand for vaping as a cessation tool to drop by around 30 percent even though the outbreak was caused by illicit THC cartridges, not nicotine. Former CTP Director Dr. Brian King argued strongly that the FDA should take a more proactive role in correcting these dangerous misperceptions. And by using evidence-based approaches, MRTP authorization is precisely that approach.

The evidence from General Snus' 2019 MRTP authorization is somewhat encouraging. The authorized claims reached the intended audience, daily smokers, and who were more likely than never smokers to perceive the product as less harmful. Sales are increased relative to higher risk smokeless products, although declining in absolute terms, suggesting some beneficial substitution. And critically, there was no increase in youth use. Every MRTP authorization is conditional and subject to post-market surveillance. If problems emerge, FDA can withdraw the authorization.

Nearly 30 million adult Americans still smoke and cigarettes kill almost half a million people a year. These tobacco-free, smoke-free pouches offer a dramatically safer alternative. The science is clear. The public health case is compelling, and we urge the committee to recommend approval. Thank you for your time and thank you for your work in evaluating the application.

Cristine Delnevo:
Thank you. Speaker seven.

Raquel Mitchell:
Hi, my name is --

Cristine Delnevo:
You're muted.

Raquel Mitchell:

Okay. Sorry. I'm Raquel Mitchell. I am the deputy political director speaking today on behalf of Moms for America Action. And while I cannot answer the question about any financial connection, I can say that we don't work or do anything with anybody whom we do not agree. So, on behalf of Moms for America, which is a national organization of mothers fiercely dedicated to empowering families, protecting our children, preserving our freedoms, and fighting for the health and future of American homes.

As mothers, we know the heartbreak of watching loved ones suffer, the empty chair at family gatherings, the grandchildren who will never know their grandfather, the devastating toll of preventable loss. That is why we are so passionate about pragmatic, evidence-based approach to tobacco harm reduction as a vital part of the broader Make America Healthy Again movement, the MAHA movement. This movement championed by leaders like Robert F. Kennedy, Jr., is about real world solutions to chronic disease, restoring family health, empowering parents with truth, and cutting through misinformation to save lives.

In our role with the MAHA movement, we embrace tolerance and practical policies that offer innovative, lower risk alternatives to dramatically reduce the heartbreaking harms of combustible smoking while never compromising our fierce commitment to protecting children through strict age verification, child resistant packaging, and ironclad enforcement against any youth access. Today, with urgency and hope, we strongly endorse the modified risk tobacco product applications for ZYN nicotine pouches submitted by Swedish Match USA, Incorporated for the Morris International Company. These tobacco-free, smoke-free pouches are supported by overwhelming scientific evidence showing dramatically lower exposure to harmful chemicals compared to cigarettes.

The FDA's own rigorous review during the 2025 premarket authorization confirmed that ZYN contains far fewer dangerous substances, substantially lowering the risk of cancer, heart disease, lung disease, and other devastating illnesses that rob families of precious time. Think of the millions of American adults, parents, grandparents, spouses, until 6 years ago—even myself—who are trapped in the grips of cigarette addiction, unable to quit cold turkey, despite desperately wanting to be there for their families.

Combustible cigarettes cruelly claim more than 480,000 American lives every single year. The leading cause of preventable death in our nation, I quit cold turkey. I had a choice, either quit or suffer another stroke more devastating than the one I had. For those who struggle to quit completely, ZYN offers a powerful evidence-based lifeline, a way to completely switch away from deadly combustion that causes so much suffering.

Approving the proposed modified risk claim, using ZYN instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, chronic bronchitis would deliver truthful life-saving information straight to these adults and the families who love them. Thank you. Think of the families. Think of the mothers. Thank you so much for your time today.

Cristine Delnevo:
Thank you. Speaker eight.

Mario H. Lopez:
Hi there. Am I good?

Cristine Delnevo:
You're good.

Mario H. Lopez:
Okay. Thank you. Good afternoon. My name is Mario H. Lopez, and I'm president of the Hispanic Leadership Fund. We are a nonpartisan public policy advocacy organization promoting liberty, opportunity, and prosperity for all Americans. I'm here today to support authorizing the modified risk tobacco product application being considered today. According to the CDC, nearly half a million people die every year in the United States due to smoking. And smoking-related illnesses cost over $300 billion yearly, including medical expenses and lost economic productivity. But despite massive public campaigns and other large-scale and costly efforts, the reality is that millions of Americans will continue to smoke.

In a physical sense, what smokers are after is simple: nicotine. Nicotine does not cause disease or death, but it is what keeps people using tobacco products. The toxic mix of thousands of chemicals contained in tobacco and tobacco smoke makes its use deadly, causing serious health effects, including fatal lung diseases and cancer. We thus appreciate the FDA's recognition that health risks for different tobacco products exist on a spectrum. This is a critical linchpin for moving more people away from the harms inherent in tobacco combustion.

Modified risk tobacco products are important because of their role in providing harm reduction options for adult smokers who cannot or will not quit nicotine entirely. MRTP designation shows scientifically evaluated evidence of reduced harm and risk of tobacco-related disease compared to combustible cigarettes. Such a designation provides consumers with credible, regulated information, rather than marketing claims. Smokers benefit from clear guidance about which alternatives are genuinely less harmful. MRTP status gives them confidence that switching can reduce health risks, empowering them to make decisions based on science, not speculation.

Adult smokers deserve access to truthful, scientifically backed information about the risks and benefits of all tobacco products. The MRTP process was specifically designed to address this issue. Denying the MRTP in question would undermine this process and deprive consumers of a critical tool used to make better choices. The public health benefits are simply too great to ignore. The FDA has an opportunity to continue to acknowledge the realities and science involved in various methods of tobacco consumption and allow consumers to use products that will substantially lower the negative effects to their health.

The Hispanic Leadership Fund respectfully urges the Tobacco Products Scientific Advisory Committee to recognize the merits of approving the MRTP application in question. Thank you.

Cristine Delnevo:
Thank you. Speaker nine.

Lindsey Stroud:

Hello again. And again, I really appreciate this. I'm Lindsey Stroud here again. And this time, I am founder and president of Tobacco Harm Reduction 101 or THR101, which is a Florida-based 501(c)(3) nonprofit advancing science-based smoke-free strategies to reduce the harms of combustible tobacco, and it's my baby. THR101 welcomes FDA review of whether to issue modified risk tobacco orders for ZYN oral nicotine products. We believe the agency should issue these orders.

A growing body of evidence shows oral nicotine products are substantially less harmful than combustible cigarettes. These products are also associated with statistically significant reductions in both smokeless tobacco and cigarette use. FDA itself has acknowledged these findings through its PMTA determinations, which kind of makes the whole MRTP process a little bit redundant. Ultimately, FDA does remain constrained by a regulatory framework that is increasingly disconnected from consumer behavior and public health outcomes.

Historically, the American free market has driven innovation across industries from medicine to transportation to computing. Under the 2009 Tobacco Control Act, however, it has become nearly impossible to bring the reduced risk tobacco product to market without extraordinary financial resources. PMTA demands increasingly resemble pharmaceutical drug approval, while disregarding the real-world experience of tens of a million of U.S. adults who have used these newer products since 2007. The result is a severely constrained legal marketplace.

To date, only 87 products have received PMT authorizations from 10 manufacturers. Actually, really it's eight after you consider acquisitions. One manufacturer alone has more than 41 percent of those orders. The MRTP pathway is even narrower, only 24 products from four companies, actually it’s really three. These regulatory failures reflected in the growing unauthorized market, including oral nicotine products. Notably, this expansion, though, has occurred with historical declines in smoking. According to the CDC's Behavioral Risk Factor Surveillance System survey, adult smoking fell to 11.6 percent in 2024. It's the lowest rate ever recorded in that survey. And among ages, young adults age 18 to 24 years old, smoking was just 5.9 percent.

Since 2007, with these new products, adult smoking has declined more than 42 percent. And it's also among young adults, it's declined more by 80.5 percent. In the prior TPSAC meeting, I made a kind of a tongue-in-cheek observation that Americans have greater access to fast food fried chicken sandwiches to legally authorized alternative cigarettes. And they did a little bit of research on that. During the fried chicken sandwich wars that kind of spurted in 2019, at least 20 fast food chains introduced new sandwiches. That is twice the number of manufacturers of PMTA product orders, and then more than six times the number of companies with MRTP orders.

For a country that has known the dangers of smoking for more than 50 years, this is wholly inadequate. For a federal regulator committed to a reduced harm approach, it's deeply concerning. Ironically, since that meeting in October, FDA has issued marketing orders for 49 additional tobacco products. Six were for oral nicotine pouches under the PMTA pathway. The remaining 43 were traditional tobacco products approved through less restrictive pathways. It's nearly twice the number of those fried chicken sandwiches.

THR101 supports FDA's issue and MRTP orders for products with demonstrably reduced risk. But we urge the agency to critically reevaluate PMTA and MRTP reviews. Parameters regulatory policies should align with real-world evidence and accelerate, not impede, declines in smoking. Again, thank you for your time.

Cristine Delnevo:
Thank you. Speaker 10.

Drew Tardiff:
Good afternoon. My name is Drew Tardiff, and I'm a senior staff attorney at the Campaign for Tobacco-Free Kids. I have no financial connection to the applicant or the tobacco industry, and neither does my organization. On January 6, Tobacco-Free Kids submitted written comments to TPSAC explaining in detail the reasons why the applicant has failed to meet the rigorous statutory standard for authorization of its proposed claim.

First and foremost is the lack of any demonstrated benefit. FDA's briefing document correctly concludes that the applicant study doesn't suggest that the modified risk claim would result in a substantial change to tobacco use patterns. The application can and should be denied on this basis alone, without having to even weigh the potential harms, of which there are many. Perhaps most significant: the potential impact that this claim would have on youth usage. The applicant entirely failed to submit data showing how youth—meaning those under the legal purchasing age of 21—perceive this claim.

This is critical data because ZYN has features that enhance its appeal to young people. It's sold in a variety of flavors. It's easy to conceal. It can be used discreetly. And unlike General Snus, which has been authorized with a similar modified risk claim, ZYN has developed into a cultural phenomenon. It's inspired TikTok videos and Instagram posts seen by millions of youth. It's inspired memes, dog toys, even its own lingo.

PMI's marketing of ZYN has greatly contributed to ZYN's popularity. Buying ZYN is the only way to secure tickets to exclusive shows featuring performers with young fan bases like Nate Bargatze and Noah Kahan. ZYN rewards use of its products with merchandise that appeal to youth, like iPads and Dyson hair stylers. Studies show that these types of reward programs encourage higher consumption. And just last month, PMI announced that it will expand its partnership with Ferrari to add ZYN branding to Formula One race cars potentially exhibiting ZYN to the more than 4 million children that Formula One says actively follow the sport. Nothing like this has occurred with General Snus.

Data is just beginning to show the consequences of ZYN's rise. While nicotine pouch use rates among youth are relatively low now, they are rapidly trending upwards. NYTS data show that the percent of middle and high schoolers using nicotine pouches in the past 30 days doubled between 2021 and 2024. Monitoring the Future data show that past 30-day nicotine pouch use rates among 12th graders more than doubled between 2023 and 2025. And ZYN is by far the most reported brand used by youth and young adults. NYTS data show that more than three-quarters of high schoolers who reported currently using nicotine pouches use ZYN.

This trend mimics the early years of initially slow growing e-cigarette use among youth just before rates rose to epidemic levels due to the youth-oriented marketing of JUUL. If the proposed messaging leads to youth misperceiving ZYN as being safe, it could drive usage even higher. Authorization shouldn't be granted unless there is clear evidence that it won't, and there isn't. Thank you.

Cristine Delnevo:
Thank you. Speaker 11.

Amanda Smith:
Good afternoon, members of the committee. My name is Amanda Smith. I'm president of the Native American Business Association, a national organization advocating on behalf of Native entrepreneurs and small businesses across the United States and on Tribal lands. Cigarette smoking remains the leading cause of preventable death in the United States but this toll is especially severe in American Indian and Alaska Native communities. CDC data shows that American Indian and Alaska Native adults have the highest smoking rates of any racial or ethnic group, 15.8 percent in 2024 compared to 10.7 percent for white adults. Some Tribal communities reach 50 percent.

This disparity drives devastating outcomes. Cardiovascular disease and lung cancer are among leading causes of death in our communities both strongly linked to smoking. American Indian and Alaska Native women have the highest rates of smoking during pregnancy at 12.7 percent, nearly double that of white women. Secondhand smoke harms our children and takes our elders before they can pass down Tribal customs and traditions. It is essential to distinguish between sacred traditional tobaccos, which are used for prayer and healing, and commercial combustible cigarettes, which are mass produced, addictive, and deadly.

Our public health strategies must respect Tribal sovereignty while accelerating harm reduction for adults who smoke. The FDA's modified risk tobacco product process is rigorous and evidence based, authorizing truthful information about smoke-free alternatives like ZYN nicotine patches can empower adult smokers, especially those who cannot and will not quit, to make better informed choices.

Scientific reviews confirm that noncombustible products expose users to substantially fewer harmful chemicals than cigarettes. Granting MRTP status for ZYN, if the evidence supports it, would help lower the disease burden, advance health equity, and support economic productivity in Native communities by helping more adults move away from combustion by far the most harmful form of nicotine use.

So, on behalf of the Native American Business Association, I urge the FDA to uphold its rigorous standards, and if warranted, grant MRTP status for ZYN. Our communities deserve accurate information and less harmful alternatives to build healthier futures. Thank you.

Cristine Delnevo:
Thank you. Speaker 12.

Gretchen Wartman:
Good afternoon. My name is Gretchen Wartman. I am vice president for policy and program of the National Minority Quality Forum. The forum is a 501(c)(3), not-for-profit research and advocacy organization based in Washington, D.C. The mission of NMQF is to reduce patient risk by assuring optimal care for all. Our vision is an American health services research delivery and financing system whose operating principle is to reduce patient risk for a minimal morbidity and mortality while improving quality of life. We do not have a financial conflict of interest.

Accordingly, tobacco harm reduction is a priority for NMQF. Combustible cigarette smoking remains the leading cause of preventable disease and death in the United States, resulting in significant economic burdens due to health care costs and lost productivity. As has been mentioned by prior speakers, according to the Centers for Disease Control and Prevention, smoking-attributable medical costs exceed $250 billion annually, and productivity losses amount to approximately 372 billion. These figures highlight the impact of tobacco-related illnesses on family livelihoods and local economies, including small businesses and tribal enterprises that bear the brunt of reduced labor force participation and increased absenteeism.

The FDA modified risk tobacco review process demands robust evidence that the ZYN nicotine products could reduce harm. NMQF believes that providing science-based smoke-free alternatives to legal age adult smokers who are unable or unwilling to cease their use of combustible cigarettes is an essential component of a strategy to improve the health of the public within the context of the individual as well as of the community as a whole.

NMQF, therefore, is submitting this public comment in support of the FDA modified risk tobacco product review process for ZYN nicotine pouches. NMQF supports FDA's rigorous review standard and believes that when evidence meets legal and regulatory requirements, the resulting fact based non-misleading communications about lower risks of ZYN nicotine pouches relative to continued smoking will help adult smokers make better informed choices. Providing comprehensive support to help people transition away from smoking combustible cigarettes is crucial. For individuals who are not yet able to quit nicotine, safer alternatives should be available.

In closing the National Minority Quality Forum respectfully urges the FDA to continue its stringent, transparent MRTP review. If the evidence meets the necessary requirements, granting a modified risk tobacco product designation for ZYN would enable more effective communications to adult smokers about the reduced risks relative to continued use of combustible cigarettes. Thank you for the opportunity to speak this afternoon.

Cristine Delnevo:
Thank you. Speaker 13.

Jasjit Ahluwalia:
Thank you to the FDA and Chair Dr. Delnevo and the TPSAC members. My name is Jasjit Ahluwalia. I'm a physician scientist and a professor at Brown University School of Medicine and School of Public Health. I do have a conflict of interest with Qnovia. It is a startup pharmaceutical company that completed phase 1 clinical trials that's working with CDER at the

FDA for prescription product, a nicotine replacement product in particular. I've read all the FDA/manufacturer documents for today and was quite impressed with the thoroughness and actually, a symmetry between the two. And I've enjoyed the discussions this morning.

I'm here because I'm passionate about this topic. I have been doing this since, in a way, 1986 when I was a med student and invited C. Everett Koop, the then surgeon general. You'll have to be old enough to know who he was. And really, he had a massive impact on me. As a resident at Chapel Hill in North Carolina, I took care of a patient that I'll never forget that had end state COPD. And in order to sleep in the hospital, they had to sleep backwards on a chair because if they lay down flat, they would suffocate.

That is one of many reasons why I've been in this space for 34 years doing randomized trials with every FDA-approved cessation medication and led the first RCT with fourth-generation e-cigarettes published in JAMA Network Open in the year 2000. During this time, I was a peer reviewer for an article that was on nicotine pouches, comparing it to oral nicotine products. I was sort of new to this space back then because I have not heard much about it. I was stunned that the in vitro HPHCs were essentially no different and were below-level quantifiable in some cases compared to oral NRT. So, not cigarettes, obviously, but oral NRT.

This led our team to conduct a pilot trial, a very small pilot trial of 45 people comparing use of e-cigarettes versus pouch versus smoke your own. This was published in 2024. The particular smokers in this study, 77 percent were on Medicaid, and 70 percent had less than a high school education. Our findings were that those that got pouches, the mean number of cigarettes per day fell from 15 to 8 cigarettes per day. We definitely need more work in this space. And I hope that there's continued funding and more work, both by the industry, but especially by those not in industry.

All this work reminds me, and should remind us, that if harm reduction is a strategy that we want to pursue, we need to target the people who smoke cigarettes. And as pointed out earlier by others, this includes lower socioeconomic people, dual addictions, those with mental diagnoses, in particular Native populations, and as mentioned earlier, also those greater than 50 in age.

I always say that if you smoke, quit. First, use FDA-approved medications. If you can't and don't want to quit, use safer nicotine products. If you don't use nicotine, don't start using it. To me, speaking as a physician and scientist, the evidence to date is quite strong to grant an MRTP. It's very important, however, if this is granted, that continued surveillance, especially regarding youth usage and other things by the manufacturer and the FDA is, of course, warranted. Thank you very much for giving me the time.

Cristine Delnevo:
Thank you. Speaker 14.

Leah Vukmir:
Good afternoon, chairman and members of the committee. My name is Leah Vukmir, and I am the senior vice president of state affairs at National Taxpayers Union. I am a former state senator and certified nurse practitioner. I am drawing on experiences from all three roles, and I am here

today in support of the MRTP application for ZYN. No one is paying me to express any convictions that are different from the ones I have long held long before joining NTU. And beyond that, NTU protects the identifiable information of all of our thousands of supporters.

We all know that combustible cigarette smoking remains the leading cause of preventable disease and death in the United States. Yet, despite decades of prevention and cessation efforts, as has been said by many, 28 million American adults still smoke and quitting completely remains difficult for so many. Public health policy rightly prioritizes cessation, but it must also recognize that for adults who cannot quit, safer, noncombustible alternatives can meaningfully reduce harm. And this is precisely where the MRTP process plays an incredibly critical role.

Not all tobacco products carry equal risks. Adults deserve accurate science-based information about those differences. A major barrier to harm reduction is widespread misunderstanding about nicotine. Many adults believe nicotine itself causes cancer and heart disease. In my clinical experience, when patients believe all nicotine products are equally dangerous, they're less likely to switch and are more likely to continue smoking cigarettes, the most dangerous option.

What's even more confounding to me is the misunderstanding is not just limited to the public. It also extends to health care providers. We have large surveys that show that the majority of physicians, including 70 to 86 percent in the United States, incorrectly believe nicotine causes lung cancer, COPD, or atherosclerosis. When both patients and clinicians overestimate nicotine's harm, smokers are denied information they need to make better choices.

This is why allowing accurate evidence-based communication about reduced exposure from noncombustible products like ZYN is so important. Goal is not about promotion. It is informed decision-making for adults with strong safeguards against youth access. From a taxpayer perspective, harm reduction also delivers meaningful fiscal benefits. Smoking drives hundreds of billions of dollars in annual public health costs and reducing that can save taxpayers money across the board.

In closing, providing truthful science-based information about lower risk products supports public health, it respects adult choice, and it reduces taxpayer burden. The MRTP pathway, when applied carefully and responsibly, can help move smokers away from the most dangerous products, while maintaining strong protections for youth. Thank you very much for the opportunity to speak to you today.

Cristine Delnevo:
Thank you. Next speaker, speaker 15.

Christina Smith:
Hello. My name is Christina Smith, director of the Consumer Center at the Taxpayers Protection Alliance. Thank you for the opportunity to speak today on behalf of the millions of taxpayers and consumers that we represent. The Taxpayers Protection Alliance is a nonprofit, nonpartisan organization dedicated to educating the public by researching and analyzing the unintended consequences of government intervention. TPA advocates for greater consumer access to harm reduction products such as nicotine pouches as a less harmful alternative to traditional tobacco

products.

Today, over 30 million American adults smoke cigarettes with few legally available and quality controlled options for adults attempting to quit the deadly habit. More than half a million deaths occur annually in the U.S. from smoking. A conventional cigarette contains more than 6,000 ingredients, which when burned, release more than 7,000 chemicals. Traditional cigarette use is associated with a host of diseases and chronic illnesses. Additionally, traditional smoking burdens a health care system and costs taxpayers hundreds of billions of dollars annually.

Fortunately, harm reduction products such as nicotine pouches offer users much of the satisfaction they gain from combustible tobacco products at a small fraction of the risk to their health. Evidence supports that adults may be using nicotine pouches for harm reduction, given that the use is highest amongst those who have recently quit another tobacco product, and this substitution strategy is very wise.

As Dr. Vaughn W. Rees, director of the Center for Global Tobacco Control at the Harvard School of Public Health, notes, ZYN has very low toxicity compared with smoking. So, even without long-term studies, we know that long-term disease risk is likely to be lower than combusted cigarette products. Most importantly, the FDA itself has acknowledged this substantial body of evidence.

In its January authorization of ZYN nicotine pouch products, the agency stated, "Due to substantially lower amounts of harmful constituents than cigarettes and most smokeless tobacco products, the authorized products pose lower risk of cancer and other serious health conditions than such products." Allowing the manufacturer to market the products with a modified risk claim is the next logical step for the FDA and is consistent with the evidence.

As the Tobacco Products Scientific Advisory Committee convenes to review modified risk tobacco product applications submitted by Swedish Match USA for ZYN nicotine pouch products, we urge the committee and FDA to consider the substantial evidence that nicotine pouches are a less harmful alternative for consumers than cigarettes. We also would urge the FDA to more generally adopt a flexible approach and regulatory framework that allows consumers to access harm reduction products. I thank you for your time and attention to this important issue.

Cristine Delnevo:
Thank you. Speaker 16.

Sherwin Herring:
Good afternoon. My name is Sherwin Herring, and I'm the owner and CEO of SouthCo Distributing Company located in Goldsboro, North Carolina. We are a family-owned business that has served convenience retailer for more than four decades. And today, we supply over 1,500 stores across five states. I appreciate the opportunity to speak about the modified risk tobacco product application for ZYN nicotine pouches.

As a distributor and member of several trade organizations, we get to see trends all across the

nation, thousands of retail locations, and millions of transactions. One thing is very clear, adult smokers are actively seeking smoke-free and less harmful alternatives. ZYN has become one of the most requested products in our warehouse because it offers a noncombustible, discrete option that aligns with harm reduction principles.

Modified risk tobacco product modification authorization is critical for two reasons. First, it ensures that any reduced risk claims are scientifically vetted and FDA reviewed. Distributors and retailers need clarity and confidence when communicating with adult consumers. Without MRTP, we cannot responsibly share the facts, even when science supports harm reduction. Second, MRTP authorization strengthens compliance and trust.

At SouthCo, we work closely with our customers to uphold strict age verification and responsible sales practices. Carrying FDA-authorized products like ZYN reinforces our commitment to public health and also protects our consumers and customers. We have seen firsthand that when adults have access to truthful, easy-to-understand information, they will make choices that move them away from combustible cigarettes. That's a win for public health. It's a win for tobacco users and for communities that we live in and serve.

I respectfully urge TPSAC to recommend modified risk tobacco products authorization for ZYN nicotine pouches. Doing so will empower adult smokers with accurate information, support harm reduction, and reinforce the role of responsible distributors and retailers in advancing public health. Thank you for your time and consideration.

Cristine Delnevo:
Thank you. Speaker 17.

Akashleena Mallick:
I am Dr. Akashleena Mallick. I'm a physician and public health researcher with the nonprofit National Center for Health Research. We have no disclosures. A modified risk authorization requires clear benefit to public health. That standard is not met here. I will explain why. I want to begin by supporting the concerns previously raised by UCSF and Tobacco-Free Kids about the use of nicotine pouches by about a half million U.S. middle and high school students.

I will now focus on the medical, pediatric, and public health harms of ZYN. A modified risk order requires proof of less disease. FDA found no such data on the health impact of ZYN. Relying on General Snus data is inappropriate because these products differ in use, toxicology, and marketing. We agree with FDA that data on Swedish adults do not apply to the U.S. teenagers. That's why FDA's General Snus MRTP is not a valid precedent for ZYN. Claims of reduced risk for cancer, heart disease, and stroke would require decades of follow-up to make it comparable to risks of cigarettes. No such data exist.

Short-term biomarkers and toxicant comparisons cannot prove disease reduction. Nicotine itself harms the heart and blood vessels, as concluded by the American Heart Association and the European Society of Cardiology. Nicotine raises blood pressure and heart rate and worsens vascular function, which are key pathways for heart attack and stroke. Without long-term data showing fewer cancers, heart attacks, or strokes, any claim of reduced risk is misleading and

probably incorrect.

U.S. Poison Center data show nicotine pouch exposures rose dramatically from 181 cases in 2022 to over 900 cases by early 2025. Nearly three-quarters of these cases involve children under the age of 5, mostly from accidental ingestion. A peer-reviewed national study found that nicotine pouch ingestions in young children rose more than 760 percent in just 3 years and were more likely than other nicotine products to cause serious harm or hospital admission.

These injuries are happening now. ZYN has a record of aggressive marketing with a rewards program that encourages more frequent use, including in children and adolescents. If the goal of ZYN was to give a safer alternative to smoking, why is ZYN successfully focusing its marketing strategies on children and teens, most of whom don't even smoke? Independent research shows that modified risk claims are often misunderstood as safe, leading to dual use, delayed quitting, and use by nonsmokers who then become addicted.

Some states apply lower taxes to MRTP products and companies push for those cuts. Lower prices increase use among both smokers and nonsmokers. FDA said e-cigarettes would help adults quit. Instead, it helped fuel a youth nicotine epidemic. Nicotine pouch sales have already risen more than tenfold from 126 million units in 5 months in 2019 to over 800 million units in 3 months in early 2022. There is no long-term evidence that ZYN reduces mouth cancer, lung cancer, heart disease, or stroke but there is clear evidence of pediatric poisonings, likely cardiovascular harm, problematic marketing, and increasing risks to public health. For these reasons, ZYN nicotine pouches do not meet the legal standard for modified risk authorization. Thank you.

Cristine Delnevo:
Thank you. Speaker 18.

Scotte Ellis:
Good afternoon. My name is Scott Ellis, and I have no financial affiliation. I wanted to thank you for the opportunity to provide testimony. I have spent much of my life in environments where tobacco use was common and often accepted, beginning through my involvement in sports at a young age and later during my career in law enforcement.

I'm here today to share my personal experience and why I believe harm reduction should be an important part of public health policy. I began using tobacco at a young age, at a time when it was widely normalized. Although I knew the health risk associated with tobacco, understanding those risks did not eliminate my dependence or cravings. Over many years, I continued using chewing tobacco despite repeated efforts to quit. What ultimately made a meaningful difference for me was the access to a tobacco-free alternative.

After switching to ZYN nicotine pouches, I was able to stop using tobacco entirely and significantly reduce my exposure to harmful components associated with traditional tobacco products. Traditional chewing tobacco exposes users to tobacco leaf and range of harmful additives, including tobacco-specific nitrosamines, which are strongly associated with oral disease and cancer. Regular use can damage gums, teeth, cause chronic irritation of the mouth,

and lead to conditions such as gum recession, tooth decay, and precancerous lesions.

ZYN nicotine pouches are fundamentally different because they do not contain tobacco leaf or do not expose users to the same tobacco-derived carcinogens found in smokeless tobacco. They're placed in the mouth without abrasive plant material, reducing irritation to oral tissues. While no nicotine product is risk free, tobacco-free nicotine pouches like ZYN represent harm reduction option by significantly lowering exposure to the substance most responsible for the oral and dental damage caused by traditional chewing tobacco.

I want to thank you for the opportunity to share my perspective and personal experience. I appreciate the department's time and consideration. And I respectfully encourage thoughtful evaluation of harm reduction approaches that can help adults reduce their exposure to the most dangerous forms of tobacco. Thank you.

Cristine Delnevo:
Thank you. Speaker 19.

Jessi Troyan:
Hi, members of the committee. Thank you for the opportunity to speak today. My name is Jessi Troyan, and I serve as the Director of Policy and Research at the Cardinal Institute for West Virginia Policy. My home state faces a public health challenge with deeply personal and economic implications. West Virginia has the highest adult smoking rate in the country at 20.4 percent and the second highest rate of new lung cancer cases, according to the American Lung Association State of Lung Cancer Report.

These aren't abstract numbers. My own mother falls into both of these categories. But for me as an economist, this reality forces an uncomfortable but necessary question: What do we do when ideal solutions are statistically unlikely? Nationally, about 11.6 percent of adults smoke. In West Virginia, it's nearly double that. While, yes, the ideal solution would mean people quitting smoking entirely, data from the CDC shows that sustained quitting is difficult. Every year, a majority of smokers say they want to quit, but only a small fraction reaches long-term success.

For the millions of Americans who still smoke cigarettes, policy is a matter of tradeoffs, not perfection. If outright quitting is unlikely for many smokers, the next best questions focus on harm reduction. How can people move away from the most dangerous form of nicotine consumption toward alternatives that pose less risk? To me, this is where product innovation and consumer choice matter. A broader range of noncombustible nicotine products give smokers more realistic off ramps. Allowing accurate communication that these products are lower risk than cigarettes would help smokers make informed decisions and move away from the deadliest options.

As already mentioned, the physical and health care implications in my state are significant. We're consistently ranked among the unhealthiest in the nation, and smoking is a major contributor. According to the West Virginia Department of Health and Human Resources, tobacco-related illnesses drive substantial Medicaid spending and long-term health care costs borne by taxpayers. If even a portion of smokers shift to lower risk alternatives, the downstream savings could be

enormous for government budgets, families, employers, and communities.

Again, from an economist's perspective, this is about aligning incentives with reality. Harm reduction respects individual choice while reducing public choice—public costs. This doesn't endorse nicotine use. It acknowledges imperfect human behavior and mitigates the most damaging consequences. Thank you for your time.

Cristine Delnevo:
Thank you. Speaker 20.

Jennie Salyer:
Yes. Thank you for the opportunity to comment. My name is Jennie Salyer, and I represent Gallatin Redrying and Storage Company, a dealer and processor of fine leaf tobacco based in Gallatin, Tennessee. We are a supplier to Swedish Match for their moist snuff products, but we have not been paid to speak today. With over a century of experience in the tobacco industry, we have supported the tobacco farming community by collaborating with farmers to promote good agricultural practices and strengthen the tobacco economy.

As a proud business owner, we create jobs and contribute to our state through commerce, donations, and taxes and honor our heritage. Tobacco has been a foundation of Tennessee's economy since before it became a state. Its historical and economic importance extends across the U.S. as tobacco was the first commodity traded by American colonists with England over 400 years ago and played a role in the American Revolution. Our financial stability and success rely on recognizing market trends showing leadership and embracing innovation in our industry. For example, in 2015, we hosted a CTP site tour at our facility to give the FDA a chance to learn more about our business and tobacco agriculture.

The development of nicotine pouches made from tobacco-derived nicotine, such as ZYN, demonstrates the innovation taking place in the nicotine sector today. Authorizing ZYN through the FDA's modified risk tobacco product pathway can benefit small businesses and tobacco farmers by creating legal opportunities for new tobacco-based products that could sustain demand for domestic leaf tobacco as cigarette use declines supporting specialty crops and enabling farmers to grow high-value, proprietary crops that meet FDA requirements for specific nicotine content.

The MRTP process offers a rigorous, science-based approach to distinguish legitimate, domestically sourced tobacco products from illicit or unregulated alternatives. The regulatory clarity helps stabilize the legal market for both farmers and businesses. FDA's actions today can strengthen local economies and support small agricultural-based businesses. Your favorable recommendation is crucial to our business and to the U.S. tobacco farmers. Again, thank you for this opportunity to speak.

Cristine Delnevo:
Thank you. Speaker 21.

Tim Hwang:

Hello to the members of the committee. I appreciate the chance to provide comment to you all. My name is Tim Hwang. I'm a senior fellow at the Foundation for American Innovation. I do not have a financial interest. FAI is a think tank that looks to advance pro-innovation, pro-progress policies. And at FAI look after our national security and defense work.

So, why am I here? We live in an era where geopolitical tensions and great power competition is really leading the U.S. military to evaluate very closely and take seriously the notion of its military readiness and the readiness of its service members. If you've been watching the news, Department of War Secretary Hegseth has said that the country needs to be on a wartime footing and that, for his part, the sort of lethality of the Armed Forces is a key part of that picture.

And so, what does that mean in practice? A big part of it will be taking seriously the health of the DOW's 2.1 million service members at this pretty critical time. And that means looking after their physical standards and their long-term health. Current DOW policy is really constituted when it comes to tobacco products around something called Instruction 1010.10. And it basically commits the department to a sort of categorical tobacco-free policy. That means sort of bans on the use of any tobacco or nicotine products in training, on bases, in facilities, in the field, or otherwise.

And so, I think I'll cross-reference a lot of the health evidence that's been presented by many of the other speakers in the need to start creating a policy that differentiates between combustible products and products like ZYN. It's very relevant for the acute health impact of these products on the physical endurance of service members into the field. But outside of that health evidence that I think applies to this analysis for the general population, I want to kind of put two sort of interesting dimensions to this into the record when it comes to the military.

The first one is in the field. You know, this is an adversarial situation where enemy combatants, adversaries may be looking to actively harm our service members. And here, actually, the difference between combustible and products like ZYN may really have a real impact on the safety of our service members. The second one is many service members serve in places where combustibles are not viable, in submarines, in flight, in tactical concealment. And these are all places where active encouragement of the use of products like ZYN would make a big difference.

And so, I think in the campaign to revise the DOW's policy, MRTP would be of a lot of scientific grounding for revision of that policy and to allow them to differentiate between these two types of products. And so, when it comes to national security, there are implications of what the committee will do here today. And I thank you for your time.

Cristine Delnevo:
Thank you. And I want to thank all of our open public hearing speakers for their attentiveness to the time. So, that concludes the open public hearing. At this point, I'd like to introduce Dr. Benjamin Apelberg, Deputy Director of the Office of Science at CTP.

Benjamin Apelberg:
Okay. Great. Thanks, Dr. Delnevo. And thanks to all the individuals who participated in today's

open public hearing. You know, public participation in the regulatory process, it's really an important part of the work we do here at FDA. So, I just wanted to say thank you to those who spoke today. As Dr. Delnevo said, I'm Dr. Ben Apelberg. I'm the Deputy Director in the Office of Science at the Center for Tobacco Products.

For the rest of today's meeting, our committee members will be asked to discuss and deliberate about four discussion questions, which CTP developed based on our preliminary evaluation of the MRTP applications for these ZYN products and reflect the topics most relevant to our evaluation of whether all the statutory standards are met. I wanted to let everyone know that we have many staff here from the Office of Science who will be paying close attention to the committee's discussions, and these discussions will be used to inform our evaluation of the MRTP applications.

Just a few things that I wanted everyone to keep in mind before I turn things back over to our Chair. First, you know, we encourage committee members to focus on the questions that CTP has developed. A great deal of thought went into these questions, and they really do reflect the areas of scientific evidence where we are most seeking TPSAC scientific input and advice. You know, also, as scientists, we encourage you to use your scientific expertise to objectively consider the evidence that's been presented, and keep in mind why we're here to provide scientific advice to CTP as part of our evaluation of these MRTP applications.

So, with that, I'd like to turn it back over to Dr. Delnevo to lead what I'm sure will be a robust and engaging discussion about the evidence that's been presented. I look forward to it. Thank you.

Cristine Delnevo:
Thanks, Ben. Next slide. Next slide. Next slide. So, we're going to start with Discussion Topic 1, the Accuracy of the Proposed Modified Risk Claim. As a reminder, for background, the proposed modified risk claim is: “Using ZYN instead of cigarettes, puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.” The majority of constituents—harmful constituents, are below the levels of quantification in ZYN. And the biomarker studies of people who use nicotine pouches are consistent with the product chemistry data.

In the absence of the long-term health risk studies of nicotine pouches, Swedish Snus epidemiological studies show that snus use is lower risk compared to combustible cigarette smoking for mouth cancer, heart disease, stroke, lung cancer, emphysema, and chronic bronchitis. And so, now I'd like to open it up to the committee to discuss whether the proposed modified risk claim is substantiated by the scientific evidence. Dr. Rigotti.

Nancy Rigotti:
Thank you. I'm just getting onto the screen here. So, hello everyone. I think we could—I would make this simple, because I think the answer to this question is yes, that the proposal has met the criteria. I think the other ones—the other questions will be more controversial. But I think that this one, while we don't have perfect information, we don't know exactly what ZYN, when used for many years, will do, I think it's very reasonable to use the Swedish experience and the

evidence that's been shown. So, I would—I would say yes. Thank you.

Cristine Delnevo:
Thank you. Dr. Benowitz.

Neal Benowitz:
I would agree with Dr. Rigotti. There were some comments saying that there was concerns about the long-term risks of ZYN being different than Swedish Snus. I don't understand the biological plausibility of that. There have been many studies of Swedish Snus documenting a high level of nicotine absorption. There have been many studies looking at biological effects and health outcomes. And in terms of cardiovascular effects, certainly, nicotine has got cardiovascular effects. But again, the literature looking at the risk of developing cardiovascular disease, atherosclerosis, heart attacks, strokes, basically, the risk is very low or nil and much, much lower than cigarette smoking. So, I don't think that there's any concerns about risks being much, much lower than smoking. I do think—and this may go to a different question—the data where people were asked about the perceived risk after looking at the warning, still showed that most people—smokers or not—think that nicotine is very, very harmful.

And again, to get back to the question of getting older smokers to quit, if they think that using a pure nicotine product is almost as bad as smoking or even half as much, they've got an excuse not to change. One thing I think that, not so much Swedish Match, but FDA and public health really need to explain the actual risks of nicotine per se versus cigarette smoking. I think that would encourage people to switch to a less harmful product. So, I've got some comments about some of the other things, but I think those are the main ones involving health effects.

Cristine Delnevo:
Thank you. Dr. Jordt.

Sven-Eric Jordt:
Thank you. I generally support the claims about mouth cancer and lung cancer. However, I have concerns about the claims related to respiratory conditions. There have been studies out of Nordic countries showing that when, yeah, children are starting to use like snus, for example—and we got here the Swedish example—have a higher incidence of asthma developing, right? And that cannot be really differentiated from chronic bronchitis. It may not be as bad as from smoking, but we will have new populations forming that need to be traced that have—where adverse health effects over the long term are manifesting with the use of ZYN. Thank you.

Cristine Delnevo:
Thank you. Dr. Scout.

NFN Scout:
In general, I really only want to bring up one thing here. I know I added a prior meeting too, but I urge FDA to update the HPHC list so that it's more accurate for noncombustible potential toxins, and that future science is based upon that.

Cristine Delnevo:

Thank you. Dr. Postow.

Lisa Postow:
Yeah. Thanks. Yeah. So, I would agree with what I think most people are saying. I think that the statement is true almost certainly. If there are other constituents in the product that aren't in tobacco products, they're almost certainly going to be less harmful than cigarettes. There are very few things that are legally accessible that are worse for you than cigarettes. So, I think it's a pretty low bar to be safer than cigarettes.

And the most important aspect of this, in addition to not being combusted and not containing tobacco, is that this is taken orally and not inhaled. We know a lot more about what's safe to take orally than what's safe to be inhaled. Almost nothing is safe to be inhaled, but lots of things are safe to take orally. So, while I am sensitive to the idea that there may be some pulmonary conditions that are going to be more likely with this product, they are almost certainly less so than cigarette smoke. Although, like I'm going to say through this whole thing, I think the product has not been on the market long enough to say anything for sure and if this proposal is granted, that we really need to keep an eye on it.

Cristine Delnevo:
Thank you. I'm actually going to move us forward to the next discussion topic. And if committee members have things they want to come back to Discussion Topic 1, you can. But I am agreeing with Dr. Rigotti and kind of reading the room that we're going to have some more robust discussions on some of the additional discussion topics. So, next slide.

So, Discussion Topic 2 is Consumer Understanding and Perceptions. As a reminder, by way of background, the applicant had provided evidence about whether consumers understood the risk reduction described in the claim that ZYN confers lower risk than combusted cigarettes. That although conferring lower risk than combusted cigarettes, ZYN still confers health risks, as well as how to use ZYN to confer lower health risks, which is complete switching.

So, we're now going to discuss the available evidence about consumer understanding of the proposed modified risk claim and their perceptions of ZYN. And opening it up, Dr. Scout.

NFN Scout:
A couple of points on this one. First of all, I'm curious about the framing of using the phrase "tobacco-free" so heavily in the marketing of the product. Because, as you see, buried somewhere in their information, a substantive portion of users perceive this as nicotine free, and that's certainly a concern. Because that means that that's a substantive portion of people researched thought that it was potentially not addictive. And that's definitely an issue, and I suspect that's probably what is being intended with the tobacco-free claim.

As well, I am certainly concerned about the dual-use information and the fact that we only have dual-use data off of a different product, and not this product, knowing that they're chemically not the same, and the use of tobacco salts makes uptake different. So, that is definitely a weakness as far as this information we've been given.

Cristine Delnevo:
Thank you. Dr. Popova.

Lucy Popova:
I have a couple of points here. One is when evaluating consumers' understanding according to FDA guidance to the industry on modified risk tobacco product applications, MRTP studies should measure not only comparative risk between the product and cigarettes, but also different other things like the product and e-cigarettes, product and other products of this category, product and NRT and product and complete cessation. These data are available in the application that PMI submitted. And I urge the FDA to look at the data that is not publicly available to see what those comparative risk perceptions are for a variety of those products.

In terms of the question of whether switching is understood, the SM was brought up earlier by Dr. Wackowski. The evidence for that comes from understanding—comes from Swedish Match General Snus studies, not from this study. Unfortunately, the language here is using "instead of cigarettes," and that means it's—a lot of people can understand that as, "Oh, I switch a few of them, and that gives me the benefit." We have studies where we show when even when we provide a very detailed explanation for a phrase saying, "switching completely," which means smoking only this product or using only this product and not smoking any cigarettes. When we ask people, "How many cigarettes can you smoke if you switch completely," it only increases the number from like 12 percent to 20 percent and the rest of people still think, "Oh, you could smoke some." And this is particularly prevalent among smokers. If you look at the population as a whole, including people who don't smoke, then these numbers drop. Because people usually, especially young adults who do not smoke, they usually have pretty correct perceptions. But among people who smoke, they're very inclined to still think, "Oh, I can still smoke and not switch completely." And even when they use them behaviorally, you say, "Did you switch completely?" They say, "Yes." And then you ask them, "How many cigarettes did you smoke yesterday?" They're like, "Oh, five."

So, oftentimes it is unclear whether when people in the study data that were presented earlier today, if people are saying, "Oh, we switched completely," if they actually switched. There was no validation other than self-report, which could be incorrect. So, thank you.

Cristine Delnevo:
Thank you. Anyone else have some questions, comments? So, Dr. Rigotti, you had your hand up before. Oh, back up again. You're on.

Nancy Rigotti:
Okay. Here, I would say that I felt like the quality of the material that was in the application made to the FDA was not as good as it might should have been, or might have been, let's say. in the sense that it didn't show all of these. And you know, sort of, how to use ZYN to confer lower health risk, which is the third part of your—of the question here is the implication was that you had to switch completely. And I'm not sure that that got through.

But beyond that, there's also that perhaps there might be ways that you can use ZYN and there might be ways that you can overuse ZYN. And perhaps there could be some information

provided in the marketing of the product, which I know is not exactly what we're discussing now, but it's something for the company to think about that about how to use it properly so people don't overuse it at all.

But I would say that given what was there, it seems like this was reasonable to think that people do understand that the effect is that it's less harmful than cigarettes. I think that message got through. And I think getting that message out to the public, even people who don't smoke, is very helpful because there's such misunderstanding in the U.S. right now about reduced harm products. Thank you.

Cristine Delnevo:
Thank you. Dr. Popova.

Lucy Popova:
Just to follow up with Dr. Rigotti. You were saying that the message that ZYN is less harmful than cigarettes came through. Based on what we see, we don't really see that this was the effect of the message itself. The slides we should have seen today for the lung cancer risk perceptions that the FDA showed in their backgrounder showed a very, very minimal change between people who from—between the control group and test group. So, people who didn't see the modified risk claim thought it's less harmful, and people who saw a modified risk claim thought it was less harmful, maybe by a few percent points. We don't know. There were no, as FDA pointed out, there were no statistical significance testing done.

So, in that sense, what we are seeing is that people already have that belief that it is less harmful. Showing them the message in this one study was shown once. We don't really know what would be the effect of it if it's shown again and again. And based on—I was really hoping we have evidence by now from the General Snus marketing, but we do not. So, based on all of that, we do not see that putting this message on the product, and not even on the product but just on the advertisements for that, that we will see actual change in the beliefs about the risk of product in terms of its comparison to cigarettes, because it's already quite different.

Cristine Delnevo:
Yeah. Dr. Wackowski.

Olivia Wackowski:
Sorry about that. Yeah. Just to follow up on some of Dr. Popova's points, I think too that it was a little bit surprising that the relative risk perceived differences between the test and the control ads that they were quite narrow, quite modest differences. But I agree that, you know, a limitation in the study was that they were only shown this one ad one time. The claim itself doesn't—there's a lot of text in the ad. The claim itself doesn't particularly stand out. So, you know, we do wonder what it would be like if there was more exposures, more prominent exposures. And so that that was one point.

I do think that to the second point about whether people still perceive that ZYN confers health risks, I think that was pretty clear in the data that we saw. And then as far as how to use ZYN to reduce risks, I think yes, going back to the previous point about switching completely, it did

seem like a missed opportunity, a limitation of the study, to not ask about that for this particular product in this study, and to only rely on the General Snus one. Although I do think the evidence from the General Snus study was, you know, good in terms of showing that people did understand it. But it seems to be a limitation that that couldn't be asked again for this particular product and study.

Cristine Delnevo:
Thank you. Dr. Benowitz.

Neal Benowitz:
I think this whole issue of rating the risk is problematic because of public knowledge. The warning just says it's less harmful. But the actual data said 50 percent of people or more thought that pure nicotine would cause cancer, for example. And Swedish Match doesn't provide data on actual cancer risk among Swedish Snus users. So, there's no sort of general knowledge of the public about what this would mean.

So, it doesn't surprise me that there's very, very little difference if you say reduced risk. What does that really mean to people if they think nicotine is responsible for cancer and for heart disease? So, I think this is not just a failure of this study. I think it's a failure of public health to educate people so they know what's going on. You know, if you don't know anything about nicotine and someone says this product is less harmful, what does that mean? So, again, I think it's a problem with the whole concept of just saying something is less harmful without having a context.

Cristine Delnevo:
Thank you. Any other committee members want to weigh in on this discussion topic? If not, I'm going to—oh, Dr. Rigotti.

Nancy Rigotti:
Just to—someone previously mentioned the fact that the plan is not to put the statement about reduced risk other than on promotional materials, which I'm not quite sure how widely that will be seen by the public, as opposed to sort of on the product or right on the cash register or right on the display in the stores. So, I just think that it would be more useful if we—while there's a limit on how much perhaps we understand what this is saying, I think at least we—what its saying is true. And it would be good to get more people to get the message if granted by FDA to get the company to use it more broadly to make sure that the message gets across. I'll stop there.

Cristine Delnevo:
Dr. Popova.

Lucy Popova:
Yeah. Just to piggyback on that is Dr. Rigotti, we were talking about—we don't necessarily want those messages at where people who are not using tobacco products to see. So, the point of sale where there's candies in there, we don't want this sitting there where kids can see that. But the tobacco companies do have a lot of ways to reach smokers with those messages, specifically all the mailings they do to the emails, direct messaging. So, all of that was like, promotion should be

done.

And in addition, like, my point is like, we're always putting this on the product itself. These messages should be on cigarettes. So, when the people who are using those most harmful products, they should be the ones getting the message on those harmful products. Again, something for the companies to think about in the future.

Cristine Delnevo:
Dr. Jordt.

Sven-Eric Jordt:
Yes. I strongly agree with Dr. Popova. At this time, the cans only have warnings about the addictiveness of ZYN. So, I agree that a lot of the other health risks have to be listed there. The cans should basically have the same information as NRTs about cardiovascular risk, about also potential adverse effects, and what to do if you experience these effects like heart palpitations, anxiety, other things. And there should especially be warnings on there that pregnant persons should not use these products. And also, if you want to become pregnant, you should not use these products, right? That should all be listed on the cans. I think that would be the most direct way to educate the customer. Thank you.

Cristine Delnevo:
Thank you. Dr. Madl.

Amy Madl:
Hi. Yeah. I would just like to bring it back to some of the main points that were presented by the Swedish Match, as well as FDA. And from the evidence that's provided in the MRTPA, it's very clear that the consumers understand that the label claim presents that the product ZYN is a reduced risk product and there'll be reduced risk for a number of disease outcomes, including mouth cancer, heart disease, lung cancer, et cetera.

And that consumers understood that the use of the—to really receive that health risk reduction, they had to completely switch away from combustible cigarettes. And from the evidence provided, it also seemed to be very apparent that nonusers, just reviewing the label claim that that would not facilitate the initiation or reinitiation of the tobacco product. Thanks.

Cristine Delnevo:
Thanks. Actually, I had more of a question perhaps for FDA, if you could clarify for us if there is an expectation that consumers need to understand the claim, or that the claim should be able to move people in a direction of improved understanding. They're two slightly different things. But I think some of the data did show, when you looked at the control and the test groups, that consumers do understand that non-inhaled, non-tobacco products do have a different risk profile than combustible cigarettes. And so, I don't know if anyone from FDA can kind of quickly clarify that for us in the context of this discussion. Dr. Chang.

Cindy Chang:
So, I can start and maybe Ben, you can jump in. But yes, FDA would be concerned with both

understanding and also the impact of the claim. And from what we've seen, the trend is—it seems to be going in the right direction. But Ben, you may have more to weigh in.

Benjamin Apelberg:
Yeah. Dr. Delnevo, just to clarify, you're sort of asking is the focus more on generally, do consumers understand or sort of the impact of the claim on kind of changing understanding.

Cristine Delnevo:
Right. What is what is the criteria?

Benjamin Apelberg:
Yeah.

Cristine Delnevo:
Is it that they understand the claim or that the claim must move people in a positive direction?

Benjamin Apelberg:
Yeah.

Cristine Delnevo:
Because those are—they are two different things.

Benjamin Apelberg:
And obviously, I mean, you know, the way we approach it is, like, to look at the statutory requirements. And in the Acts, you know, would sort of have a whole section about consumer understanding, you know. I think that ultimately, you know, we're trying to sort of our—Apoorva presented on this earlier kind of, like the aspects that we're looking at, like the dimensions of understanding that we try to focus on. Because even just sort of the concept of understanding itself is fairly broad but, you know, what that actually means.

I think I would just say that, you know, generally, we look at, is there evidence that consumers generally understand? We talked about the various dimensions that includes that the risk is lower for the particular conditions, how they're supposed to use the product to get that benefit, and that it's not risk free, and sort of those dimensions. I think we all recognize in like the experience to date for those of you who have been on other committee discussions about MRTPs is some of what was already sort of talked about in terms of, like—we understand that people have sort of strongly held beliefs about nicotine, about sort of various tobacco products in general and recognize that there's going to likely be limitations to particular studies that are looking at one time exposures and things like that, in terms of really expecting much movement.

So, I do think part of what—so it's kind of a complicated response, but it's in these various dimensions, and also sort of the nature of the misunderstanding if it is so, is it a matter of, like, "Well, look, just not enough people sort of actually believe this," versus "No. This is pushing people to believe something that could result in behaviors that are going to be counterproductive, you know, or sort of negative for public health."

So, I think ultimately, I mean, I'd just say we really look to sort of hear from you all in terms of what this evidence demonstrates, whether it's sort of absolute levels of kind of understanding or the impact of a claim and how you would sort of interpret that and that would all be part of what we take into account in our evaluation.

Cristine Delnevo:
Thank you, very helpful. I'm going to move us to Discussion Topic 3 now, so next slide. So, Discussion Topic 3 focuses on the Impact to People Who Use Combusted Cigarettes. By way of background, the data suggests that nicotine pouch use is most common among adults who recently quit other tobacco products. Twenty-four percent of participants in the PMTA Pattern of Use study of those that use ZYN completely switched from other tobacco products to ZYN by the end of the 10-week study. And in the Consumer Perception and Likelihood Use study, viewing the proposed claims did not impact intention to use ZYN among those who were using tobacco products.

So, considering that background, the discussion topic posed to us is if ZYN is marketed with the proposed claim, we're to discuss the evidence regarding the likelihood that people who currently use combusted cigarettes will completely switch to ZYN and/or will duelly use in and combusted cigarettes long term. Dr. Popova.

Lucy Popova:
So, the way I read the evidence is that there is no evidence in the application that the claim itself is going to have an impact on behavior. What we are seeing is the current status quo with ZYN on the market has an impact on behavior already. And people who are—for whatever reasons—coming to use the product probably because partially driven by the beliefs they already have that this is less harmful, or this is, you know, all of that, what we're seeing there is evidence of this. So, there's evidence that ZYN being on the market makes some people in this nonrepresentative study switch. What we are not seeing is a question being asked, does adding modified tobacco risk claim to that will result in people switching? There's no evidence for that.

Cristine Delnevo:
Dr. Scout.

NFN Scout:
I do agree with Dr. Popova that we are attempting to establish the overall risk profile to the population according to the evidence that we've been given and if there is this additional warning attached. And we currently do not have evidence that it is particularly going to reduce the risk if the warning is attached for either combustible cigarette users interested in potentially switching or enticed to potentially switching and/or other existing users. So, I'm afraid on this, it's a strong meh according to the science we've been given.

Cristine Delnevo:
Dr. Rigotti.

Nancy Rigotti:
I would agree that we don't have the information that we need to answer the question. I would

add that it didn't seem that I saw in any of the evidence we saw that while we don't know that it's going to help, that it would hurt—that having this claim would hurt—would lead nonusers to be thinking that they would be switching to the products. Because I think that the data showed that that didn't seem to be the case. Not very strong evidence but just want to make that point.

Cristine Delnevo:
Yeah. I just want to add too, right? So, what we know thus far about the patterns of use for nicotine pouches, in terms of who is using the products on a regular basis, there is evidence there that the product category—we did not see data specific to ZYN—but the product category itself in the research literature does show that the product has had appeal among people who use combusted cigarettes and have quit combusted cigarettes.

But whether or not the claim itself is going to kind of accelerate the adoption or the experimentation or the switching, there is no data presented here to necessarily answer that question quite yet. Dr. Benowitz.

Neal Benowitz:
I agree with you on what these data show, but I'd just like to comment that e-cigarettes as a model actually are widely used for people to quit smoking, especially in some other countries. And a study from USC by Harlow has basically been showing that among youth that e-cigarettes are being—that e-cigarette users transition to nicotine pouches, and they stop using e-cigarettes in part because the perceived risk is less.

So, I think the phenomenon is real and realistic to expect that this would occur. Again, I think it gets back to public education about what the real risks are of nicotine versus of smoking. But I think nicotine patches have got the potential both to reduce cigarette smoking any cigarette use, including among youth. And sorry for the background noise,

Cristine Delnevo:
Dr. Gogova.

Maria Gogova:
Okay. Just to build on what Dr. Benowitz was talking about. So, what we know is that adult tobacco consumer, specifically smokers, who have correct perception about the relative risk or even lower—or the nicotine doesn't cause—is not the primary cause of smoke-related diseases are twice or three times more likely to switch to smoke-free alternatives.

So, although this study was only showing us exposure to—one time—to the reduced risk claim, I believe that, you know, maybe over multiple times exposure when adult consumers or smokers can internalize the information, maybe can have future impact on accelerating switching of adult smokers to the ZYN or another kind of oral tobacco products. So, I think evidence is not there but there is likely that those adult smokers who have correct perception about the relative risk are more likely to move to smoke-free alternative.

Cristine Delnevo:
Dr. Upson.

Dona Upson:
Thank you. Yeah. I agree with the comments so far that there are lack of data for changes in behavior. And I guess my question is for PMI in terms of since their data show that people—that the claim itself is not going to change behavior, what's the reason to pursue the claim from a marketing perspective? Thank you.

Cristine Delnevo:
Thank you. Yeah. I mean, I think one of the things I'm looking at the discussion topic and kind of asking myself is the question of if it's marketed with the proposed claim. There's the question of the effectiveness of the proposed claim to spur new uptake and product switching, right? But also, in addition, how is the marketing of the product actually going to be occurring? And we did not get a lot of detail regarding that. And we did hear earlier in discussion points, concerns for certain populations of people who smoke, older adults, older Americans that may potentially not be reached by the particular channels that might be used in the marketing. And so, to some extent, the answer to this question is really going to depend on what the marketing strategy is actually going to look like with the context of the proposed claim itself. Any committee members have additional things they would like to weigh in here with this particular item? Dr. Popova.

Lucy Popova:
Well, just to—since we're broadening up a little bit, not just in terms of people who—the question narrowly asks, would people who smoke switch? We do not have the evidence of that. What other things should be considered that FDA is not asking, would people who are—we keep talking about smokers who are unwilling or unable to quit. There are a very few of them out there, most people are willing and trying to quit.

And when we talk to them, they're not interested in switching. They're saying, "I don't want to switch my addiction, one addiction to another." They want to quit and they just sometimes unable to. And for them, we just need more support. And we also need to look at people who are interested in quitting. How are they being cannibalized by switching instead of quitting? So, just again, keep that in mind.

Cristine Delnevo:
All right. We're actually moving fairly swiftly through the materials and the questions. So, I'm actually going to take Chair's discretion, and we're going to move the break now from 2:45 to 3:00 p.m. And we will resume at 3:00 p.m. and discuss the fourth topic question.

[break]

Welcome back, everyone. Can we move on to the next slide? Next slide. Go back. I think we're going to go back a couple. Go back another one. Back one more. Go to topic three, please. Thank you. Before we move on to topic 4, Dr. Upson, I wasn't sure if you had a question directly for PMI that you wanted them to answer. I want to make sure we weren't—I wasn't misreading the room. Did you have a question directly for PMI to answer?

Dona Upson:
It's something I've been thinking about since the data showed that it's not going to—that their

data showed it doesn't impact whether people are more likely to take up use of the product. And so, I think you addressed part of that. I'm wondering how it's going to be used in marketing. And if they have other information that suggests that it might increase uptake of the product. It's a lot of work to get the approval, you know, by everybody. And so, if they don't think it's going to increase use of it, I'm just wondering what the, you know, what their thinking is about it, I guess. And it's unclear to me.

Cristine Delnevo:
Go ahead. You can have a couple of minutes to respond to that.

Keagan Lenihan:
Thank you. I appreciate the question. I think while the data is limited with the one time that the folks in the study were exposed to the claim, we do believe there's a lot of opportunity with continued marketing to adult cigarette users that the claim will resonate with increased exposure. So, I think there's a lot of opportunity with the increase. I think you've heard today from many folks that there's a lot of misinformation out there around nicotine and smoke-free products. So, I think the more you communicate to adult smokers with this type of claim, it will only increase, hopefully, the use of switching to a product like ZYN in the future.

Cristine Delnevo:
Thank you. All right. Moving on to the fourth discussion topic, next slide. So, our last topic is focused on Impact to People Who Do Not Use Tobacco Products. And by way of background, at least the data that we had been presented with thus far, use of nicotine pouches among youth has been relatively low, and that viewing the proposed claim did not increase intentions to use ZYN. And so, we're tasked with discussing the question that if ZYN is marketed with the proposed claim to discuss the evidence regarding the likelihood that persons who do not use tobacco products will start using ZYN.

And I'm actually going to start us off with the discussion. You know, I think everyone here would love to know what the more recent data from the NYTS look like, what the 2025 tell us about nicotine pouch use. Specifically, it won't be a surprise that among people that are using and have new uptake of nicotine pouches, with ZYN being the clear market leader with 50 percent of the market share use among those populations is going to seem somewhat unavoidable. And the way that the marketplace is changing broadly, it's hard to imagine that there's not going to be increased initiation of pouches, broadly, and ZYN of people who have not used tobacco products previously.

I think one of the challenges here is the context of the MRTP, and whether or not the marketing itself is going to help accelerate—would it accelerate initiation? And how do you square what's available in the marketplace with the claim in and of itself. And so, that's something that I'm just broadly thinking about, and kind of welcome others jumping into the discussion. Dr. Upson.

Dona Upson:
Thank you. This is my greatest concern with the uptake by youth because we've seen it dramatically with e-cigarettes. We're seeing it now. We don't have the data, unfortunately, but we're seeing it in our communities. And as was just mentioned, viewing the claim once didn't

increase uptake in ZYN among people who use tobacco. There's as much likelihood, if not more, that with increased exposure to the claim that youth will increase their use of the product.

And we're seeing it—again we don't have the data—we're seeing it in our hospitals. We have physicians who are using ZYN who never use tobacco products, who are not in a high-risk group for using tobacco products, and they're using ZYN. So, I'm very concerned about this part, and I don't think that we have the information to make a decision about it. Thank you.

Cristine Delnevo:
Dr. Rigotti. You're muted.

Nancy Rigotti:
You'd think 6 years in, one would know how to use ZYN -- do this. But in any case, I'm also very worried with, as you both said, about what's happening with ZYN use patterns, especially among young adults and also kids. We know the sales are rising, and we have a delay, as you pointed out, in the use patterns.

But I guess I was also thinking about what difference will it make if we allow the company to put on a statement which we think is scientifically true, that use of this product reduces your risk compared to smoking, will it make a difference for young adults? How important are the health risks or the health claims in whether or not they pick up ZYN? I have a feeling it's not going to be a big effect. But I know in that case, Dr. Upton and I are disagreeing, I guess. And the fact is, we don't know. We're just making our best guess.

But the question that we're sort of faced with here is a very concrete one, whereas our concerns are much bigger and broader about what's happening. And then so that if the FDA decides to allow for this modified risk designation, I guess the question would be, what things do they have the ability to do around making, you know, sort of making sure that surveillance and marketing restrictions or marketing is surveilled carefully, to do whatever the FDA can to try to keep this out of the hands of nonsmokers, which is what we're all trying to do.

Cristine Delnevo:
Thanks, Nancy. I'm reminded of our discussion around General Snus' MRTP renewal, which was the first renewal that came to TPSAC. And I think the committee as a whole was a little disappointed with the quality of the post-market surveillance data. And so, I think that in the context of your comment, you know, a reminder about how important that post-market surveillance data is going to be, I think is an important one. Dr. Jordt.

Sven-Eric Jordt:
Thank you. Yeah. We were told by PMI that the United States should follow the Swedish example. Because, yeah, the uptake of ZYN and snus is reducing smoking. But if you want to know what might happen in the United States in terms of youth uptake, we should look at Sweden. They have a catastrophic increase in youth use of oral tobacco products. It's sixfold increase over the last 7 years. Now, almost 30 percent of Swedish youth are using either snus or nicotine pouches. So, I'm just—and I'm sure in Sweden, ZYN was marketed with very similar claims. So, if we look at Sweden, we should not follow these policies. Thank you.

Cristine Delnevo:
Dr. Scout.

NFN Scout:
Well, I think that we have an excellent example here, particularly with all the evidence that we've been given of a "look here, not there" campaign. And if we had a cardboard tube and we only wanted to look at one end of the population, then we might be able to substantiate the fact that this might be valuable. But we are charged with estimating the impact on the full population, and we have not been given any information on impact on teens at the exact same time that news stories about the incredibly dramatic change in teen uptake related to this—again, a tobacco-naive population—uptake of an addictive product. They're popping up everywhere from New York Times to Psychology Today.

And in light of that repeated, consistent reporting of a dramatic increase in uptake, what we're hearing here is things like the point prevalence is low. Great. But what is the angle of that change on the point prevalence? When you look at it, it's doubling over, as has been brought up a few different times, over a very short period of time. If that continues, it's a logarithmic level of growth. And we are going to be—as Dr. Jordt was bringing up—in a very problematic area, specifically with tobacco-naive people using these pouches very, very quickly.

So, it's really concerning that we have absolutely no science on the exact area when there is so much public report of dramatic uptake. And I also have to say that whether it's a paid advertising campaign or not, a lot of those reports are talking about how robust the social media ads are related to ZYN use. And I asked earlier if PMI had any plans to counter those whatsoever and was met with a nonresponse that, yes, youth are exposed to lots of bad things, and so everybody should be worried about that.

But whether or not, again, that's a paid advertising campaign, if we were to put the risk reduction label on this, we are putting it on that free advertising campaign, which appears to be aimed at or at least significantly motivating youth. And so, we have to adopt all ends of that equation. Not just the older folks who are using it to get off of combustible cigarettes, but the people who are not currently addicted to anything and would soon be addicted to anything with these current trends. So, I have to say that on full balance here, harm reduction is not harm reduction if it increases harm for another group, particularly if it increases harm for our youth.

And for us as scientific advisors, to ignore that incredible sign of distress and uptake among one population, ignore the fact that we have no science related to that, and only look at science for another smaller subset of the population, I honestly think is really bordering on negligent. And, you know, again and again, I'm the target age demographic for this. And yet, if I talk with my colleagues, they have no idea what ZYN is.

And yet, when I go to colleges, when I talk with them about tobacco control, what they bring up again and again is ZYN, ZYN, ZYN. Something that's put in a package that looks very much like the candy that's available. And yet again, you can't even describe it to the people your own age because we have so little exposure to it. So, this is a big problem. I wish that we could vote on whether we think that this is reasonable or not, and if so, I would heartily and strongly vote

absolutely not. We have too many signs of big danger here.

Cristine Delnevo:
Dr. Popova.

Lucy Popova:
I agree with Dr. Scout, and I wanted to emphasize the point slightly differently. If by itself, the modified risk claim that we're discussing today—if there was no advertisement, no social media, if we just put that claim on ads that go directly to smokers, it will not have an impact on youth. That wouldn't be a problem. However, in the real world, where we do have this pervasive social media ZYN influencers, which, again, what is PMI going to do with those? Pushing of the products, as was mentioned on sponsoring Formula One, sponsoring music festivals like Indie Cars Music City Grand Prix in Nashville, sponsoring National Pickleball Championship or advertising there. How is this targeting old folks?

But anyways, given a world where we do have all this marketing targeted at young people, putting the modified risk claim in there might be just one other little thing that pushes people who would otherwise never use tobacco product into using it. And we don't have evidence of that, but this is something to consider. And especially appreciate Dr. Jordt bringing up the Swedish experience, where in Sweden, they do have limits on marketing, and they restrict it much harder than we do here.

And even there, if we're seeing such an increase in youth use, here with the marketing and with all of that in ZynCoin, which is another cryptocurrency which is coming up. Having this pervasive presence in social life, adding a modified risk saying this is a less harmful product. Who knows where it's going to go? So.

Cristine Delnevo:
Dr. Benowitz.

Neal Benowitz:
While I firmly agree with the concern about the Swedish youth use of pouches, which is very prevalent with high addiction. I doubt that this claim is going to have any effect on the U.S. Most kids know that smoking is really the worst thing you can do. They moved to e-cigarettes, I think they moved from e-cigarettes to pouches. I think it's got nothing to do with this MRTP. There's just a perception—a general perception that nicotine is not that hazardous. And I think the main controls are going to have to be access controls. Maybe it shouldn't be sold in gas stations and convenience stores. Maybe it should be sold only in tobacco shops. I think that's going to be the only way to control it.

In terms of young adults, you know, the issue there is there's real questions about cognitive enhancement. You know, many people use these products occasionally or just for certain tasks perceive improved attention and focus. Golfers are using this, and there is some credibility to the fact that some people may gain benefit from it. That's hard to regulate with something like this. So, I think that it's hard to fight this. It's hard to fight this tide of a perceived cognitive enhancement. But I think in terms of kids, it's not going to matter if this MRTP gets approved or

not. I think it has to be better access control. That's my opinion for e-cigarettes as well.

Cristine Delnevo:
Dr. Rigotti.

Nancy Rigotti:
I would agree with Dr. Benowitz that better access control is essential. I think that we don't want to forget that there are a lot of smokers who still need help to quit and are not quitting with what we already have. And I think that it would be helpful to grant the MRTP to—for that reason, so that we can reach people who are adults, and that we don't forget that there still are a lot of smokers that need to quit even though I am very worried like everyone else about what is happening with kids and young adults.

Cristine Delnevo:
Dr. Jordt.

Svcn-Eric Jordt:
Thank you. I would like to thank Dr. Benowitz for bringing up the issue of point of sale. Restricting that would definitely help reducing youth uptake. But I also would like to address this discussion around the cognitive effects of nicotine. So, it's not just that influencers are promoting this idea, it's PMI itself that's doing it. The PMI CEO recently stated that nicotine is misunderstood and offers cognitive benefits. So, this is really encouraging people to take up nicotine who have never used nicotine before.

So, PMI is really contradicting its own message that only former smokers should use this but is promoting this idea of cognitive benefits that, as Dr. Benowitz said, is a perceived benefit and that is often compromised by addiction behavior and all the other adverse health effects that nicotine use has, for example, effects on sleep and other health parameters. Thank you.

Cristine Delnevo:
Do we have any other committee members who want to weigh in on the impact to people who do not use tobacco? I know we are eager to see new data kind of come out on youth, and there are data that are coming out from various nonfederal data sources. And as a reminder, we do still have the overwhelming majority of young people who are using tobacco and nicotine products, are using—still using e-cigarettes. And so, you know, thinking about the risk continuum, I think, is important in that regard as well. Very quiet group today.

All right. If I'm not seeing any additional comments specific to Discussion Topic 4, we're going to start to move into wrap up. And in doing so, we're going to go and give every committee member an opportunity to make a final comment or statement about the four discussion topics. And we are going to go in the same order that we did the roll call this morning. And so, I'd like to start with Dr. Guy.

Mignonne Guy:
Thank you, Dr. Delnevo. For the—I'm sorry. My computer keeps freezing, I apologize. For the initial claims—for the initial question related to whether or not the proposed claim satisfies the

requirement from—as stated, I don't have as many concerns about that as I do, really with the latter—the last question that we just—that was deliberated, which is the potential impact on other individuals. Meaning, for me personally, it would be focusing on youth in particular.

So, it's—this is a difficult thing to sort of think about, right? Because we're asking about whether or not this specific claim has potential impact to persuade young people to use tobacco products or to use ZYN in this case in particular, which is slightly problematic given the fact that these things—uptake in tobacco use—tobacco products and ZYN specifically, doesn't happen within a vacuum, right? So, it's not necessarily specific to this claim about modified risk.

However, the claim about modified risk combined with marketing, combined with potential perceived less risk, combined with a multitude of flavors, and in particular novelty flavors, all of those elements together may, in fact, contribute to increased risk specifically amongst young people. That we don't have very much data, or that uptake is low thus far, does not necessarily mean that one should move forward with approval at this point, simply because we don't have the data to dispute that it's a problem amongst youth. That's been the problem with the FDA and with regulation of tobacco products in this country to date, which is that we approve certain products go on the market. We approve specific claims related to these products, and then we have to put out the fire later on.

So, I would just caution FDA to consider specific trends with other tobacco products and uptake of other tobacco products amongst particularly individuals that are under the age of 21 or that are young. And to consider that we may, in fact, have the same trends that we have with other tobacco products, such as e-cigarettes in the future and learn from our mistakes from the past. That's my only comment.

Cristine Delnevo:
Thank you. Next, Dr. Jordt.

Sven-Eric Jordt:
Sorry about that. Thank you. So, yeah, it is clear to me that PMI strategy for the marketing and modified risk claims for ZYN is duplicitous. And for the case that MRTP status is granted by FDA, the company cannot be trusted to act responsibly and inform consumers about the actual risks associated with ZYN product use. On the one side, PMI appears to comply with federal rules. However, on the other hand, PMI is marketing seasonal products with alcohol-related product names such as Mojito and Coffee Martini that appeals specifically to youth and young adults, the population that has an exceedingly low smoking rate, with a large majority never having used any nicotine product.

These alcohol-themed product names encourage youth and young adults to use the products together with alcoholic drinks. Since these products are not listed in the current application, FDA needs to clarify whether these products are authorized for marketing and whether it has evaluated the risk these alcohol-themed product names pose for youth and young adults. PMI is further misleading consumers by claiming that some products such as ZYN Chill that is equivalent to ZYN Classic and ZYN Smooth that is equivalent to ZYN Original are unflavored. FDA's technical review during the PMTA process has concluded that all ZYN products PMI has applied

for, including ZYN Chill and ZYN Smooth, have characterizing flavors due to the inclusion of artificial sweeteners and synthetic cooling agents. The equivalent products, ZYN Classic and Original, are purely designed to obfuscate and confuse state and municipal regulators in locations with flavor bans.

Furthermore, PMI leadership is openly promoting the use of nicotine for enhancement of cognition, a claim picked up by ZYN influencers on social media. PMI CEO stated publicly that nicotine is misunderstood and offers cognitive benefits. These claims are not substantiated by current science for the intended use patterns. Even if short-term cognitive effects can be proven, these are compromised by addiction behavior and cardiovascular effects of nicotine and its effect on sleep, among other health effects. These claims again aim towards youth and young adults and contradict PMI's stated strategy in the application to restrict use to former smokers only.

The so-called Swedish experience cited in favor of ZYN uptake should not be used as a role model for the United States. It cannot be touted as a success. The Swedish model promoting snus and nicotine pouches comes at the expense of a catastrophic increase in youth tobacco product use in Sweden. Sweden's public health agency has recently documented that snus and ZYN use—or pouch use has increased sixfold over the last 7 years with now almost 30 percent of underage the population using these products.

At this time, the health warning on ZYN cans only refer to the addictiveness of nicotine. In the context of FDA's review, FDA should mandate that the health warning stated on cans need to be expanded to include oral health risks, risk to pregnant persons, risk to persons who try to conceive, and risk to persons with cardiovascular disease, potential complications, and adverse effects related to ZYN use need to be clearly listed on the package, as done for oral NRTs.

PMI also needs to state that with ZYN use, you might actually take up more nicotine than from cigarettes. Recent studies have shown that the uptake of nicotine from nicotine pouches can exceed what you get from a cigarette. And if you use a lot of these pouches, you can actually exceed nicotine intake. And with the associated health effects, in my opinion, it’s concerning that in the Consumer Perceptions and Likelihood of Use study viewing the proposed claim did not impact intentions to use ZYN among those who were using tobacco product. There's a risk that the claim may eventually appeal to populations that have not smoked or never used any nicotine products. That's why it's essential that health risks are stated. There's a—due to this great risk of unintended consequences, if I had to vote, I would vote against assigning MRTP status to ZYN at this time. Thank you.

Cristine Delnevo:
Thank you. Our next member will be Dr. Popova.

Lucy Popova:
Thank you. I really like the framework that Dr. Jordt talked about in terms of what the tobacco company says they want to do and what they're doing in the real world, and I think the contrast is definitely there. And I also want to bring—recall that we have granted—the FDA has granted modified risk claims to the same company in the past with General Snus and it hasn't really done anything. So, given the evidence from the application, given the evidence from history, we don't

really have evidence that putting this claim on the product is going to move smokers.

And also, I don't really—that we keep bringing up the misperception that people misperceive this product as equally as harmful that they have that. If you look at the data, depending on how the question's asked, the answer changes. And if you look at the data presented in the application, there's actually also—they ask questions in both ways to look at the data in there.

In general, smokers do have an understanding that those are less harmful products. And as we're seeing now, without the modified risk claim, some are using. But we're also seeing that the increase of rates of use is really high among youth. And so, that is, as everybody kept saying, is extremely concerning in the world where we have the social media influencers, just the overabundance of the marketing whether or not Swedish Match and PMI are behind it, youth might be really impacted.

And in terms of the overall, again, if it's just a claim and it doesn't have to do anything to do, yes, we can pass it. But what the tobacco companies should commit to is actually doing something and getting this claim to the smokers meeting, as I keep saying, we need to meet smokers where they are. Meet them first by saying, "You should quit. And here's how we can help you quit." And us in the public health too, we have done great work with reducing smoking. It's been presented and framed as like, "Oh, it's really—smoking rates are really high still, and all these people still smoking." It's much lower than it was before, and people are smoking a lot less today, and with a lot—instead of pushing the products that people don't necessarily want to use, to them, we just need to work on policies that actually help. And we are doing this particularly at the state and local levels, not so much at the federal level, unfortunately. So, overall, this claim, by itself, probably wouldn't have much of an effect. In combination with everything else happening in the world, it might have a negative effect on youth. Thank you.

Cristine Delnevo:
Thank you. Dr. Rigotti.

Nancy Rigotti:
Well, I would agree with the two people who came before me and agree with all the concerns that they have about the behavior of—and the marketing behavior of the company about the concerns about youth, about the lack of information that we have. All of those are very important. However, I would say that as an internist who's taken care of a number of adults over the years who have trouble quitting smoking, and a number of my colleagues who really misunderstand that products like non-inhaled products are safer, I think it's important that—I think that it's reasonable to, I would say somewhat reluctantly, I think we should—I think FDA should approve the modified risk proposal. I think that the evidence we've seen supports that.

I guess the question would be a larger one of whether the product should stay on the market at all. But that's an issue that we don't decide here. That's an issue that when the authorization, I believe, comes up again for renewal, that these things will come up. And it gives the company an opportunity to sort of recalibrate what it's doing in the meantime. And also, hopefully, the FDA could do whatever it has authority to do within the law to try to steer things in the right direction as part of this application, if they decide to approve it. So, there's a reluctant yes.

Cristine Delnevo:
Thank you, Nancy. Dr. Robinson.

Risa Robinson:
Thank you. So, when I look across the four questions that we've been asked to consider and the data that was presented today, to me, there's a clear distinction between what evidence can—is supported and where the uncertainties remain. The scientific basis for the claim is strong for adults who do completely switch. The toxicants, the biomarkers, the epidemiological data all point in the same direction, and that is substantially lower exposure and a plausible expectation of lower long-term risk compared to continued smoking, though that data wasn't presented.

Adult comprehension also appears adequate. Adults generally understand that the product is lower risk, but not risk free, and that complete switching is required. But that understanding has not been demonstrated in youth, in individuals under 21 or in nonusers. And those gaps matter because these are the groups that are most likely to misinterpret any claims of reduced risk. On the switching behavior, the evidence is modest, in my mind. The biomarker study does not measure switching, and the exclusive use was not verified. Switching data came from a highly selected group of committed ZYN users, but not from a representative sample of smokers. Meanwhile, the national data show that dual use is common, and we do not have evidence that this claim would shift behavior towards exclusive use.

And finally, the greatest uncertainty in my mind lies with the youth and the nonusers. Use remains low, but it is rising. As we've heard today, awareness is increasing. Pediatric exposure is climbing. We have no youth perception or comprehension data that was presented, no evidence on how a reduced risk claim might influence initiation or perceived harm in this age group. Even with marketing safeguards, youth behavior is shaped more by experimentation and peer influence than by formal messaging.

Without youth-specific data, the potential for unintended consequences remains a real concern in my mind. So, while the claim is scientifically accurate for adults who completely switch, the evidence is incomplete for understanding how the claim will function in the broader population, particularly among youth and nonusers.

Cristine Delnevo:
Thank you. Dr. Scout.

NFN Scout:
I think in considering all the science that we've been shown today and our charge that we are supposed to under the Tobacco Control Act assure that this is a proven benefit to the population, according to that science, that we are, in essence, to use an analogy being asked to look at a house and comment on how nice the living room looks and ignore the fact that there's smoke coming from the kids' bedroom. We don't know anything about that. Don't look that direction. And worse yet, Dr. Jordt is telling us that it happened two houses over and it was a fire.

So, the idea that we would be able to say that we have proof that this is a benefit to the population with the science given to us is, in my mind, incredulous. So—and Dr. Upson asked an

interesting question, why would you go through this level of effort to get the modified risk claim on when the evidence of actually improvement for combustible cigarette smokers looking to move to ZYN with the risk statement added is middling at best? Well, there is a theoretical potential for that, is why you'd go through that much effort is that maybe your win is with the youth population.

And again, we've got more smoke coming from the kids' bedroom. And so, overall, very heartily, I would have to say this has not met the burden of proof. If anything, if we decide to add the claim through some interesting twisting of science, in 10 years, it sounds like we will have all the evidence to see what kind of a mistake we've made at this juncture.

Cristine Delnevo:
Dr. Upson.

Dona Upson:
Thank you. The benefit of having a last name starting with the U is that I get to just build on what everybody said already. I agree that we have a significant lack of data, especially data from randomized, peer-reviewed, published studies that we can actually look at and see the questions that were asked. We do not have any long-term data. As we've seen with e-cigarettes, it's the longer-term data—still not long term—as those data are coming in, we're seeing more harms than were expected from e-cigarettes.

And in particular, we have no data on the health effects of dual use. We know that dual use of e-cigarettes and combustible tobacco, the risks are higher. At our last meeting, we talked about IQOS. And even there, there's, you know, beginning to be a suggestion that there may be increased risk of dual use with IQOS and other tobacco products.

In the future, we may be seeing very low nicotine cigarettes. And one could guess that once those are exclusively on the market, if and when that happens, that people who are heavily addicted to nicotine are going to hopefully completely switch to something else than combustible tobacco. But maybe it will just increase dual use of cigarettes or combustible tobacco and these other products that we have. And we don't know what that dual use is going to do to people.

I think if—and as I said, and I agree with the others that the increasing uptake by youth and other people who don't—who are nicotine naive is extremely concerning. So, we need surveillance by FDA because it's already happening—not necessarily the surveillance, but the increased uptake. And we need to have better public education, partly about the reduced risk to cigarette smokers who completely switch. That's important. But also on the risks of nicotine, as Dr. Jordt reviewed.

And I think, I can't really overstate the importance of renewing and increasing research funds to study the effects of tobacco, all forms of tobacco, and reinstatement of the CDC Office of Smoking and Health, which had dramatic progress in reducing youth initiation of e-cigarettes and combustible cigarettes. Thank you.

Cristine Delnevo:
Thank you. Dr. Bailey.

William Andy Bailey:
Yeah. Thank you, Ms. Chair. I'm just going to make some broad [inaudible] MRTP approval for General Snus back in 2019. And then it's, I think, what I thought was a very easy renewal in 2024 due to the substantial harm reduction that was seen with the use of snus versus cigarettes. It's exciting that there has been very clear evidence presented here today that ZYN provides even greater harm reduction compared to snus versus cigarettes. I'll also say it was also clear to me that ZYN is not an introductory product that leads to the use of cigarettes or more harmful products by youth or adults.

I just want to mention a couple more things talking about the claim perception. And I would agree with PMI that, you know, if you look at just one exposure to the claim by a relatively small subset of users in these studies, it's probably difficult to get a clear picture of what that true perception is going to be. And it really would take a bigger subset because you get the real true picture. I think a big subset of users is going to require approval of this MRTP. And so, and that's where I would agree with the others that stated about the post-market surveillance is so important to really see the impact of those claim perceptions after the MRTP is approved, and those claims are seen repeatedly by users.

I also wanted to mention that there's also been a push within the industry for tobacco that's used for nicotine extraction for ZYN and other products here to be produced here in the U.S. In the past, it may have been produced in other parts of the world. And if it's produced here in the U.S., it's a lot more traceable, a lot more transparent than it may be if it's coming in from other places. That's definitely going to help our U.S. tobacco growers, which I am in full support of here. And I think we can also have a lot better handle on what the ingredients is in this nicotine product, if we're producing the raw product here in the U.S.

And so, for these reasons, I think the MRTP status should be granted for ZYN nicotine pouches. I think we have seen more than adequate evidence here. There's going to be a substantial harm reduction compared to cigarettes and other products. Thank you.

Cristine Delnevo:
Thank you. Dr. Gogova.

Maria Gogova:
[unintelligible] communities that the MRTP claim which was presented today by Swedish Match is targeted towards adult smokers. And there are 30 million of adult smokers in the U.S. who continue to smoke, and many will suffer from morbidity and mortality associated with their smoking over their lifetime. We also know that the PATH data indicated more than half adult smokers are looking for smoke-free alternatives. And as we discussed today, there is a [unintelligible] great misperception around nicotine as well as a relative risk perception among the smoke-free alternatives that can be a barrier for adult smokers to make the adoption or transitions to those smoke-free alternatives.

Therefore, I believe that providing them with true and accurate information is critical for them to make informed choices. And I believe that today, based on the evidence, the MRTP claim presented by Swedish Match is scientifically substantiated. The target audience clearly

understand the relative risk. They also understand that it's not risk free, and that adult smokers must switch completely to realize the benefits.

And of course, the benefit to the population as a whole, we should be all concerned about the—around youth. And we all want to make sure that they no youth use any kind of tobacco products. And therefore, to realize the benefits of the MRTP, we want to make sure that now manufacturers has clear, responsible marketing practices, limit access to the products—to the youth, so that they can actually realize the tobacco harm reduction potentials to adult smokers.

And I also think that it's really unreasonable to believe that we can fully mitigate or fully predict in a pre-market setting what will happen once the MRTP claim is authorized. However, I also believe that FDA has added tools such as post-market surveillance, where they can monitor what's actually happening in the real world, in the real times, to mitigate any unintended consequences, so that now we are actually realizing there are harm reductions in the [unintelligible] population as a whole.

Cristine Delnevo:
Thank you. Dr. Madl.

Amy Madl:
Hi. So, I fully support FDA's authorization of the modified risk claim for ZYN. And based on the evidence that's been provided, the proposed claim is accurate and is fully supported by the scientific evidence that has been provided by Swedish Match, PMI, as well as reviewed and critically evaluated by FDA. Some of the points that I think are important to reflect here that resonated with me and my support of the authorization is that ZYN is—presents a significant health risk reduction that the HPHC profile is on order of 98 to 100 percent less than combustible cigarettes, and also has significant health risk and exposure reductions compared to other modified risk products, including General Snus.

We've seen that ZYN is—the abuse liability potential of ZYN is less than a cigarette but is comparable to other smokeless tobacco products. From the actual use study that was presented, there appears to be a very promising trend: upwards of 24 percent of smokers who used ZYN completely switched away from combustible cigarettes and others that continue to use cigarettes, nearly 60 percent of smokers reduce their cigarettes per day by at least 50 percent.

And so, based on the experience of the Swedish Snus experience, where we've seen that population transition significantly over to oral nicotine products that it presents a reasonable and scientifically justifiable population to see where the risk reduction profile will be in terms of risk for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

When we look at how consumers evaluate or perceive the claim, they understand the claim that ZYN products and as well as the product category as a whole is a reduced harm product. They understand how to use the product that to get the full benefit of this reduced harm product, they have to have complete switching away from combustible cigarettes. And there didn't appear to be an appeal that would initiate nonusers or former users to take up ZYN products.

And then while—you know, as the committee has talked here today of concerns about youth use, I think that is a concern of everyone, including Swedish Match and PMI. And they've put measures in place to try to restrict youth access to these products. And luckily, up to this point in time, the evidence that we have is that youth uptake of this category product is relatively low. But it's really up to PMI as well as FDA to really outline what an appropriate post-market surveillance program should look like to continue to monitor youth use, as well as different populations of use of this product.

So, with that, these are the elements that resonated for me in terms of support and authorization for the modified risk label claim. Thanks.

Cristine Delnevo:
Thank you. Ms. Becenti.

Alberta Becenti:
Okay. As far as scientific evidence that substantiates the proposed claim is that ZYN and nicotine pouches provided evidence of reduced levels of harmful chemicals that poses lower risk of cancer, stroke, emphysema, and chronic bronchitis. However, there's no data on the health effects of diabetics, pregnant users, potential impact on developing fetus, and the long-term effects of ZYN use.

And one of the other concerns that I have is about the proposed claim the regarding nonusers. I'm concerned about the use of nicotine pouch among youth. Although commercial tobacco use among the general population have declined. However, commercial tobacco use among American Indian/Alaska Native youth and adults remain relatively high. As the data that was presented also, nicotine sales have tripled, and ZYN was the most popular nicotine pouch among middle schoolers and high schoolers and also concerned about the late uptake with use pattern among youth, just like it was with e-cigarettes.

And one of the ways, I guess, we need to consider is to address the point of sales and to have clear health risk warning labels that youth will comprehend. And also take in consideration, maybe conduct a study on youth perception of the health risk of using ZYN products. Okay. That's all I have. Thank you.

Cristine Delnevo:
Thank you. Dr. Postow.

Lisa Postow:
Yeah. So, I'm just going to say a lot of what other people have said before me. I think there's general agreement that the claim is true, that these are less harmful than cigarettes, which was true for General Snus as well. And I also think that there is a general misunderstanding in the population about the relative risk of these products. I do think that the general population thinks that non-combusted, non-inhaled products are more dangerous than they probably are.

Where this differs from the General Snus example, though, is in the use patterns and the explosion of use among youth, and potentially youth who don't have a history of smoking. And I

think it's unfortunate that the data that was available at the time that this application came in is not really capturing that explosion. I don't think that we know those numbers yet and we weren't able to really fully absorb how many—how popular these are currently or will be next year among youth.

So, in a situation where in the data, the smokers and nonsmokers both have sort of a middling reaction to the message. What we really need to understand is the relative effect of the message in the relatively small group of smokers who might want to quit and use ZYN to do so versus the large population of youth who might potentially start using these products, and, you know, who the message works most effectively on and who the message is most likely to convince to start using these products. And I think that that's just data that we don't have yet.

And so, that's all I have. I don't have an answer. But I think, if the MRTP is granted, there does need to be a large amount of post-market surveillance. And I think the FDA needs to think really hard about what data they would need if a renewal application were to come in.

Cristine Delnevo:
Thank you. Dr. Benowitz.

Neal Benowitz:
So, I'd like to make three comments. The first is the biggest population at risk for dying from tobacco smoke are adult smokers who are 50 years and older. And if we can get them to quit smoking as soon as possible or reduce risk, we will save millions and millions of lives. So, to me, that's got to be a top priority in terms of immediate health risk. I think that while smokers think that pouches are less harmful, again, as Dr. Postow said, they don't have a quantitative measure.

And so, if they knew that the risks are 10 percent or less of them developing cancer, for example, or whatever you talk about, and that they could get the nicotine that they want for whatever reason, that they would switch in a much greater number. I think smokers think that e-cigarettes are almost as harmful as smoking, and many don't use those for that reason. I think they would believe that nicotine pouches are less harmful than e-cigarettes. So, I think there's a great potential to save a lot of lives. Now, whether the MRTP would have—would make a difference where this is a public health issue, I'm not sure. But that's my comment about adults. I think there's a good role for ZYN in saving lives.

For kids, I think it's a cultural phenomenon. I don't think that the MRTP would make a difference one way or the other for kids. They're just all over. Kids know about ZYN. Many kids think ZYN are safer than e-cigarettes, and they're switching. You know, as Dr. Jordt said, there's a huge risk for a big surge in adult addiction to ZYN or any nicotine pouches. And I think that's got to be dealt with by enforcement of access. I don't think it matters if there's an MRTP or not. I think it really is an access issue.

The third thing I want to bring up has to do with nonsmoking adults who choose to use ZYN-type products for cognitive enhancement or whatever. There's no way to ban that. I don't think it should be advertised by Swedish Match. But that that's really a societal question. You know, do

we want to ban nicotine or have no one use nicotine in society, if they want to or not, if the risks are low? And that's a tough question.

You know, we went through that for cannabis at one time, and we decided that cannabis shouldn't be used by society and now it is. So, that's a third—I know this committee is not addressing that. But that, I think, is going to be the ultimate question about what's the place of nicotine pouches. So, thank you for inviting me to participate.

Cristine Delnevo:
Thank you. Dr. Wackowski.

Olivia Wackowski:
Yes. So, I agree with many of the committee members that the claim itself is generally reasonable in terms of accuracy, as far as what we know about the characteristics of the product, and how its HPHC levels compare with those of cigarettes and snus. And the fact that the claim is really making a comparison to smoking, it's not making a claim that the product is free of these risks, but lower risk than smoking.

In terms of consumer understanding, I think the study had some limitations that may have precluded some stronger evidence. But in general, I think we saw trends in the expected directions. And it's possible that effects could be stronger in the real world with repeated exposures. And I think people may potentially have a greater buy-in and acceptance of this claim for this ZYN product versus General Snus, which, you know, carries the same claim because this product doesn't have tobacco. And so, I think there's—it's easier to believe. It's easier to kind of buy into it. And so, I think that that could help, even if people have misperceptions about nicotine itself.

I agree with the data that nicotine pouch use is mostly used by adults with prior tobacco use and see that it has good potential to serve as a harm reduction product. And I think that it's important to note that, you know, even if this claim isn't authorized, this product will still be available. And so, it can still be used as a harm reduction product by people. But if the claim is authorized, it may help further motivate some smokers to switch. We didn't necessarily see great evidence of that here, but there is other evidence from longitudinal studies showing associations between people having lower product risk perceptions and using those products.

And in addition to potentially impacting consumers directly, I can also see how an FDA authorized claim like this could also make people who work with smokers like health care providers or tobacco treatment specialists to feel potentially more comfortable to talk to patients about these products, to recommend switching to these products for harm reduction if they haven't been successful with traditional methods.

I also agree with concerns about youth use that have been raised, and agree that it's likely to grow, though it was good to see from the data that interest was low in general and lower than that of the adult tobacco users. But if the claim is authorized, I think paying attention to the marketing and placement of these claims can hopefully help to mitigate youth use. And I also agree with other points that have been made about the importance of future post-marketing plans.

And I think in addition to assessing, not only switching and youth uptake, I think it would also be important for those plans to assess actual exposure to claims in the real world to help us better understand actual exposure to these claims and effects of these so that we know for future applications and renewal potentials.

Cristine Delnevo:
Thank you. All right. So, just to close us out, some final comments from me. So, in the context of an MRTP, I tend to think of two pieces of the puzzle, the product and the people. As we heard for the data we saw that we discussed under questions one and question two, I do feel that the data provided supported the conclusions about the reduced—the risk profile of this particular product.

With regards to people, thinking about question three and about adult smokers. There's 30 million adult smokers currently in the United States. And there is a tremendous opportunity where harm reduction can play a critical role to help facilitate complete product switching. The extent to that though, with this particular MRTP, if it is authorized, is going to depend on both the reach and the effect of the marketing and the effect of the claim. And I think that's something that will be important to kind of keep an eye out for. But there is, I think, we need to recognize great opportunity from a harm reduction perspective for those that continue to smoke.

However, with regards to question four and particularly with youth, I share people's concerns about increases in youth use. Yes, the use is still low. And as a reminder to folks that when prevalence is very low, a doubling of prevalence from 1 to 2 percent, you know, that's 100 percent increase. So, I think we need to be kind of tempering our ourselves when we're looking at that data and considering prevalence overall. But, you know, without question, nicotine pouch use is going to rise among youth. I don't see another marketplace where—you know, the tobacco marketplace, where that's not going to happen. And so, it's going to be incredibly important to have robust post-market surveillance. And then, I would argue, action by FDA, if there starts to be indicators that are problematic, if the MRTP is authorized. And with that, I would like to invite Dr. Apelberg back for his closing remarks.

Ben Apelberg:
Okay. Great. I'll keep this short because it's been a long day. But first, I just really wanted to thank Dr. Delnevo for leading the committee discussion today and doing it so well. It was really a very fruitful set of discussions and conversation. I'd like to close out our meeting today by once again, thanking the applicant. You know, we know that there's a lot of work that goes into these submissions and presentations before the committee. So, thank you for that.

I'd like to thank the members of the public who submitted comments and spoke today, you know, as well as the many CTP staff members who worked for months to ensure a successful meeting. You know, in particular, I'd like to thank our technical project lead for this application, Dr. Cindy Chang and our DFO Dr. Rachel Jang, and our presenters, Dr. Apoorva Rajan-Sharma and Dr. Amanda Fidalgo. Thank you all for your work. And really, most importantly, thanks to the committee members and our two guest consultants who joined us today.

You know, as I said earlier, the referral of MRTP applications to TPSAC is a crucial part of

CTP's evaluation of these applications. You know, we take these discussions seriously, and we'll take the committee's scientific advice and recommendations back and consider them as part of the totality of evidence that we evaluate when making determinations about this application. So, thanks so much to everyone who made today's TPSAC meeting a success. And now I'll turn it back to Rachel to close this out. Thanks again.

Rachel Jang:
Thank you, Dr. Apelberg. In closing, I would like to thank everyone for their hard work and efforts, especially the committee members, Dr. Delnevo, CTP staff, and A/V staff. This concludes today's meeting of the Tobacco Products Scientific Advisory Committee. Thank you, everyone. It is now 4:08, and the meeting is officially adjourned. Have a wonderful evening.

[end of transcript]