FDA is committed to ensuring digital accessibility for people with disabilities. We are continually improving the user experience for everyone and applying the relevant accessibility standards. At the time of initial posting on July 31, 2024, the attached PDF may not be fully accessible to users using assistive technology. A fully accessible version of the PDF is in preparation and will be posted as soon as it is ready. We regret any inconvenience that this may cause our readers.

Please let us know if you encounter accessibility barriers by contacting the Center for Tobacco Products at 1-877-287-1373 or CTPOutreach@fda.hhs.gov.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)
CENTER FOR TOBACCO PRODUCTS (CTP)

+ + + + +

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

+ + + + +

WEDNESDAY
JUNE 26, 2024

+ + + + +

The Advisory Committee met in Building 31 Great Room, FDA White Oak Campus, 10903 New Hampshire Avenue, Silver Spring, Maryland, at 9:00 a.m., Dr. Cristine Delnevo, Chair, presiding.

PRESENT
CRISTINE DELNEVO, Ph.D., Chair
MIGNONNE C. GUY, Ph.D.*
SVEN-ERIC JORDT, Ph.D.
DEIRDRE LAWRENCE KITTNER, Ph.D., M.P.H., Ex Officio (CDC)
ADAM LEVENTHAL, Ph.D.
LUCY POPOVA, Ph.D.
LISA POSTOW, Ph.D., Ex Officio (NIH)
NANCY A. RIGOTTI, Ph.D.
RISA ROBINSON, Ph.D.
SCOUT, Ph.D., M.A.
DONA UPSON, Ph.D.
TARYN WATSON, M.Ed., Ex Officio-ALT (IHS)

ALSO PRESENT
SERINA A. HUNTER-THOMAS, M.S.A., R.N.,
Designated Federal Officer
BENJAMIN APELBERG, Ph.D., Ph.D., FDA
JENNIFER BERNAT, Ph.D., FDA
ERIN M. ELLIS, Ph.D., M.P.H., FDA
MARIA GOGOVA, Ph.D., Industry Representative
ANNETTE KAUFMAN, Ph.D., Consultant
AMY MADL, Ph.D., DABT, Industry Representative
JENNIFER MULLIGAN, Vice President and Director
of Marketing Services, Swedish Match USA
TRYGGVE LJUNG, Ph.D., Vice President,
Scientific Affairs, Swedish Match USA
ALEXANDER PERSOSKIE, Ph.D., FDA
GERRY ROERTY, J.D., Vice President Legal and
General Counsel, Swedish Match USA,
NICOLE TASHAKKORI, M.P.H., FDA
SAMANTHA VENRICK, Ph.D., FDA
OLIVIA WACKOWSKI, Ph.D., Consultant

*via videoconference

P-R-O-C-E-E-D-I-N-G-S

(9:00 a.m.)

MS. HUNTER-THOMAS: Good morning, everyone. There's one slight change to the agenda, which is we're going to have Dr. Brian King start with opening remarks and then we will go from there.

Mute your phones, everyone. Thank you.

DR. KING: Yes, thank you. Good morning, everyone. I will need some breadcrumbs to get back to my seat. So lovely to see everyone this morning, it's a pleasure. I am Brian King, I am the Director of the Center for Tobacco Products. And appreciate everyone taking the time to be here today.

I will say that, on a 96-degree D.C. day, there is no place I would rather be than the White Oak Campus at FDA. We've got some air conditioning, we've got some government grade seating that's mildly comfortable, and a

government rate lunch that you can purchase at your own expense during the break.

So, great to see everyone. I know it's been a while since we convened. I do want to reinforce just the critical juncture of today's session. Of course, we know this is the first discussion of a modified risk tobacco product application renewal, so certainly a first of its kind. It's been about four years since we've discussed an MRTP, which of course we are required to do by the Tobacco Control Act.

I know it was four years because I was on the Committee at that time. I remember it for multiple reasons, one, it was right at the cusp of the pandemic, we'd just got it in. And it was also on February 14th, which totally killed my Valentine's Day dinner plan. So rest assured that will not happen again.

But we definitely are at a critical juncture of the Center, which also, coincidentally, just celebrated 15 years this

past weekend. And so I appreciate everyone coming together and continuing to implement the components that Congress intended of us in the Tobacco Control Act.

I'm also mindful, it's been about a year since we've convened this group. Of course, folks know that we had an external evaluation in December of 2022. Seems like eons ago, but as part of the 15 recommendations, one of them was to continue to enhance the work of this critical group, which I completely and wholeheartedly agree with as someone who was on the Committee for over a decade.

And so we've committed to have at least one of these sessions a year. We'll aim to do more when the merits permit and allow. But I also want to note one component of that evaluation as well was our intent to expand the scope of the dialogue around this Committee as well.

And so frequently, we're focusing on

applications, specific topics, but we also made a commitment to expand the scope to focus on broader level scientific issues, to capitalize on the time and expertise. And so that's exactly what we're doing today.

And so this afternoon as part of the session, there's going to be a broader level discussion around various components of consumer understanding related to modified risk tobacco products.

And so I think this is a critical juncture for us to continue to expand on those dialogues moving forward and I hope that they continue and so it’s a first of many.

That said, in terms of today's session, I would like to just comment on a few higher-level points, including on the myriad people that come together to make this happen. One, I know we've got some folks in the audience, which is critically important. I'd like to see those numbers increase over time.

But of course, in a hybrid

environment, we can certainly hope to maximize that. But I want to thank you all for coming today. I think it's a critically important part of the work that we do in terms of tobacco product regulation, you bring people to the table to participate in the regulatory process, it takes a village.

And so thank you for those who are going to speak today verbally, but also those who have submitted written comments to the docket and otherwise participated. It's a critical component of the work that we do and it needs to continue.

I also want to give a shout out to our staff at the Center for Tobacco Products. I joke frequently that tobacco product regulation is not for the weary. I'm certainly not in it for my health, I've likely lost years off my life as a result of doing this.

But we have a critical purview in scope of the work that we do do. That said, I want to commend our staff for doing a hell of a

job, working day in and day out to conduct comprehensive scientific reviews. That's the crux of our Center. That has always been the case, and that will continue.

We have many of them here today, some of which will be speaking. But they're representative of hundreds and hundreds of staff across the Center who are working tirelessly to ensure that we continue the important scientific integrity of our portfolio, including product reviews. They bring a new meaning to the word civil service, and I want to make sure that they're recognized for that work.

I also want to acknowledge the Committee. Having sat on this Committee in the past, I know this is not glamorous work, well, I guess, depending on your interpretation of glamorous, but it's an important work.

And I realize that it takes a lot of time and effort and expertise, including to prepare for these sessions, and also to make

sure that we have a constructive and fruitful dialogue. And so, thank you for trekking up to FDA and for your continued service to not only the agency but also to the public health of this country.

And finally, I also want to acknowledge the applicant as well. I know that a lot of effort goes into these applications. And we continue to ensure that scientific integrity is utmost importance in everything we do.

And so I appreciate the thoughtful presence, and also the information that you will share today to make sure that we are using science to guide our ultimate decision.

So, with that I will close my bureaucratic mouthpiece, but again I want to thank you all for being here. I, unfortunately, cannot stay for the duration of the session. I'll stay for about half the morning.

I found I can be in three places at

one time, but four is pushing it. And so, I'm going to stay as long as I can, but I know you're in good hands with Serina, et al., and I look forward to your productive dialogue throughout the day. Thanks so much, bye.

CHAIR DELNEVO: Thank you, Brian, for your opening remarks. Good morning, everyone, welcome and thank you for joining us today.

I'm Cristine Delnevo. I am Chair of the Tobacco Products Scientific Advisory Committee. I want to make a few opening statements and then we will move into introducing the Committee.

For 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 meeting will be a fair and open forum for discussion of these issues. And individuals can express their views without interruption.

Thus, as a gentle 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 forum of the meeting.

We are aware that members of the media are anxious to speak with 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 breaks.

And with that, I would like to ask the Committee members, our expert consultants, as well as the FDA staff that are playing a critical role in today's meetings, to introduce themselves. And we're going to start at this

end of the table with Dr. Annette Kaufman.

DR. KAUFMAN: Good morning, everyone. My name is Annette Kaufman. I'm a Program Director and Health Scientist in the Tobacco Control Research Branch at the National Cancer Institute. And my role today is serving as expert consultant.

DR. BAILEY: Hey, good morning. Andy Bailey, University of Kentucky, Extension Tobacco Specialist, and I'm here to represent tobacco growers.

DR. MADL: Amy Madl with Valeo Sciences, also with University of California at Davis. I'm a board-certified toxicologist and my role is to represent small businesses in industry.

DR. GOGOVA: Good morning. My name is Maria Gogova and I am a Vice President Chief Scientific Officer at Altria. But today I am representing tobacco industry.

MS. WATSON: Good morning, Taryn Watson. I work for the Indian Health Service,

attending on behalf of Alberta Becente. Thank you.

DR. KITTNER: Good morning. I am Dierdre Lawrence Kittner, the Director for the Office of Smoking and Health and the Centers for Disease Control.

DR. POSTOW: Hi, I'm Lisa Postow. I'm a Program Director in the Division of Lung Diseases at the National Heart, Lung and Blood Institute at NIH.

DR. POPOVA: Good morning. Lucy Popova, Associate Professor at the School of Public Health, Georgia State University.

DR. LEVENTHAL: Adam Leventhal, Director of the University to Southern California Institute for Addiction Science.

DR. JORDT: Sven Jordt, Associate Professor of Anesthesiology, Pharmacology, and Cancer Biology at Duke University School of Medicine.

DR. ROBINSON: Good morning. Risa Robinson. I'm a Professor of Mechanical

Engineering at Rochester Institute of Technology.

DR. SCOUT: Good morning. I'm Scout. My pronouns are he/they. I'm the Executive Director of the National LGBTQ Cancer Network and I'm here representing the general public.

DR. RIGOTTI: Hello, I'm Nancy Rigotti. I'm a Professor of Medicine at Harvard Medical School in Boston and the Director of the MGH Tobacco Research and Treatment Center, MGH being Massachusetts General Hospital.

DR. UPSON: Dona Upson, Professor of Medicine, University of New Mexico, adult pulmonologist at the VA.

DR. WACKOWSKI: Good morning. Olivia Wackowski, Associate Professor at Rutgers University, and I'm participating as an expert consultant.

DR. KING: Brian King, Director of the Center for Tobacco Products.

DR. APELBERG: Good morning. I'm Ben Apelberg. I'm the Deputy Director for Regulatory Science in the Office of Science at CTP. I also wanted to let everyone know that our Office Director, Dr. Matthew Farrelly, had intended to attend today's meeting in person. Unfortunately, he's come down with COVID, so he's not going to attend in person. But he is listening in virtually and sends his regrets.

DR. BERNAT: Good morning, everyone. My name is Jennifer Bernat. I'm a Branch Chief of Social Science, Branch 2, in the Office of Science at Center for Tobacco Products and I'm the technical project lead for the review team.

MS. HUNTER-THOMAS: Dr. Guy, are you on the line to introduce yourself?

DR. GUY: I am, thank you. Mignonne Guy, Professor at the Department of African-American Studies and Faculty Investigator of the Center for the Study of Tobacco Products at Virginia Commonwealth University. And my apologies that I was not able to join you in

person, I had some transportation issues.

MS. HUNTER-THOMAS: Thank you. Good morning everyone, my name is Captain Serina Hunter-Thomas and it is my pleasure to serve as the Designated Federal Officer for this Tobacco Product Scientific Advisory Committee or TPSAC meeting.

First, I would like to thank the many hands that were involved in the planning and preparation of this meeting leading up to today. It truly took a village and I thank you all.

Today's session will cover one topic that is open to the public in its entirety. The meeting topic is described in the Federal Register notice that was published on Monday, May 6th, 2024, with an amendment that was published on Wednesday, June 12th, 2024.

The transcriptionist for this meeting today is Mr. Devin Gildea. I would like to remind everyone to please check your pagers and cell phones and make sure that they

are either turned off or in silent mode.

When making your comment, please first state your name and speak loudly and clearly for the record. We would like everyone to be heard for the benefit of all Committee members, FDA staff, and public attendees here in the room as well as those listening via webcast. I will now proceed to read the conflict-of-interest statement for this meeting.

The Center for Tobacco Products of the Food and Drug Administration is convening today, June 26th, 2024, for a meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act of 1972 and the Family Smoking Prevention and Tobacco Control Act of 2009.

The Committee is composed of scientists, health care professionals, a representative of a state government, a representative of the general public, ex officio participants from other agencies, and

three industry representatives.

The following information on the status of this Advisory Committee's compliance with applicable Federal and conflict of interest laws and regulations is being provided to participants in today's meeting as well as to the public and is available for viewing at the registration table.

The purpose of today's meeting, which is being held in open session in its entirety, is to discuss the renewal of a risk modification order submitted by Swedish Match USA for loose snus and portioned snus products as itemized in the Federal Register notice.

Accordingly, this meeting is categorized as the particular matter involving specific parties or PMISP. With the exception of the industry representatives, all Committee members, either special government employees or regular government employees from other agencies, are subject to federal conflict of interest laws and regulations.

Based on the categorization of this meeting and the matters to be considered by the Committee, all meeting participants, with the exception of the three industry representatives, have been screened for potential conflicts of interest.

FDA has determined that the screening participants are in compliance with applicable federal conflict of interest laws and regulations.

With respect to the Committee's industry representatives, we would like to disclose that Drs. Maria Gogova, William Andy Bailey, and Amy Madl are participating in this meeting as non-voting representatives from the industry.

Dr. Gogova is representing the tobacco manufacturing industry. Dr. Bailey is representing the tobacco growers industry. And Dr. Madl is representing the tobacco small business pool industry. Their roles at this meeting is to represent these industries in

general and not any particular company.

Dr. Gogova is employed with Altria Client Services. Dr. Bailey is employed with the University of Kentucky Research and Education Center. And Dr. Madl is employed with Valeo Sciences.

This concludes my reading of the conflict of interest statement for the public record. And at this time, I would like to hand the meeting back over to the Chair, Dr. Delnevo. Thank you.

CHAIR DELNEVO: Thank you, Serina. And with that we're going to have our first presentation. So I'd like to introduce Dr. Jennifer Bernat who is the Technical Project Lead at FDA for the Swedish Match MRTP application.

DR. BERNAT: Good morning, everyone. My name is Dr. Jennifer Bernat, and I'm the Chief of the Social Science Branch 2 in CTP's Office of Science. I'm going to present an overview of Swedish Match USA, Incorporated's

renewal modified risk tobacco applications currently under review.

Please take a moment to read through the disclaimer on this slide. Okay. This is an outline of what I will be discussing. I will begin with the history of Swedish Match's risk modification order, including a brief overview of federal Food, Drug, and Cosmetic Acts risk modification order standard and details about Swedish Match's previous modified risk tobacco application or MRTPA.

Then I will move into a summary of the current renewal MRTPA under review. This summary will include details about the renewal request, FDA's post-market surveillance and studies, or PMSS requirements, and the marketing and sales landscape post-Swedish Match's risk modification order.

Lastly, I will walk through the lines of evidence submitted by the applicant in support of their renewal application and the questions we are posing to the Committee.

When determining whether to issue an order under 911(g)(1), FDA must assess not only whether the proposed modified risk claim is scientifically accurate, and consumers understand it, but also whether the product as it is actually used, will reduce the risk to people who use tobacco products and benefit the population as a whole, taking into account both people who use tobacco and people who do not use tobacco.

FDA's evaluation of an MRTPA can be thought of in terms of a few key overarching questions. Each of these involves the evaluation of many specific questions which draws from multiple scientific disciplines.

In evaluating an MRTPA, FDA has to consider the product with the proposed modified risk information. The questions include: Is the proposed modified risk claim scientifically accurate?

What are the health risks of the MRTP to people who use tobacco? How do

consumers perceive and understand the modified risk claim? And what are the potential benefits and harms to the health of the population as a whole?

In Swedish Match's previous MRTPA, FDA conducted thorough scientific review of all the available scientific evidence, including, but not limited to, long-term epidemiological studies assessing long-term health impacts as well as behavioral changes, and perceptions and intentions data.

On October 22nd, 2019, FDA issued Swedish Match a modified risk granted order under Section 911(g)(1) of the FD&C Act for eight General Snus smokeless tobacco products listed on this slide. Throughout this presentation, we refer to these eight products as the General Snus products.

The applicant's currently authorized modified risk claim is using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer,

stroke, emphysema, and chronic bronchitis.

Now that I've provided an overview of the risk modification orders, how we evaluated the original MRTPA, and the history of Swedish Match's risk modification order, let's discuss the current renewal application.

The risk modification order is for five years and expires on October 22nd, 2024. On July 17th, 2023, FDA received a renewal MRTPA from Swedish Match which states that the applicant is seeking to continue to market their General Snus products with the same modified risk claim.

FDA is reviewing the scientific information submitted and the renewal MRTPA to determine whether the statutory requirements for authorization provided in Section 911 continue to hold.

In addition to the evidence presented by the applicant, we will consider recommendations made today by the Committee, public comments, and any other scientific

evidence or information that is available to the Agency.

Under Section 911(i)(1) of the FD&C Act, FDA must require post-market surveillance and studies, or PMSS, for any product for which an applicant received an order under 911(g)(1).

This is in order to determine the impact of the order issuance on consumer perception, behavior, and health to enable the Secretary to review the accuracy of the determinations upon which the order was based and to provide information that the Secretary determines is otherwise necessary regarding the use or health risks involving the tobacco product.

The specific PMSS requirements for Swedish Match include the following: monitoring the use of the eight General Snus products that were authorized to be marketed with the modified risk claim in terms of uptake, dual use, and complete switching. Particularly assessing the extent to which

people who newly started using the MRTP were not using any other tobacco products; smoking combusted cigarettes or using other tobacco products before initiating the MRTPs and the extent to which people who newly started using the MRTPs, exclusively used the MRTP, or used the MRTP with combusted cigarettes or other tobacco products over time.

An assessment of consumer's perceptions of the products and understanding of the claim, particularly that to reduce their risk of disease relative to smoking, they must use General Snus exclusively, and surveillance of General Snus sales and distribution, adverse experiences, and new research findings.

The applicant was required to submit PMSS protocols for approval. The applicant did so, and FDA reviewed and approved the PMSS protocols before the studies began. The applicant submitted reports outlining their progress on PMSS activities each year as a part of their annual reports.

Now that you know the applicant's PMSS requirements, I'm going to describe the marketing and sales landscape after they received the risk modification order.

The applicant's advertising and marketing is limited in scope, budget, and impressions. Impressions are the number of times the intended audience had an opportunity to view the advertisements.

This limited advertising and marketing consisted of a branded website, trade print advertisements, Facebook only social media posts, paid digital advertising, earned media, and point-of-sale advertisements using the modified risk claim.

Earned media refers to unpaid media publicity that the applicant did not commission or pay for, for example, a news article about the product.

On this slide is an example of a print advertisement displaying the modified risk claim. Overall, sales of General Snus are

declining. As part of their PMSS requirements, the applicant submitted sales and distribution data showing declining sales since the risk modification order.

The applicant's data show that during 2019 through 2023 both wholesale unit and dollar sales decreased. Wholesale units by cans decreased from 4.94 million cans to 3.47 million cans. And wholesale dollar sales decreased from 17.52 million to 14.96 million.

FDA conducted an internal analysis of General Snus sales data using Nielsen IQ Retail Measurement Service or RMS data, between 2019 and 2023.

Sales of General Snus products with modified risk granted orders were evaluated on a quarterly basis and we matched General Snus products in the Nielsen IQ RMS data by the UPC codes provided in the renewal MRTPA. Overall, sales of General Snus products in Nielsen IQ RMS data have fallen from 6.6 million to 4.9 million.

Now that I've discussed the renewal application, let's shift to the lines of evidence we received and reviewed and TPSAC's focus for discussion. Today we are asking the Committee to focus on a few key areas.

First, we will assess the evidence related to the use of the MRTP and impact to the population. We will begin by describing data from observational studies and the applicant's General Snus Patterns of Use Study to describe characteristics of people who use snus, patterns of tobacco use among people who use General Snus, and transitions from combusted cigarette smoking to exclusive use of General Snus. TPSAC will be asked to discuss the use behaviors with respect to the modified risk tobacco products.

Second, we will present the applicant's study results relevant to consumer understanding and perceptions. TPSAC will be asked to discuss the evidence related to consumer understanding and perceptions of the

modified risk claim.

There are two questions that we are posing to TPSAC. Question No. 1: FDA reviewed the literature, the applicant's data, and conducted internal analyses of the applicant's data to describe the characteristics of people who use snus, patterns of tobacco use among people who use General Snus, and transitions from combusted cigarette smoking to exclusive use of General Snus. What does TPSAC think about the use behaviors with respect to the modified risk tobacco products?

And Question No. 2: FDA reviewed the applicant's data on consumer understanding and perception of the modified risk information. What does TPSAC think about the evidence related to consumer understanding and perceptions of the modified risk claim?

That concludes my introductory presentation. Now I think I will hand it back over to the Chair. Thank you so much for your time.

CHAIR DELNEVO: Thank you, Jennifer. We're going to continue to move through the agenda. And I'd like to now ask the team from Swedish Match to come up and give their presentation.

MR. ROERTY: Thank you, Serina, appreciate that. Yes, my name is Gerry Roerty. I'm the Vice-President and General Counsel of Legal Affairs for Swedish Match U.S.A. Thanks for joining us today, really, really appreciate you all being here.

Also like to thank my wife for picking out this fabulous tie to match my suit, so thanks, Julie. I'm very proud to be standing here representing not only Swedish Match, but also our General Snus consumers, tens of thousands of them who -- in the U.S., many of whom have transitioned away from cigarettes to our products. We're proud of our commitment to a cigarette free America.

But everyone in this room should be proud to participate in a forum that shows

transparent data-driven discussions can improve American public health. As Director Brian King said when unveiling the Center's five-year strategic plan, this is a critical moment in the history of tobacco product regulation.

The Center's mission is to make tobacco-related disease and death a part of America's past. Today, together, we can meaningfully advance that goal. Swedish Match was not only the first company to receive an MRTP, but also the first to go through this MRTP renewal process. We're also proud to be a pioneer in modified risk products.

When FDA reviews an MRTP, they must assess the product against the criteria established by Section 911 of the Food, Drug, and Cosmetic Act.

Namely, an applicant must demonstrate that the product and claim will significantly reduce harm in the risk of tobacco-related disease to individual tobacco users and also benefit the health of the

population as a whole, taking into account both users of tobacco products and persons who do not use tobacco products.

And this is the conclusion that FDA reached when they granted our modified risk order. Five years ago, FDA authorized us to inform smokers that a reduced risk product can make a real difference to their health, if they will switch completely from cigarettes.

As specified in the award letter, our authorizations were limited to a term of five years. So, we are back before TPSAC to present our case for renewal of the existing order. The Agency's decision was based on these four key conclusions.

General Snus has the potential to significantly reduce harm and the risk of tobacco-related disease. Consumers understand the relative risk of General Snus compared to cigarettes, and their need to switch completely.

General Snus when marketed with the

modified risk claim promotes complete switching and reduction in cigarettes. And General Snus does not appeal to youth.

Since the claim authorization, we collected additional post-market evidence which demonstrates that General Snus products continue to fulfill these criteria.

Today, we will summarize that evidence, update you on recent research, and demonstrate how our responsible marketing practices maintain low levels of use by unintended populations.

Swedish snus's category has been available in Sweden for over 100 years, and the General Snus brand has been around for quite a long time. Swedish snus is a smokeless tobacco product, traditionally produced in Sweden. It is non-fermented, and air cured.

The modified risk products include eight General Snus varieties that have been made available in the U.S. for more than a decade.

As you may know, these eight products received the first ever PMTA authorizations in 2015. As a result of the MRTP authorization, we are able to use General Snus, excuse me, General Snus's website to communicate to consumers the following: Using General Snus instead of cigarettes puts you at a lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

Having these products marketed with this claim is essential in helping move adult consumers down the continuum of risk. The claim works. It must be allowed to keep working.

Now, five years later, the products have entered the stage of the process and are up for renewal of the MRTP. So, what was required for renewal of an MRTP? And how does this differ from our initial MRTP application? Because of final guidance governs the renewal approach, we relied upon the FDA's draft MRTP

guidance to shape our approach.

Related to renewals, the key points of this guidance are: One, the data provided by the applicant should continue to show that the product is APPH; and two, the applicant should comply with required post-market surveillance and studies. This emphasizes the importance of post-market evidence which will demonstrate that the product continues to satisfy the requirements.

General Snus has been extensively studied through both the PMTA and RMTP pathways. It's important to emphasize that through these complementary pathways, the Agency assessed the benefit to the population on the whole and monitored post-market surveillance throughout the authorization period.

The key differences for the MRTP pathway include an assessment of whether the product significantly reduced the harms and risks associated with tobacco-related disease.

The MRTP pathway also includes an assessment of a modified risk claim, including whether the claim is both supported by scientific evidence and understood by consumers. Finally, MRTPs are subject to renewal.

Now let's talk a bit about process. The MRTP process is a rigorous, often multi-year endeavor that includes multiple phases of review to achieve authorization. The process begins with pre-submission meetings between the Agency and the sponsor to discuss key aspects of the application. Once submitted, the application moves through acceptance and filing reviews.

And finally, through a substantive, scientific review process, which for our initial application involved FDA going over more than 100,000 pages of scientific data. There is also an opportunity for public participation in the review process through the combination of a public comment period and a

TPSAC meeting.

And then FDA takes action by issuing a decision on the application. In the event of an authorization, products enter the post market- surveillance period where information is routinely provided to the FDA based on the requirements established in their authorization.

Finally, after the end of the authorization period, an MRTP renewal must be submitted, and the process begins again. The key take away here is that the MRTP process is science based and rigorous.

And Swedish Match has already completed the four phases of this process as part of their initial MRTP, including ongoing post-market reporting on an annual basis.

We are now in Phase 3 for this renewal. Given that this meeting is focused on an MRTP renewal, we will only briefly discuss the history of the products and the large body of scientific evidence that has been collected

and reviewed at multiple points over the last 10 years.

The General Snus products were first authorized as appropriate for the protection of public health through the pre-market tobacco product application process in 2015, following a PMTA submission earlier in that same year.

Since then, Swedish Match has submitted eight annual reports over as many years, the last four of which were combined with MRTP annual reporting.

The General Snus products were submitted for consideration through the MRTP process in June of 2014. A TPSAC meeting was held, and the FDA issued a partial decision in December 2016, where they determined that additional information would be needed in order to grant the modified risk tobacco product authorization.

Swedish Match amended and submitted a second MRTP in September of 2018, which was followed by a TPSAC meeting, and a later

authorization in October of 2019. The MRTP renewal for the products was submitted in July of 2023, triggering the third TPSAC meeting on these products, which is being held today.

In total across the PMTA and MRTP processes, Swedish Match has submitted four applications, presented at three TPSAC meetings, including today, and submitted eight years of required annual reporting to the FDA regarding the General Snus products.

Throughout the eight-year surveillance period, Swedish Match has not received any communication or concerns from the FDA regarding the APPH status of these products.

To summarize, the evidence surrounding General Snus is extensive and led the FDA to authorize both a PMTA and MRTP for these products. Based on the PMTA, FDA concluded the marketing of General Snus is APPH for both users and non-users.

Based on the MRTP, FDA found that

General Snus, as actually used by consumers, will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole, taking into account both users and non-users of tobacco products.

The results of our post-market surveillance and studies, have not raised new questions of public health. And therefore, support and reinforce FDA's prior actions.

For the remainder of this presentation, we will discuss the real-world evidence and post-market surveillance and studies that continue to demonstrate that General Snus's APPH, and that the MRTP authorization should be renewed.

When we received authorization for the eight General Snus products, FDA's assessment was comprised of four main evaluations. The first of those is health to individual users. The second is consumer understanding and perceptions. The third is

tobacco use behavior and the impact to the population. The fourth and final is responsible marketing and controls.

Similarly, all of these were components of our required post-market surveillance and studies, which we will discuss today.

This leads us to the agenda for the remainder of the presentation. And I'll first turn it over to Dr. Tryggve Ljung, the VP of Scientific Affairs at Swedish Match, who will discuss the scientific assessment of General Snus products.

Jen Mulligan, the Director of Marketing Services at Swedish Match, will then discuss how we are responsibly marketing the General Snus products with our authorization claim. So at this point, I would like to pass the podium to Dr. Ljung.

DR. LJUNG: Thank you, Gerry, for the introduction. Again, my name is Dr. Tryggve Ljung, and I am the Vice-President of

Scientific Affairs at Swedish Match.

Today I would like to walk through the conclusions made in the original MRTP and the post-market evidence collected since then, which collectively show that the authorized General Snus products remain appropriate for the protection of public health.

As Gerry mentioned, we will cover the post-market scientific evidence in three parts. First, the health risks to individual users; second, consumers understanding and perceptions; and finally, tobacco use behavior and impact to the population.

We will begin with a discussion of the health risks associated with General Snus use relative to other tobacco products. In their 2019 review, the FDA concluded that the scientific evidence supported the conclusion that exclusive users of General Snus had lower risk relative to cigarette smokers for mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

This conclusion was based on long term- epidemiological data coupled with the fact that harmful and potentially harmful constituents, or HPCs, in General Snus are significantly lower than other smokeless tobacco products that were on the U.S. market during the same period.

In this case, prior evaluation of HPCs, they stated that and I'm now going to read from the slide, the levels of NNN and NNK in these General Snus products are lower than those in the vast majority of smokeless tobacco products on the U.S. market.

And when used exclusively instead of other smokeless tobacco products, the General Snus products offer the potential for reduction in or of cancer risk. This shows that General Snus use poses lower risk than use of cigarettes and even other smokeless products based on their HPC profile.

Swedish Match has been focused on reducing the presence of HPCs in our products

for decades. And the implement of the use of the GOTHIATEK standard to further explode.

The GOTHIATEK standard is a manufacturing standard that has requirements for ingredients, processing, and levels of harmful and potentially harmful constituents. This chart depicts the evolution of HPCs in General Snus measured as part of the GOTHIATEK standard we have all used for decades.

What you can see is that over time, Swedish Match was able to dramatically reduce the levels of HPCs to a place where they are now incredibly low.

If we are looking at the redline, we are looking at typical levels of tobacco-specific nitrosamines, which are known carcinogens. Those TSMAs are made up of primarily NNN, the light green line, and NNK, the dark green line.

In addition, the black line is showing levels of benzene pyridine, another potent carcinogen. It shows also being reduced

to very low levels in General Snus. The low levels of these HPCs were recognized by the FDA during their original evaluation. And as you can see, the levels have remained low over the course of the authorization period.

When comparing to other smokeless tobacco products, we can see that the levels of TSMAs in General Snus, particularly NNN, are exceptionally low. This figure shows the levels of NNN measured in a series of smokeless tobacco products.

The first and second bars show levels of NNN in loose and portioned moist snuff. When compared to these smokeless products, the levels of NNN in General Snus, shown by this third bar, is reduced by more than 80 percent.

Further demonstrating the importance of considering HPCs in assessment of health risks, the FDA proposed a tobacco products standard in 2017 that would limit levels of NNN in smokeless products to less than 1 microgram

per gram, shown by the red dotted line.

This proposed product standard is expected to reduce tobacco-related harms by requiring lower levels of NNN in smokeless tobacco products. And thereby reducing the risk of oral and possibly other types of cancer in smokeless tobacco product users.

General Snus is one of very few smokeless tobacco products that already complies with this proposed product standard. And therefore, the collected post-market evidence indicates that General Snus continues to maintain exceptionally low levels of tobacco specific nitrosamines and benzene pyridine levels over time.

This is likely to translate to improved health outcomes among smokers who transition exclusively to General Snus. While HPCs are useful tools in assessing potential exposure risk associated with tobacco use, long-term epidemiological evidence is the most reliable indicator for evaluating individual

and population health risks. This is a rather busy slide, which I will walk you through.

Over the course of the post-market period, new epidemiological evidence was published regarding three of the disease outcomes specified in the claim, mouth cancer, heart disease, and stroke.

No new evidence was identified regarding lung cancer, emphysema or chronic bronchitis. In this chart, the examiner has agreed to, for the disease outcomes specified in our claim, which are shown on the left of the slide.

The pre-market evidence for snus, which the original authorization was based, is shown in black, and in blue indicate new post-market evidence for snus, which should be compared to data in red which represents smoking.

As you can see, the new post-market evidence continues to support that snus users are at reduced risk of mouth cancer, heart

disease and stroke compared to smokers. And therefore, the collective evidence demonstrates that the claim remains scientifically accurate.

As a final topic related to health risks, we also want to discuss the outcome of our annual reporting of adverse experiences associated with General Snus use.

Throughout the post-market surveillance period which spans our annual reporting submitted through October 2023, new, serious, or unexpected adverse experiences were reported, and our online monitoring does not seem that any concerns regarding adverse experiences related to General Snus prolonged use.

In the previous section, we discussed how HPCs coupled with GOTHIATEK standard make General Snus a lower risk tobacco product. And that the HPCs remain consistent since authorization.

For the rest of this portion of our presentation, we will focus on the evidence

collected after the MRTP authorization during the post-market surveillance period.

Now, we will focus on the post-market evidence regarding the modified risk claim and whether tobacco product users understand the information in the claim.

During their initial evaluation of our MRTP application, the FDA looked at our license of use study. The FDA determined that consumers generally understood the proposed modified risk claim, and also understood that the relative risk of General Snus is lower compared to smoking.

As part of their trial method for the post-market survey and studies, we conducted a longitudinal cohort pattern of use study, or PAU study. In the course of 24 months, we looked at General Snus users, how they use the product, their use of other tobacco products, and their perceptions of absolute relative risk.

This was to make sure that the

information in the claim continued to be understood following its authorization.

Here we are looking at the design of General Snus PAU study which consisted of a self-reported longitudinal study examining the understanding of the modified risk claim and patterns of past 30-day use of tobacco nicotine products, or TNPs, in long General Snus users at baseline and again, among the same General Snus users at 6-month, 12-month, and 24-month.

There were two respondents, cans of General Snus were sold at retail with a sticker directing the purchaser to a website where they could opt in to the study.

Participants were screened for pre-defined social criteria, including past 30-day use of any General Snus product at a minimum age of 21 years. We provided FDA with a study plan, which they approved in April 2020.

As part of this study, we asked consumers, does using General Snus instead of cigarettes place you at lower risk, the same

risk, or higher risk, or no risk?

As you can see, the results of this question demonstrate that consumers continue to comprehend that General Snus use causes a lower risk than cigarette use. Across all four waves of the study spanning 24 months, you can see that the vast majority of responders correctly reported that disease risk associated with General Snus is lower than that of cigarettes.

Furthermore, this data demonstrates that the consumers' perceptions were consistent with those measured before authorization and those perceptions did not change during the 24-month- study period.

The PAU study confirmed FDA's prior conclusion that consumers understand that completely switching to General Snus would reduce the risk of disease compared to smoking.

And the perceived health risks associated with using General Snus are lower than those associated with smoking. The study also examined perceptions of dual use and

consumers' understanding of the need to switch completely to General Snus.

In 2019, when the Agency authorized the use of the modified risk claim, they noted the claim did not lead smokers to believe that partial substitution of General Snus for cigarettes would reduce their disease risk.

The Agency also confirmed that the claim enabled consumers to understand that dual use of General Snus with cigarettes is more harmful than exclusively using General Snus.

Again, as part of our PAU study, we asked General Snus consumers how many cigarettes can be smoked in addition to using General Snus to maintain a lower risk of disease.

The respondents could choose from one of the following answers: zero cigarettes, up to five cigarettes, up to twenty cigarettes, or as many cigarettes as you want.

Across all four waves, you can see that the vast majority, over 80 percent of the

respondents, correctly noted that General Snus users must not smoke any cigarettes to maintain a lower risk.

Once more, the post-market evidence confirmed FDA's prior conclusion that the consumers understand the need to completely switch from cigarettes to General Snus.

Throughout our scientific assessment, we will now discuss how consumers are using General Snus and other tobacco products in the real world. As part of our two-year PAU study, we looked at exactly this.

A critical component of assessing tobacco product use behavior is assessing transition from one tobacco product to another. As part of their prior analysis, the Agency found that the marketing of General Snus was expected to result in the population health benefit by switching smokers to snus.

The Agency also suggested that General Snus use could facilitate switching from other smokeless tobacco products, which

would also reduce both HPC exposure and oral cancer risk in this population.

Here we are showing you information from the PAU study about participants' prior fairly regular use of various TMPs. The majority of established General Snus users reported fairly regular prior use of cigarettes or traditional smokeless products, comprising 84 percent of users studies.

Four percent reported exclusive use of Snus products and 11 percent reported prior use of another TMP. Only 1 percent of all study participants reported no prior use of TMPs.

This data suggests that the majority of established General Snus users have a history of cigarette and/or smokeless tobacco use and therefore could benefit from transitioning to General Snus based on available epidemiological data.

Now given that the authorized claim speaks directly to switching to General Snus

from cigarettes, we also assessed switching behavior among smokers. To be clear, our PAU study was not designed to just switching, but we can provide some evidence on this topic.

If we look at subjects who were every day smokers at the start of the study, we can see a reduction in every day smoking down to about 50 percent at wave four. Also about 17 percent of study participants who were daily smokers at baseline, are no longer smoking at wave four.

So for half of sample, two years appears to be in transitional state, which enables consumers to switch or reduce the use of cigarettes with time.

In addition to the same changes in daily versus some days of smoking, we also see a reduction in cigarettes per day in long General Snus users. In waves three and four, people who were every day smokers at baseline reported smoking on the average, six cigarettes per day or CPD.

This represents about a 50 percent decrease from the average baseline CPD. This data confirms that under real-world conditions, many smokers who use General Snus, were able to successfully switch or reduce their CPD over the course of 24 months.

As you remember, when we discussed how the FDA evaluates MRTPs under Section 911, they assess potential benefits to the individual user of that product and evaluates the impact on the population that do not use the product, non-users and former users, and in particular, non-users who are youth.

In their review of the original MRTP application, the FDA found that although youth are in general at risk of tobacco use initiation, surveillance data on U.S. tobacco use, said as to snus, it's not of particular interest among youth.

Based on data from the National Youth Tobacco Survey as studied by FDA and CDC, this remains true today. When we look at past

30-day use of a variety of traditional tobacco products, you can see that snus has a very low prevalence of use among youths as shown in the blue line on the bottom.

If we focus on the period since the MRTP was authorized, shown in the yellow box, we see that rates of youth use of snus are low across the authorization period.

As of 2023, the percentage of youth using snus is about 1 percent, which is lower than the 2019 estimate, those seem low to estimates from the past several years.

So even with the current tobacco marketplace features, numerous brands, strengths, and flavors of snus, post-market data confirms FDA's prior conclusions, the data continues to demonstrate an absence in appeal and uptick of snus among youth.

To conclude our scientific assessment, we will recap the findings from our post-market surveillance and studies. No serious adverse experiences were reported in

the U.S. or internationally.

Respondents in the PAU study continue to understand that the relative risk of General Snus use is lower than cigarettes, and the need to switch completely. Over the 24-month period of study, about 17 percent of every day smokers using General Snus completely stopped smoking.

One-third of every day smokers using General Snus because some day smokers. And every day smokers using General Snus showed a 50 percent reduction in CPD. This demonstrates the potential for smokers to use General Snus to switch from or reduce their cigarette consumption.

And finally, the prevalence of use of snus in youths is approximately 1 percent. This totality of the evidence confirms and reinforces the FDA's prior conclusions that led to the MRTP authorization.

And therefore, TPSAC should recommend that the FDA grant the MRTP renewal.

Now, I will turn it over to Jen to discuss marketing assessment for the General Snus products.

MS. MULLIGAN: Thank you, Tryggva. Good morning, everyone. My name is Jen Mulligan, and I'm the Director of Marketing Services at Swedish Match. I will be walking you through Swedish Match's responsible marketing practices and controls as they pertain to General Snus.

At the core of our responsible marketing is our intended audience. Our intended audience is adults that are over the age of 21 who are current tobacco and nicotine consumers.

All of our marketing practices and controls and FDA's efforts related to marketing surveillance are designed to ensure that our products reach adult tobacco and nicotine consumers and do not reach unintended audiences.

With this in mind, the Agency

outlined the following marketing information to be routinely submitted for their review through annual reporting. Swedish Match complied with these requirements throughout the product authorization period, giving the FDA a thorough understanding of our marketing practices, controls, and materials.

In addition to annual reporting, Swedish Match also complies with all FDA mandated marketing rules and regulations as well as those required by law.

But as a company, we take additional voluntary measures to ensure responsible marketing practices are applied to our entire portfolio of tobacco and nicotine products, including General Snus.

We have a history of taking conservative approaches to marketing, instituting age dating marketing practices before they were required because it was the right thing to do as a company and the right thing to do for our consumers.

Let's take a closer look at some of those responsible marketing practices and controls. First, we will discuss proactive transparency.

We value and promote transparency with consumers, policymakers, and regulators to ensure our marketing practices and restrictions meet our stakeholders needs. We provide consumers with truthful information within the confines of the regulation.

Next, careful retail placement. We require our retailers to place General Snus behind the counter to ensure that consumers have been age-verified by the retailer before having access to the product.

Moving to restraint with advertising, General Snus voluntarily avoids outdoor advertising like billboards, and does not advertise through TV or other mass media vehicles to ensure that our marketing is viewed only by our intended audience.

We select models for advertisements

who are visibly over the age of 35. This image is an example of a social media post on the General Snus Facebook page, which is age restricted.

We restrict our social media marketing to only those platforms that have age restriction capabilities. And finally, Swedish Match does not partner with or sponsor professional athletes or social influencers. These are examples of our responsible marketing practices and the activities that we avoid.

Now we'll go through some examples of consumer facing materials. Here, we show a few examples of our marketing materials for General Snus, including point of sale materials, as well as an email, and a direct mailer that is sent to age-verified consumers within our database. All of these materials were provided to the FDA as part of our last annual report.

What you will notice is that none of these sample marketing materials contain the

claim. And that's because the claim is currently limited to use on our age-gated website.

The General Snus website is age-gated by third-party age verification partners, limiting access to anyone under the age of 21. Consumers must successfully verify their age, confirm they are a current tobacco and nicotine user, and create an account to access the website.

This ensures that all website visitors meet criteria for our intended audience. To be clear, the claim which was authorized as part of our 2019 MRTP is currently only communicated on the General Snus website behind the previously discussed age-gate.

Now I would like to show you the steps that a consumer would take to gain access to the General Snus modified risk claim on our website.

First, the consumer would need to

visit our website at generalsnus.com and click on the box to register now. This will prompt a pop-up requiring the consumer to answer the question, are you a current tobacco or nicotine user.

If the consumer answers no, their access to the website registration process is denied. The website then states that General Snus products are only for current tobacco and nicotine users age 21-plus.

Since you are not a current tobacco or nicotine user, there is no need to register on our website because General isn't for you.

Again, this is a completely voluntary practice that Swedish Match implemented to ensure that we are not reaching unintended audiences. This is far above the standard practices for tobacco and nicotine products.

If a consumer selects "yes" that they are a current tobacco or nicotine user, they are admitted to begin the registration

process. The first step in the process is age verification.

The consumer is asked to give their birthday and other personal information which is then sent to our third-party age verification partner to be matched to existing government databases for confirmation.

If a consumer's information cannot be verified, the registration process is stopped. If a consumer is successfully age-verified, they move on to the next step in the registration process.

In the second step, we capture consumer communication preferences and other consumer profile information. Then they move on to the final step in the registration process.

Here, the consumer creates an account username and password to access the website. Once a consumer has been age-verified and created a registered account on generalsnus.com, they are admitted to the

website.

Here they can access the modified risk claim by either scrolling down on the home page or of clicking on the navigation menu and selecting "modified risk" designated by the yellow box on this slide.

After clicking on "modified risk," the consumer is redirected to a page about modified risk and the claim appears roughly midway down that page.

To summarize, the consumer must go through a very rigorous process to access the authorized modified risk claim. They must visit generalsnus.com, select register now, identify as a current tobacco or nicotine user, provide personal information for age verification, provide their communication preferences, create a username and password, and click on "modified risk."

While this process drastically limits the likelihood that the claim will be viewed by unintended audiences, it also limits

the utility of the claim, making it difficult to reach the intended consumer who could achieve a reduction in health risks by switching completely to the product.

While we use multiple marketing channels for product advertising, our brand website is the only platform we currently use to communicate the claim.

Smokers are up against a wall of misinformation about smoke-free products and it's easy to be confused. It's hard to find science-backed information, and this Committee can help change that.

The renewal presents a great opportunity to discuss the potential to expand the use of the claim beyond our brand website. As shown in yellow, we would like to expand the use of the claim to align with the Agency's thinking to include email and direct mail to 21-plus age-verified consumers within our database, point of sale materials, print advertising and publications where 85 percent

or more of the audience is 21-plus, and other age-verified platforms such as social media and other digital platforms.

By expanding use of the claim, we could not only align with the Agency's current thinking, but also have a greater impact on public health.

Other apparently authorized MRTPs like Copenhagen, which is also a smokeless product, are permitted to use their MRTP claim within these boundaries.

With this in mind, we are prepared for a discussion with the Agency on the ways to adjust the use of the claim to reach more smokers and smokeless tobacco product users who could benefit from our products. And with that, I will turn it back over to Gerry.

MR. ROERTY: Sorry, I'm not getting any younger, it takes me a while to get up here. Jen, thanks so much. So the evidence presented here today does support MRTP renewal for General Snus.

We have consistently met all post-market requirements for both our PMTA and MRTP over the course of the last eight years. Further, the post-market evidence surrounding General Snus has not raised any new questions of public health.

And finally, the reduced risk information, including in the claim, remains accurate and is helping to achieve our and the Agency's desired outcomes for individual tobacco users and the population on the whole.

The preponderance of the real-world scientific evidence and data continues to demonstrate the harm reduction potential of General Snus with a reduced risk claim. And the General Snus modified risk grant orders should be renewed.

This process has been really, really, really hard, being the first is just never easy. But the claim -- the process should be hard. Because we're talking about, you know, very, very important issues of public

health.

But we're really proud to be a part of it. The CTP offices have been great to work with. They've challenged us, as they should. But we want to thank them especially for helping us get through this process and achieve the great achievement of having the first MRTP and PMTA.

So in closing, I want to thank the TPSAC Committee, each of you, thank you; the FDA, members of the public, the team, thank you, thank you, really. It was a collaborative effort to achieve the first ever MRTP authorization. And we look forward to having a continued discussion with you all. So at this point, we are happy to -- are we -- questions, is that the plan?

CHAIR DELNEVO: Yes, so we have -- I'd like to keep us on track, but thank you for staying within your time. So I think we have about 10 minutes to open it up for clarifying questions.

And I would like to start with one. Regarding the post-market surveillance study, I have two questions there. Did you measure continued use of General Snus at all of the waves?

And how you define -- you referred to them as established General Snus users, but if I understand correctly, at the first wave, they had used General Snus at least once in the past 30 days.

And so is that your definition of established use? And did you measure continued use throughout the waves?

MR. ROERTY: Yes. Thank you for that. You know, when we sat down with CTP to come up with a study design, the decision was made to start with existing General Snus consumers. So we did know that they were at least purchasing General Snus products.

With respect to the various measures within the POU, perhaps I could invite Dr. Ljung to join as at the podium to address your

questions.

DR. LJUNG: Sure, thank you. And what we did was that we recruited respondents by stickers. And as a consequence, we could say that 52 percent of the study participant had been using General Snus for at least 36 months, so they were in general well-established.

We tried to find a cohort, a stratified cohort with new users, but we recruited very few of them. It did continue to measure, you know, snus use through all the waves. Thank you.

CHAIR DELNEVO: While you're still up there, a follow-up question. So you presented data showing that there were changes in cigarette smoking behavior over time.

But did you also look at use of other tobacco products potentially explaining that, and whether or not that the patterns you are seeing are different for the individuals in the General Snus post-market surveillance study

versus just secular changes in tobacco use behavior among adults in general over that time period?

DR. LJUNG: So we did ask for one or ten different TMPs during that post-market surveillance study. And what you can see in general is mainly a stable usage pattern. The only things we actually saw some differences was a slight uptick of nicotine pouches over time, and actually -- and are key.

CHAIR DELNEVO: Adam, and then Lucy, and then Nancy, I think after that.

DR. LEVENTHAL: So, you know, the MRTP is in relation to using your product instead of cigarettes, right. So my question is about your intended audience and consumer base.

And I noticed in some of your research that you presented, that a fairly modest proportion of the General Snus users in your research smoke. And many of them use other tobacco products including nicotine

pouches and other smokeless.

So my question for you is to what extent, if the majority of the people who are using your product and purchasing it, are not people who smoke combustible cigarettes, but are using other non-combusted products, to what extent does that influence the designation for the APPH? And I have one follow-up question.

MR. ROERTY: Thanks. I appreciate that. So if I could, perhaps I could pull up Slide 2, from and this, if I could draw your attention to this. And again this was 2015 PMTA, but again, remember there's a whole collection of evidence that went into what we were attempting to do here.

And as you see, and the CTP concluded, that we're seeing a, you know, a switching away from the most deadly product, cigarettes, to a product like snus. And what we -- what we had seen over time is that the reason we went the direction we did with the claim is because cigarette smoking is quite

candidly the most deadly form of tobacco.

Now the fact that we had an added benefit of moving some smokeless tobacco consumers, moist snuff and things like that, that have higher levels of HPCs down the risk continuum, of course, is a bonus. But again, the POU study, not meant to be a switching study, meant to be a check on whether the conclusions that the CTP found, that is as a population level benefit, General Snus fits.

And there was nothing in the research or the studies that would have undermined what CTP said before, so. Not a perfect study by any means, you know. We worked with the CTP to get there, but we find that the, you know, the population harm is -- the gain is still there.

DR. LEVENTHAL: And one follow-up question related. So I notice that your colleague talked about extending the marketing channels to point of sale and one of the slides showed the General Snus product being sold

right next to some of the nicotine pouch products.

And so one question for you is I think that there's some evidence, a study by Lieber showing that pre- and post-MRTP authorization of your product, all different types of snus brands show the slowing, it was a reduction, but it was slowing, relative to other smokeless products raising questions as to whether MRTP claims may have halo effects where by the consumer misperceives that the MRTP applies to not only different products within the general category, but other products.

So getting back to my point, if there's an extension of the MRTP claims in point of sale or other types of marketing channels where there are other products where there's no evidence, to my knowledge, that General Snus is less harmful than these other products, how can you ensure that that type of misperception would not happen?

MR. ROERTY: Couple of questions in there, but I think I've teased it out. When you say as for the shelf space, we don't have any control over that.

Honestly, the -- I think there's some competitors out in the audience that have a lot more to do with that by virtue of their retail agreements.

So the product winds up where it does, not very often by our choice. With respect to the halo effect and I'm going to invite Dr. Joyce up here in a minute to talk about the study that you referenced if that's okay. Ms. Chairman, I know we're trying to keep this quick, but we'll try to do that quickly.

But what I will say is that the CTP concluded with the Copenhagen folks that the MRTP claim could be at point of sale and be consistent with the mission of the MRTP program, that's why we included it within our wish list.

So perhaps that's a question you could post to them this afternoon. And then very quickly on the study, Dr. Joyce would you like to come up and briefly talk about that?

DR. JOYCE: Good morning, my name is Andrew Joyce and I'm the President and CEO of Consilium Sciences. Our firm provides consulting services on scientific and regulatory matters for companies in the tobacco harm reduction space.

While I am being compensated for my time today, I just want to make it clear as a disclaimer that I have no financial interest in the outcome of this particular meeting.

So I will attempt to comment on this particular halo effect, just very briefly. I don't know that we have strong data that from the snus category indicating that there is a halo effect that translates to a nicotine pouch and that sort of thing.

And I just want to make it clear that a consumer is going to be exposed not only

to the claim, but also to the health warnings that go with it.

So if we look at Slide 2, just to enumerate, the consumer's going to be faced with a variety of other contextual pieces of information to make judgments on the relative safety of the products, especially vis-à-vis cigarette smoking, so.

CHAIR DELNEVO: Lucy?

DR. POPOVA: Thank you. I'm sorry, I'm going to ask the question facing this way.

In your POU study, did you evaluate, did you measure the exposure to actual claim, either as a recall or any other way? And did you do any analysis with that?

MR. ROERTY: Sure, sure. Yes, so FDA pointed out in their briefing materials that consumer was not shown the claim as part of the POU study. It was an intentional choice actually.

DR. POPOVA: Well, I'm not asking about intentionally showing them, they were in

real-world, the claim was there. Did you measure if they had seen it or not?

MR. ROERTY: Don't believe that was the -- we didn't ask that -- we did not ask that question. Instead what we tried to do was contextualize had they received the information in such a way that they could answer the survey. So no, we did not measure whether they had actually seen it.

CHAIR DELNEVO: Nancy?

DR. RIGOTTI: I had a question about your longitudinal analysis of the post-marketing survey. There's a large drop out, a very large drop out. And so I wondered whether, and since we know that people who tend to stay in studies are those who have good things happening.

Was wondering if you had adjusted for potential founders or otherwise adjusted to try to make sure that your conclusions would be without bias?

DR. ROERTY: Sure, sure. We're

aware of the attritional analysis that the CTP has in their -- in their materials. You know, I guess what I would say is that, you know, we were the first, and so we tried to put together the most cohesive plan we could and the results were what they were.

And so we just shared with you who was left and what they -- what they said. But I think what I would -- what I would offer is that even with attrition, you know, we think there's some information in there that says hey, this can work and this does work. And if we can meet more smokers where they are with this information, we hope we could achieve, you know, even greater results.

CHAIR DELNEVO: Olivia?

DR. WACKOWSKI: Hi. I want to follow-up on Dr. Popova's question. So you said you didn't measure exposure to the claim itself, but did you measure perhaps, the extent to which they were exposed to marketing materials where the claim may have been,

whether they used the website or received mailings? So that was one question I have.

MR. ROERTY: There you go, he shook his head. There is the answer, no we didn't -- we didn't do that.

DR. WACKOWSKI: Okay. And my second question is can you just clarify why the claim is only on the website? I'm not clear if this is sort of a self-imposed thing or what was authorized or not authorized.

I think in the beginning, we did see the claim in emails and direct mailings but somehow it shifted over time. But can you say a little bit about that?

MR. ROERTY: Yes, sure. I guess the answer to your question is yes. So we have a -- our authorization letter is very general. It talks in terms of you can use media that you can really measure and get lots of data on. You know, we don't want any unintended audience to see this information.

And so when we put the application

together, we put the marketing plan and we had all those, we had POS, we had other things like that. Over time, as we were having discussions with people outside the Office of Science, they began to say, you know, can you really show us that this particular way of marketing checks all these boxes in terms of avoiding unintended audiences from seeing these things and what measures do you have?

And we just could not figure out a way to get there, you know, we just couldn't. And we were struggling like crazy and said, you know what, in the end the only place we know for absolute sure that we can meet what the folks outside the Office of Science were asking, was the website.

Which is disappointing, but we just didn't know what else to do. And then we saw the Copenhagen decision and it was like, okay, so people had begun to -- I'm not going to call it a safe harbor by any stretch, but it just appears that the change -- there's been an

evolution in thinking and perhaps they have, the Center's gotten that information and they feel better about those channels.

So we're kind of hoping just to be put on the even playing field with other smokeless products. I hope that helps, I, you know, as a I said, a little self-imposed, a little by dialogue with others.

CHAIR DELNEVO: We're going to go to Sven and then Dona and then we're going to wrap this segment up.

DR. JORDT: Thank you. I have two questions, one for Dr. Ljung, and one for Jennifer Mulligan.

For Dr. Ljung, I have a question about adverse events. And data out of Sweden have shown that snus users often present with oral mucosal lesions.

There are other papers linking snus potentially with Diabetes Type 2. These may not come down to adverse events, like they are more like acute. But is your company and at

the same time, FDA, monitoring these type of adverse presentations?

My second question is for Jen Mulligan. Last week, spheres matches Zyn web store was closed after a subpoena from the Washington, D.C. Attorney General, probably due to sales of flavored tobacco products in Washington, D.C.

Does this closure extend to the General Snus web store, or is their web store regionally dated to prevent sales in regions of the United States with flavor bans? Thank you.

MR. ROERTY: Thanks for both of your questions. I'm actually going to handle your second question. We are as we said, publicly, we are actively and currently investigating that information in all our practices.

I will tell you without doubt, that we are absolutely committed to compliance across the board. The surest way to ensure that compliance with all of our products was to close the e-commerce site, we could do the

investigation.

With respect to General Snus, we are similarly committed to that and really at this point, that's all I can really say about the matter. It's a pending matter.

So with respect to your first question, however, I would invite Dr. Ljung up to describe this. I do know that CTP does do surveillance, by the way, on these products.

DR. LJUNG: Yes, so as to snus lesions as you referred to them, if they were reported as an adverse event we would, of course, share that information. It's a well-known feature of snus users, and it does not qualify as a serious adverse event or unexpected adverse event.

And for health outcomes, yes, we are following the literature, we are capturing consumer complaints, of course.

But for the renewal process, I mean, if you refer to diabetes, it's not part of the claim, so this renewal is strictly related to

data presented in the claim.

CHAIR DELNEVO: Dona?

DR. UPSON: Thank you. And I also, can I ask the limitations of an unexpected adverse event in that the data you presented also showed an increased risk of cardiovascular disease and microinfarctions and stroke, lower than with cigarettes, but still a risk that we're not really addressing in the education of the public?

And my other question is or my question is whether you've looked at any impact on interaction with ENDS, electronic nicotine delivery systems?

I know you looked at cigarette, combusted cigarettes and other types of smokeless tobacco. Have you looked at anything with electronic nicotine delivery devices? Thank you.

MR. ROERTY: To the extent that there is data in the POU to show what products they use, if we have a slide, I don't know, we

can certainly show it, but I don't believe so, we don't have that.

CHAIR DELNEVO: All right. And with that, we're going to conclude this segment. We're going to take a 10-minute break and reconvene at -- a 9-minute break at 10:50.

(Whereupon, the above-entitled matter went off the record at 10:41 a.m. and resumed at 10:52 a.m.)

CHAIR DELNEVO: I'd like to invite Nicole Tashakkori from FDA for the next presentation. Oh, she was there.

MS. TASHAKKORI: Good morning, everyone. My name is Nicole Tashakkori, and I'm an epidemiologist in CTP's Office of Science. I'm going to present on the General Snus patterns of use and the impacts on the population.

So this table presents summary of relative risks from published meta-analyses or pooled analyses, of the association between Swedish Snus use and mouth cancer, heart

disease, stroke, and lung cancer compared with people who do not use tobacco.

This body of literature was reviewed in the original MRTPA. So the risks of oral cancer, lung cancer, and emphysema, and chronic bronchitis are clearly lower in people who exclusively use Swedish Snus compared to people who smoke cigarettes. The data for heart disease and stroke are mixed.

However, as shown on the table, cigarette smoking has been found to increase the risk of cardiovascular disease by a factor of about one-and-a-half to threefold.

A systematic review by Rostren and colleagues provided additional clear evidence that the heart disease risks due to Swedish Snus use are lower than the risk from cigarette smoking. Additionally, this review found that the risk of stroke due to Swedish Snus use is lower than the risk from cigarette smoking.

So since the MRGO in 2019, the newly published literature is generally consistent

with the body of literature viewed during the original MRTPA and provides additional evidence that the risks of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis due to Swedish Snus use are lower than the risk from combusted smoking.

The applicant submitted published literature regarding individual health risks as part of their PMSS requirements. In addition, FDA conducted a review of individual health risk studies published between 2019 and 2023 regarding mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis.

These are the health outcomes listed in the modified risk claim in the 2019 MRGO. So overall, we analyzed a total of ten studies that were published since the MRGO.

And among these studies, listed to two that did not focus on outcomes relevant to the modified risk claim, and one systematic review that overlapped with the other studies

selected.

Regarding mouth cancer, there was one study identified that evaluated the association with current snus use as compared to never snus use and observed no statistically significant association.

FDA did not identify any new studies published since the MRGO that evaluated the association between current snus use and either lung cancer, emphysema, or chronic bronchitis.

Therefore, there is no new information published since the MRGO to consider for these claim-related health outcomes.

FDA evaluated four studies published since the MRGO to estimate an association between current snus use and stroke or heart disease morbidity and mortality.

As noted in the side, findings are mixed, ranging from no association to having increased risk. Titov and colleagues find that people who currently use snus and have never

used combusted cigarettes, have a significant 53 percent increased risk of total stroke and a 65 percent increased risk of ischemic stroke compared to people who never used tobacco.

These results are based on a single cohort, and are consistent with prior findings that the level of risk is below the well-established stroke risk of combusted cigarette smoking.

Similarly, one study found a significant 27 percent increased risk of cardiovascular disease mortality among people who exclusively use snus and have never used combusted cigarettes. And this risk is still lower than that for combusted cigarette smoking.

Data from a contemporary cohort among men aged 55 to 74 indicate that people who smoke combusted cigarettes have elevated risk of stroke and cardiovascular mortality.

Therefore, the risk of stroke and cardiovascular disease mortality in people who

exclusively use snus are lower relative to people who smoke combusted cigarettes as FDA's prior evaluation concluded.

And the scientific evidence published since the original MRGO continues to support the modified risk claim assigned to be accurate. Additionally, neither the applicant nor the FDA's safety reporting portal revealed any adverse experiences involving the product subject to this review since the issuance of the MRGO.

So to provide some context, this section examines observation studies in the applicant's General Snus Patterns of Use Study that describes patterns of use for General Snus.

FDA will also review published literature from national representative surveys of tobacco use among youth and adults. The applicant cites results from wave one of the past study where 0.4 percent of U.S. adults were current established users of pouched snus.

Population estimates from FDA's internal analysis of pathway seven data indicate that 0.7 percent of adults reported using snus in the past 30 days.

The applicant cited 2022 NYTS data that showed 1 percent of students reporting ever use of snus and 0.5 percent indicated use of snus at least once in the past 30 days.

Results from an internal analysis of the 2023 NYTS data indicate that 0.8 percent of middle and high school students report current snus use. In the 2022 MITS, snus use was assessed separately from other smokeless tobacco products.

The applicant conducted an online survey examining use behavior of General Snus and other tobacco and nicotine products at multiple time points. This prospective study spanned two years.

Participants were asked to complete the survey at four time points, baseline, six months, one year, and two years. And in the

subsequent slide are the slated time periods and sample sizes for each wave.

Participants who completed the baseline survey were allowed to participate in any of the subsequent waves regardless of participation in prior follow-up waves. The applicant recruited purchasers of General Snus products through invitation stickers placed on product packaging.

These products with invitation stickers were available at approximately 10,600 retail stores across all locations where General Snus was sold from July 25, 2020, until August 7, 2020.

The applicant also recruited via email people who opted in and registered to receive communications from General Snus. Study participants received $40 for each completed survey and an additional $50 bonus if they completed all three follow-up surveys.

So to be eligible for the study, individuals must have reported current use of

the General Snus product at baseline, defined as using at least one within the past 30 days prior to study initiation and using it every day or on some days prior to study initiation. They also had to be U.S. residents, age 21 years or older, reported being able to read and speak English.

Lastly, they had to agree to participate in four surveys over a 24-month period and provide consent and personal contact information.

The applicant excluded individuals who selected don't know or declined to answer to survey questions about their gender or geographic region; who participated in consumer research on tobacco and nicotine products in the two weeks prior to accessing the baseline survey; who were employed in market research, marketing, advertising, tobacco and nicotine product manufacturing or as a physician.

So as previously stated, the applicant provided their General Snus Patterns

of Use Study which assessed snus behavior through the applicant's three primary objectives.

First is to compare tobacco and nicotine patterns of use. Second is to compare consumption patterns of combusted cigarettes and General Snus over the last 30 days with consumption patterns in waves two through four, and third is to assess complete substitution and cessation behaviors among people who dual used combusted cigarettes and General Snus.

The applicant originally had another primary objective comparing prior tobacco and nicotine use and demographics to people who newly use smokeless tobacco and nicotine products. But this was eliminated midway through the study due to a low sample size of new users.

The Patterns of Use Study also indicates several secondary objectives pertaining to risk perception and understanding of the modified risk claim which will be

covered in a subsequent presentation. So the figure in this slide depicts the General Snus Patterns of Use Study sample size by study wave.

The study experienced higher than expected dropout rates over a two-year study duration. A priority, the applicant estimated a 40 percent dropout rate per year, resulting in an estimated sample size of 1,200 participants in wave two, 900 in wave three, 540 in wave four.

However, the actual attrition rate was higher as the figure indicates. Overall, only 281 participants completed all study waves, indicating a 17 percent full study retention rate.

The applicant removed additional responses from each wave due to data cleaning. Differential loss of follow-up by tobacco use status could impact the studies to observe transitions in tobacco use and result in bias study results.

As a result, FDA conducted an attrition analysis on the applicant's data to evaluate potential demographic or tobacco use differences in participants who dropped out versus those who were retained at each study wave. We will discuss these results in the limitations slide.

Now that you have an overview of the study design, I will describe the demographics of who participated in the study. At baseline, respondents were predominantly male, non-Hispanic white and lived in the South or Midwest. The mean age was 36 years old.

Most had some college or associate's or bachelor's degrees and an annual household income of less than $500,000 or $500,000 to less than $100,000.

Regarding tobacco use behaviors, all participants used General Snus. Baseline participants predominantly used more than 200 General Snus pouches in their lifetime. Approximately 18 percent of baseline

participants reported currently smoking combusted cigarettes.

Thirty-seven percent reported formerly smoking combusted cigarettes and 45 percent reported never smoking combusted cigarettes.

Among those who currently smoked combusted cigarettes, over 60 percent reported a readiness to quit by a quit attempt in the past 29 days, currently trying to quit, or with high intention to quit in the future.

Participant characteristics were mostly similar from baseline to wave four. However, compared to the total baseline participants, those who completed wave four were more likely to report income greater than 100,000 per year and educational attainment of post-graduate degrees.

In terms of tobacco use characteristics, those who completed wave four were more likely to have used over 200 lifetime of General Snus pouches.

Among those who smoked combusted cigarettes, there were differences in readiness to quit between baseline and those who returned at wave four. FDA notes that participant demographics in the current study are more similar to people who report using smokeless tobacco than those who report using combusted cigarettes.

This table depicts General Snus and combusted cigarette use patterns at baseline and wave four. At baseline, approximately 82 percent reported using General Snus every day and 18 percent reported using General Snus on some days. Twenty-six percent reported using General Snus exclusively. These numbers didn't drastically change over time.

So at wave four, the majority, at around 60 percent still used General Snus every day while 27 percent used General Snus some days. Twenty-two percent still use General Snus exclusively.

The applicant defined dual use as

participants who reported using General Snus and combusted cigarettes regardless of other tobacco product use. This means that these dual use with tobacco products. This means that these dual use with combusted cigarette overall every day and some day estimates include people who use other tobacco and nicotine products like nicotine pouches or moist snuff.

This isn't depicted on this slide, but it is reported in the Backgrounder. Over half of the baseline sample reported using General Snus with another non-combusted cigarette tobacco product. And among baseline participants, approximately 33 percent reported use of nicotine pouches, 33 percent reported use of moist snuff.

Dual use with combusted cigarettes only indicates exclusive General Snus and combusted cigarette dual use. At baseline, approximately 7 percent report using General Snus with combusted cigarettes every day.

And 11 percent report dual use on some days. At wave four, three-and-a-half percent report every day dual use and 8 percent report some day dual use.

Now that we've discussed use patterns, let's discuss a participant's substituted combusted cigarette use with General Snus or to quit both products over time.

Evidence from published literature suggests that about 5 percent of people who dual use combusted cigarettes and smokeless tobacco before completely switching to a smokeless tobacco over time. This slide depicts FDA's analysis of the applicant's data. And we found higher estimates of switching behavior.

Complete substitution was defined as participants who used General Snus and combusted cigarettes at baseline, but quit combusted cigarette smoking and only used General Snus at waves two, three, or four.

Participants who completely substituted General Snus for combusted cigarettes may use other tobacco products. Cessation was defined as participants who completely substituted General Snus for combusted cigarettes plus those who quit both products.

As displayed in the table, among some day participants who were dual users at baseline, 9 percent report quitting combusted cigarettes by wave four and 8.4 percent report completely substituting combusted cigarettes with General Snus.

The General Snus Patterns of Use Study had some limitations. Thus, FDA replicated some of the applicant's findings and conducted additional analysis when needed. Namely, FDA found evidence of differential attrition.

This means that participants who were younger, had a lower household income, used General Snus non-daily and used less than

200 General Snus pouches in their lifetime, tended to drop out of the study. Also, regarding tobacco use behaviors, people who exhibited a higher readiness to quit stayed in the study.

These findings suggest that the observed tobacco use transitions may not accurately represent the actual likelihood of transition when the data appears to not be missing at random.

To account for this, FDA calculated completed substitution and cessation using people who report combusted cigarettes at baseline as the denominator, which assumes that people who smoke combusted cigarettes and drop out of the study, continue to smoke.

Overall, no new health risks were identified in the published literature. And FDA's original MRTPA review conclusions regarding claims substantiation hold.

NYTS impact data indicate low prevalence of snus use among U.S. youth and

adults, with General Snus representing only a fraction of these small estimates. The General Snus Patterns of Use Study suggests that eight and a half percent or more people who dual use General Snus and combusted cigarettes at baseline, quit combusted cigarette use two years later.

The true estimate is hard to know because of the high degree attrition, which appear to be differential with respect to smoking behavior.

While the study had some limitations, findings add to the body of evidence that some people who use General Snus use the product to help them quit combusted cigarettes.

Now that I've covered the behavioral evidence on General Snus use and the impact to the population, I'm going to hand it over to my colleague, Dr. Venrick, to discuss consumer perceptions and understanding.

DR. VENRICK: Good morning,

everyone. My name is Dr. Samantha Venrick, I'm a social scientist in CTP's Office of Science. I'm going to present results related to consumer perceptions and understanding from the General Snus Patterns of Use Study.

To start the discussion about consumer understanding and perceptions, let's review the FD&C Act's requirements for marketing MRTPs.

The FD&C Act requires that the public can comprehend the information concerning modified risk in any advertising or labeling concerning an MRTP, and understand the significance of that information in the context of total health.

Now that we know the requirements, let's dive into the information submitted by the applicant. As we just heard from my colleague Nicole, the applicant conducted an online survey titled "General Snus Patterns of Use Study."

In addition to assessing use

behaviors, the study examined perceived health risks of using General Snus and other tobacco and nicotine products, and understanding of the risk reduction as stated in the modified risk claim.

We already heard many of the details of the study. For the purposes of the objectives I just highlighted, it is important to note that participants were not shown the claim at any time during the study as advised by the FDA to avoid biasing participants in the study sample by providing them with information that they would not have had if they had not participated in the study.

The key outcomes assessed in the Patterns of Use Study include risk perceptions and understanding. The measures used to assess risk perception is shown here.

Participants were asked about the chance that a person who only uses General Snus every day would suffer from heart disease, lung cancer, and mouth cancer.

Participants were asked the same questions for a person who has never used tobacco or nicotine products. A person who only smoked cigarettes every day, only uses General Snus every day, and uses both cigarettes and General Snus every day.

Participants rated their responses on a five-point scale from very low chance to very high chance. Participants can also select "don't know".

The Patterns of Use Study also assessed participants understanding of the relative risk of General Snus compared to cigarettes with one item.

Excuse me, can I get a chair to sit on?

So, the patterns of use study also assessed participants' understanding of the relative risk of General Snus compared to cigarettes with one item. Participants completed the following sentence which is their modified risk language, verbatim, using General

Snus instead of cigarettes, with one of six responses; puts you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema and chronic bronchitis. Does that affect your risk; puts you at higher risk, none of the above, don't know, or decline to answer.

Participants who responded correctly to the previous question that using General Snus instead of cigarettes puts you at lower risk, were then asked how many cigarettes if any, you can smoke per day, if using General Snus instead of cigarettes to lower your risk of disease. Response options were: zero cigarettes, up to five, up to twenty, as many as you want to smoke, don't know, and decline to answer.

This figure shows the distribution of responses to the first understanding question across the four waves of this study. Most General Snus users that always correctly answer that using General Snus instead of cigarettes puts you at lower risk for mouth

cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis, as shown by the light blue portion of the bars.

Approximately one fifth of participants at wave four did not understand that completely switching to General Snus can reduce disease risk for a person who smokes cigarettes.

There was a statistically significant increase in understanding from baseline to wave three, among the subset of participants who completed both those waves. However, attrition was high across the pattern of -- across the General Snus patterns of use study and participants who completed waves two, three, and or four were more likely to have responded correctly to this relative risk item at baseline, compared to those who dropped out at each wave. Therefore the longitudinal findings should be interpreted with caution.

This figure shows participants' risk perceptions of General Snus across three

disease outcomes at baseline. Consumers generally viewed using General Snus as having low but present health risks, particularly for mouth cancer and heart disease. For mouth cancer, 34.9 percent of participants perceived a low risk and 34.6 percent perceived a moderate risk for heart disease. Thirty-nine point one percent perceived a low risk, and 34.1 perceived a moderate risk.

This is compared to the 13.1 percent and 18.1 percent who perceived a very low risk of suffering mouth cancer and heart disease, respectively if one uses General Snus every day. So, it's not changed over the four waves of the study.

Participants who correctly answered that using General Snus instead of cigarettes puts you at lower risk of diseases were asked an item assessing whether users understand how to use the MRTP to reduce risk. This figure shows the distribution of responses to the item from waves one through four. Participants were

asked to select only one response.

Most General Snus users at always correctly answer this question, selecting that you can smoke zero cigarettes per day if you are going to use General Snus instead of cigarettes to lower your risk of diseases. This is shown in the light blue bars. There was a statistically significant increase in correct understanding from wave one to wave two.

Further supporting that General Snus users understand how to use General Snus to reduce their risk at baseline and in each subsequent wave of the survey, participants correctly perceived dual use of cigarettes and General Snus as more harmful than exclusive use of General Snus across all three health outcomes.

In summary, the General Snus patterns of use study findings indicate accurate understanding of the modified risk claim. The applicant demonstrates that most study participants, all of whom were people who

used General Snus at baseline, understood that using the General Snus -- that using General Snus instead of smoking cigarettes, put them at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis. Most participants perceived that using General Snus every day carries some risk for some diseases.

Most participants in the General Snus patterns of use study understood that they could not use General Snus with cigarettes and experience the potential health benefits described in the modified risk claim. Further supporting consumer understanding of how to use the MRTP to reduce their risks, study participants accurately perceived dual use of General Snus with cigarettes as more likely to cause mouth cancer, lung cancer, and heart disease then use of General Snus alone.

This concludes FDAs presentation of the renewal package. At this time, we are happy to answer any clarifying questions.

And I have chocolate, so I will be okay.

(Laughter.)

DR. VENRICK: Thank you.

(Applause.)

CHAIR DELNEVO: Thank you. I do want to open it up now to clarifying questions. I do ask that folks focus their questions on clarifying questions about the content, because we will have time for discussion on the implications of the findings later.

Dona?

DR. UPSON: Thank you. Dona Upson. I had a question. I heard -- I heard you say that the gender question, people were excluded, is the answer. Declined -- Declined to answer, or -- or don't know on the gender question. And since we know in general that LGBTQIA+ people are at higher risk for tobacco dependence and complications, why -- what was the reason for excluding people who may be gender non-conforming? Thank you.

DR. VENRICK: I refer that to the Applicant, since it's their -- that was their decision.

MR. ROERTY: To -- To be very candid, in hindsight, I wish we had not. I have a -- a young daughter who's done a lot of education of this old man about these kinds of issues, and -- and now -- and now more greatly appreciate it. I can assure you it was not willful or intentional in any way. And you know, going forward -- Yeah. Thanks.

CHAIR DELNEVO: Scout?

DR. SCOUT: Was there any analysis done of the demographics of the path population to understand how that compared with the predominantly white male, thirty-six-year-old study population?

MS. TASHAKKORI: We did not do that. I don't believe the Applicant did either. So no, unfortunately, we did not.

CHAIR DELNEVO: Lucy?

DR. POPOVA: The epidemiological

studies showing lower risk of snus all compare and non-users are never cigarette users -- never cigarette smokers, with cigarette smokers. Could you remind me if there have been studies where they look at people who switched, and how the risks among those who switched compared to people who are cigarette users? And also -- because I feel like the claim talks about switching and the benefits of this, but the epidemiological study only looks at never smokers -- snus users versus smokers, but it might be a little.

MS. TASHAKKORI: Yeah. So, among the studies that were looked at, we didn't identify anything that pertained to switching in that aspect. So, no.

CHAIR DELNEVO: Olivia?

DR. WACKOWSKI: I know the claim was authorized in October 2019. The baseline study was conducted on July 2020. Do you know if the claims were running at that baseline time?

MS. TASHAKKORI: Yes. They were.

CHAIR DELNEVO: Annette?

DR. KAUFMAN: Yes. Thank you for your presentations. I have two questions. One, a more clarifying question. How many of the snus exclusive users at baseline began smoking?

MS. TASHAKKORI: I don't have that off the top of my head, but I can get back to you.

DR. KAUFMAN: Okay.

And then my second question is sort of related to those epi analyses related to the attrition of the study. Were there any considerations for multiple imputation, or assumptions that users at wave one continue to -- to use throughout all of the waves to provide estimates to that effect?

MS. TASHAKKORI: I do not believe there were.

DR. KAUFMAN: Thank you.

CHAIR DELNEVO: Lisa?

DR. POSTOW: Yeah. So, the -- the

differences in cardiovascular mortality and stroke mortality were not as big as other diseases that are in the modified risk claim. I'm wondering if there's any literature out there about user understanding of those sorts of health claims and being able to sort of parse the nuance of those kinds of things.

DR. VENRICK: So you mean understanding in terms of like, not as much reduced risk for heart diseases compared to other --

DR. POSTOW: Well, so, I'm just not sure that a -- a member of the general population would see less risk for cardiovascular disease or cardiovascular mortality, and think that that claim includes a -- a significant risk, but less risk. I'm just wondering how much understanding there is of -- of those differences.

DR. VENRICK: So, I don't think, off the top of my head, in -- in the Applicant's study, I don't think that they looked at

whether there was maybe a reduced risk, but still remaining some risk, right? I mean, we can compare that using the relative risk item that they asked about cigarettes relative to using snus.

We did look some at comparing the absolute risk perception items for like, dual using General Snus with cigarettes, using General Snus alone. And so those can provide some evidence of like if they have perceptions that there's still risk, but lower than cigarettes. So, I don't think I can give a like full sum response to your question. But, we have looked at the evidence that is out there. And from the Applicant's study, we just have the absolute risk perceptions for various use patterns.

CHAIR DELNEVO: So, I have one clarifying question, and if I missed this, I apologize, but did FDA evaluate if the eight products changed at all over -- over time?

DR. VENRICK: We did not.

DR. APELBERG: Let -- Let me just add that there isn't any evidence that the products changed. Yeah. We -- That would result in it being a new tobacco product.

CHAIR DELNEVO: Thanks, Ben.

Lucy?

DR. POPOVA: Just a quick clarifying question. You didn't measure any diseases -- perceptions of risk of diseases that were not on the claim like, gum disease or something else where that might have been this halo effect?

DR. VENRICK: Correct.

(Pause.)

CHAIR DELNEVO: Last chance for clarifying questions.

(No response.)

CHAIR DELNEVO: Okay. So, now we're going to move into the open public hearing. I will first read the open public hearing statement, and then we will proceed with the individuals that have signed up to speak.

So, welcome to the open public hearing session. Please note that 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 relationships that you may have with the sponsor, its products, and if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging, or other expenses in connection with your attendance at this meeting. Likewise, FDA encourages you, at the beginning of your statement, to advise the committee if you do not have such financial

relationships.

If you choose not to address this issue of financial relationship at the beginning of your statement, it will not preclude you from speaking.

And with that, I'd like to invite our first -- first open public hearing speaker, Tim Andrews.

MR. ANDREWS: Thank you very much for the opportunity to speak. Can you hear me?

CHAIR DELNEVO: Yes, we can.

MR. ANDREWS: Thank you. So, my name is Tim Andrews, and I'm here presenting on behalf of Americans for Tax Reform, a non -- a nonprofit group that advocates on behalf of consumers and taxpayers.

Our interest in this is on behalf of both consumers, where we believe consumers should have the right to access accurate information to make the choice to quit smoking through reduced risk products. And secondly, for taxpayers, where our interest is in the

cost burden that'll be saved on taxpayers through transitioning people from cigarette combustibles to a reduced risk product. So, those two reasons are why we are interested in this issue.

And we strongly support the application for the renewal of the MRTP. And we do this for a number of reasons. First of all, there seems to be a very clear scientific consensus, which isn't in dispute, that these are reduced risk products. These are products that there are decades of information and scientific literature about. No new information has come in the last couple of years, which would change the situation. All the post reporting by the Applicant has met with FDA requirements. So, for purely for the protection of public health perspective, the APPH standard is met, because it is very, very clear the scientific literature isn't in doubt that it will reduce tobacco related mortality and morbidity.

So, I want to speak more about that, but rather I would urge the committee to concentrate on several things in that consideration. The first is to not only look at population level data in the United States, but also look at the research that we have seen from abroad regarding this. Particularly from Sweden, where the use of snus is responsible for essentially leading to keep the below five percent population -- population level smoking rates, which make it essentially, a smoke free country, the first in the western world or the developed world, rather, that will achieve this.

As a result, we have seen in Sweden, the fact that it has some of the lowest cardiovascular, lung, and public illnesses directly attributed to public policy helping transition people through snus.

Now the question has arisen in previous discussions as to perhaps declining sales, whether this has been a halo effect from

other products or not. We would instead counteract this by saying that perhaps if there are problems with the MRTP process, and accurate information are not being given to consumers, although the consumers who purchase the product, similarly are very, very clearly aware -- We've seen this in a previous presentation.

But for people who aren't aware, that that is where a question must be addressed. Whether this be through the promotion and greater information from FDA about the benefits of MRTP and compelling misinformation. Whether this be about changing the pathway to make other products less expensive for MRTP approval. It does not, however, negate the argument for renewal of the general snus MRTP application.

The question before the committee in this session -- and I think a great conversation learned about how can we better increase understanding. But the question here

is, is the APPH standard met? And I think that the answer is yes. Is there a problem with spillover effects such as usage? The answer is very, very clearly not. Is this something that meets the statutory and regulatory requirements for renewal? Have all -- Yes. Have all the postings been completed? Yes.

So, we would once again strongly support this renewal, and our only efficient means with the taxpayer, consumers, the government, and public health. And we would only ask the committee to look at additional information as to the high level -- the population level success that snus products have achieved in other countries, and how great it is at increasing public awareness through MRTP and other processes will leads to public health benefits.

At that, I think, I will end my presentation, unless there are any further questions

CHAIR DELNEVO: Thank you.

I'd like to call Lindsay Stroud next.

(Pause.)

DR. SCOUT: Were people supposed to disclose tobacco industry funding before speaking or not?

CHAIR DELNEVO: Encouraged to do so.

DR. SCOUT: Encouraged. Okay, thank you.

CHAIR DELNEVO: I'm calling again Lindsey Stroud, next presentation.

(No response.)

CHAIR DELNEVO: Alex Clark?

(No response.)

CHAIR DELNEVO: Pete Sepp?

MS. STROUD: Oh. I'm here. Sorry, can you hear me?

CHAIR DELNEVO: Is this Lindsey?

MS. STROUD: This is Lindsey. Yes.

CHAIR DELNEVO: Okay. Go ahead.

MS. STROUD: Okay. Hi, Chairwoman, members of the U.S. Food and Drug

Administration Tobacco Product Scientific Advisory Committee. Thank you for your time today. My name is Lindsey Stroud. I'm a senior fellow at the Taxpayers Protection Alliance, or TPA.

Regarding our financial ties to Swedish Match, that is above my pay grade. I just kind of do the numbers on tobacco and vape.

TPA has long advocated for adult access to less harmful alternative to cigarettes. And we believe that the FDA's modified risk tobacco product application, or MRTP, is essential for acceleration of tobacco harm reduction in America. Yet it is inflamed by regulatory constraints inherently FDA entire tobacco product application process, specifically products that must undergo the premarket tobacco product application, or PMTA.

Swedish Match's portioned snus products were the first ever products be granted the marketing orders for the PMTA

process, the PMTA process itself requires that a product must be, quote, appropriate for the protection of the public health. In issuing Swedish Match's order, the FDA determined that the PMTA application demonstrated that the new tobacco products would, quote, result in a low likelihood of new initiation, delayed cessation, or relapses. FDA also declared the Swedish Match new products would, quote, likely provide less toxic options if current adult smokeless tobacco users use them exclusively.

As emphasized that order, the PMK did not permit the manufacturer to advertise their product as reduced risk, even though the order itself found the product to be less toxic. Swedish Match did submit an MRTP application in 2014. In submitting the MRTP, the manufacturer submitted more than a hundred thousand pages of evidence, including governmental cohort studies and clinical trial results. The FDA would issue MRTP orders for eight Swedish Match products in 2019, four

years after issuing a PMK order for their products, and five years after first applying for MRTP status.

One important tools to look at is the FDA tobacco regulations post market surveillance, including data provided by the manufacturer, and governmental surveys on use in adult tobacco product use. In recent years, when deciding applications for other tobacco products using the TMCA, the FDA has repeatedly stated that youth use for certain products outweighed the benefits for adults.

This is not the case of Swedish Match products or snus products. In fact, new use of snus products is at record lows. The Monitoring the Future, a study conducted annually by the University of Michigan, has been tracking snus use among US youth in eighth, tenth, and twelfth grade since 2012. That year, 5.7 percent of US youth have reported past or current use of snus.

In 2023, only 1.1 percent of US

students had used the snus product in the past year. This was a 30.6 percent decline from the previous year, as well as a whopping 80.2 percent decline from 2012.

But there are still constraints in the regulatory process of bringing safer products to market, and it begins first with authorizing the product. Swedish Match was prohibited from relaying FDA findings of reduced rates and the PMT order and required to submit additional application. Such processes are redundant and a waste of FDA Tobacco Center funding, all of which comes from tobacco product user base.

These processes also help to add to the growing misinformation epidemic among the public and healthcare professionals about the role of nicotine in smoking related harm. A 2018 study examining a government health information survey of American adults found that 53 percent believe that nicotine is what caused most of the cancer related to smoking.

A 2022 study, three years after Swedish Match's MRTP orders were given to them, an estimated 61.2 percent of adults who smoke believe that nicotine causes cancer.

A 2020 records lead survey of more than 1,000 physicians determined that 80 percent of respondents believe it is nicotine that directly causes cancer. A 2023 global survey of more than 15,000 doctors found that 74 percent of participants incorrectly believed nicotine caused a range of illnesses, from cancer to COPD -- COPD.

The MRTP process can help rectify this, but only as the FDA accelerates the authorization of more products to the PMTA pathway and permit it in their marketing as reduced risks.

To date, only 16 products have received MRTP orders, 15 of which -- which went through the PMTA pathway. Half of those 16 MRTP orders are for products we are discussing today. It is wholly inefficient to adequately

meet the needs of the tens of millions of US adults who still smoke and are unaware of safer alternatives.

In conclusion, Swedish Match's experience of snus highlights challenges and potential benefits of FDA tobacco product regulatory pathways, despite extensive evidence -- despite extensive evidence on snus's health effects, Swedish Match struggled to communicate reduced risk to right -- due to regulatory constraints. Further, the FDA's public education efforts and the risk continuum of tobacco products has been insufficient, causing confusion about nicotine's role in harm reduction. The FDA must balance rigorous oversight with practical measures to facilitate informed decision making among US consumers and reform the entire process for new safer products to market, as well as to inform consumers under reduced risk.

Again, thank you for your time today.

CHAIR DELNEVO: Thank you.

Pete Sepp?

DR. SCOUT: May I ask another question? I just didn't hear the organization that she was representing or they were representing.

CHAIR DELNEVO: Lindsey, can you restate your organization?

MS. STROUD: Yes. Taxpayers Protection Alliance.

CHAIR DELNEVO: Thank you.

DR. SCOUT: Thank you.

CHAIR DELNEVO: Next up is Pete Sepp.

MR. SEPP: Members of the committee, you honor me with your time today. I am here on behalf of National Taxpayers Union.

Prior to this hearing announcement, I was wholly unfamiliar with Swedish Match or its snus product. We're not here frankly to profess a scientific expertise in snus or any other combustible tobacco alternative. Rather,

we're interested in discussing, as was stated in your meeting announcement, program developments related to the conceptualization of consumer understanding, because consumer understanding is rooted, I think, and our organization believes, in taxpayer issues, and the understanding of taxpayers about what's happening here.

We've commented a great deal on PMTA, MRTP, other issues. I'd refer you to our written submission that we provided several days ago for more details on that. Let me confine my remarks today in the brief time we have to the taxpayer issue and how that's connected to consumer understanding.

We believe that taxpayer funded public health programs could fiscally benefit over the longer term by more products entering the market more quickly, and the overall net fiscal picture, and the economic picture to consumers becomes clearer as a result. You know the research. You've seen that there are

large effects that smoking exerts on the costs of Medicare, Medicaid, other government funded health programs.

The net fiscal impact is somewhat less clear, when you take into account non health programs. For example, longer lifespans, and their impact on government retirement programs. How they offset each other has been constant question among economic and scientific researchers.

I would contend that one of the reasons we need to have a more smoothly functioning product approval process in getting these products to market is that, the market itself can help to supplement some of TPSAC's very, very good work in scientifically researching the effects of these products. If you have these products to market more quickly, and in greater abundance, consumer preferences, and their understanding of the products, will help to provide valuable feedback as to what might be working with smoking cessation.

Once you do that, you can also bring in some of the other developments that are occurring throughout the healthcare sector. For example, the introduction of new pharmaceutical products that help to reduce comorbidities of smoking. We need to have a greater understanding of the net fiscal equation, not only in terms of revenues from smoking, revenues from people staying in the workforce, losses to health care programs from smoking, but also these potential new developments in health care that are going to affect the bottom line for taxpayers a great deal. You have a role in facilitating that kind of information.

Second comment I would like to make as the application process in general needs greater certainty, transparency, and alacrity to encourage the development of an investment in new products. Not a surprise, many of the witnesses here will say that. But how do we do it? There are four recommendations that were

made by the Reagan-Udall Foundation for the FDA in December 2022. All of them tied to greater collaboration and transparency with all of the stakeholders involved in this process, development of a strategic plan, a greater role in this committee in policymaking, hiring authorities, new fee authorities, and reforms. But all of those things, begin with better collaboration.

How do we do that, with all of the stakeholders involved? In our experience with other agency transformations, you can do several things here. You could adapt the job aid concept. That's under tax guidance right now. A collaborative process between regulators and the regulated to help understand each other's positions and concerns. That's adaptable for proceedings like these.

You could create an ombudsman or an advocate for individuals involved in the MRTP or PMTA process. That's worked at the IRS. It's also worked at the Small Business

Administration in creating a climate of trust and problem solving.

You could also take a look at the regulatory sandbox concept. That has primarily been confined to financial services and technological innovations. But here again, that allows companies to test innovative products with regulators to basically try out theories of what works best in the regulatory space, a very productive shirtsleeve environment that I think, has been very helpful in those areas.

The third comment, participants in the process deserve value for the considerable regulatory costs and charges they have to bear in the process. That has a direct relationship to Reagan-Udall's recommendation on fee reform. We have found three principles that have to apply to fees. They've got to be proportionate to the cost and level of the service provided. They've got to be carefully managed, and safeguarded from attempts to divert them to

other programs. They have to be transparently managed, and subject to regular oversight.

Our written comments provide a number of examples of do's and don'ts from the EPA system, which has had a lot of problems to FDA's user fee agreements governing pharmaceuticals, which seems to work fairly well, but even better models, for example, air traffic control that's practiced in other countries.

All of these best practices can help to guide you and inform you going forward. And in doing so, you're going to make inroads toward consumer understanding, while at the same time, helping taxpayers to understand the costs and benefits of your own activities going forward.

It was a pleasure being able to chat this morning, and I'll be happy to answer any questions.

CHAIR DELNEVO: Thank you.

Alex Clark?

MR. CLARK: Hello. Just make sure the microphone is working.

CHAIR DELNEVO: You're good.

MR. CLARK: Okay, thank you. My name is Alex Clark. I'm the CEO of the Consumer Advocates for Smokefree Alternatives Association. CASAA is a 501(c)(4) nonprofit grassroots consumer advocacy group.

I'm happy to be here on behalf of our 300,000 members from all walks of life. By way of disclosure, CASAA does accept donations from industry. We have accepted a donation from PMI Global Services and their competitors. My salary, and those funds are all -- the use of those funds are decided by an all-volunteer board of directors to defend access to and maximize awareness -- awareness of safer alternatives to smoking.

First of all, I think we would like to align ourselves to some of the previous comments with regard to opening up the MRTP process, making it more accessible to other

companies. We need to see more of these products on the market. People who smoke certainly need to be made more aware of the safer alternatives that they have access to.

By way of sort of personal story, the region in which I live, north of the Adirondacks, the North Country of New York, when I go and search on Swedish Match's website, I see one retailer in my area that carries General Snus. And so, this is an area where it's a relatively low income. Smoking prevalence is higher than the rest of the state. Youth vaping is higher than the rest of the state. Higher than the national average. This is grizzly and pickup truck country.

And so, if there was a region of the state, of the country, that needed to see these modified risk statements, it is -- it is where I live. And I was actually struck by, you know, knowing, going into this, having spoken in support of Swedish Match's original, modified risk application, that the messages

would be so strictly limited to existing Swedish Match customers.

To see the walkthrough of just how many steps someone has to go through in order to see this message on Swedish Match's website, it makes it clear that more has to be done to reach a wider audience of people who smoke, and inform them of what the -- the their -- their options are in terms of low risk products.

So, I -- I may have skipped this at the beginning, but we are here to speak in support of renewing the modified risk orders, and looking forward to the discussion later this afternoon about ways that Swedish Match can sort of open up the promotion and reach a broader audience. And we think that -- that reaching an audience of people, not just people who smoke, or people who are currently using Swedish Match products, is important and consistent with FTAs recent commitment to realign perceptions of risks associated with nicotine.

This is not something that should be limited to just tobacco consumers. The general public needs to be made aware of this. A lot of the encouragement or advice that we receive when we transition from -- from smoking to a smoke free product comes from friends and family and neighbors. And so, it's, I think, to everybody's benefit that we have broad awareness of low risk products.

In addition to that, in conclusion, I think, we would like to encourage the FDA to do more to draw attention to the existence of modified risk tobacco products. Certainly, we don't expect the agency to endorse any particular brand or product. But now that these products are out there, and the messages have been authorized and reviewed, and according to what we're seeing from Swedish Match's post market surveillance materials, perceptions are going in the correct direction.

I think FDA can -- can absolutely do more in terms of educating the public about the

availability of product -- availability of these products, and the benefits of, for people who smoke to switch to them.

Thank you very much, and we look forward to this afternoon's discussion.

CHAIR DELNEVO: Thank you.

For folks participating virtually, we're asking that you please turn off your cameras, because the virtual participants are only audio. We do not see you here in the room.

So next up is Yael Ossowski.

MR. OSSOWSKI: Ossowski. Yes. Thank you.

So, my name is Yael Ossowski. I'm Deputy Director of the advocacy group Consumer Choice Center. We champion the benefits of freedom of choice, innovation, and abundance in everyday life. I think I have three main points. Options matter, science based policy matters, and more bountiful choices to consumers matter. We'd like to make healthier

choices.

I think the last time that I spoke at an FDA scientific advisory meeting, it was around May 2019, and it was around regulatory questions on cannabis and CBD products. And actually much of what I say today will be very similar. At the time, we had argued for clear labeling standards, sensible age restrictions, a process for actually having a marketing provable health or risk claims, and a diverse set of product types to reduce harm and to avoid combustible products. You can see that being very relevant today.

So the reduced risk class or modified risk classification that is considered for renewal today is something we obviously support. It's been well studied, explained, and explored, thanks to many of the presentations given earlier. And we -- we can see that we're very grateful to have that, particularly in this conversation and this great venue and form for doing so. I do thank a lot of those

presentations that we have heard from earlier today.

As someone who grew up in the South, you know the rural areas, there's a lot of more of chewing tobacco. There's a lot of spit bottles. I kind of saw that growing up. And I'm actually very delighted that we now have a -- a very mature market for a smokeless, safer product that does have demonstrated reduce risk. And we have that via snus. That's because of the innovative processes of entrepreneurs in Sweden, Scandinavia, and Europe, and elsewhere.

And I think that this process -- the MRT processes is an important a part of allowing that information to be shared, spread widely, and understood by consumers. The only things that we'll highlight is that this scientifically minded reduced risk protocol is really necessary. And, if we think particularly, when it comes to marketing, consumers need to have access to that

information.

We're inundated every day with social media. We're inundated every day with different news organizations, television, radio, and if we're able to get actually good scientifically based information, not only from our policymakers and bodies such as this, but whenever we buy certain products, and we know that they will actually be better for us, we think that is a great thing.

At the same time, we should be able to spread awareness about some of the other, less harmful nicotine alternate alternatives to combustible tobacco. Things like nicotine pouches, snus, like we're talking about today, gums, lozenges. I mean, there's all kinds of different innovation that's happening there. And we very much support that.

We'd love to see more approvals of these reduced risk products, more renewals of risk modification orders. I think this would be very beneficial -- beneficial for millions

of Americans, and certainly public health overall, not to mention the large cost savings we can have.

And we can already see from examples, such as Sweden, which has an exemption in the European Union to sell snus. They do have the lowest incidence of cancers related to this. I think this is something that is an important data point that will continue to repeat, because we are seeing the benefits, particularly for younger people who are in Sweden. They're not having to lose their fathers or their grandmothers at an older age because the products that they use are combustible tobacco. I think that in itself is very powerful testimony.

In closing, I just want to say again, this forum along with the input and all the experts who are testifying or people who gave presentations -- they are very important. They give a lot of dividends to consumers who can really benefit from that choice,

particularly of reduced risk products. So, we believe options matter, scientific based policy matters, and more bountiful choices. And it was true on products such as cannabis and CBD, and we hope the conversation continues to move on that front. And it also applies here in the case of snus. So, thank you very much.

CHAIR DELNEVO: Thank you.

Next up is Stan Glantz.

DR. GLANTZ: Hello. Can you hear me?

CHAIR DELNEVO: We can hear you, Stan.

DR. GLANTZ: Okay. Yeah, we've been having a little technical problems, but they just solved that one second ago.

So, my name is Stanton Glantz. I'm a retired professor of medicine at the University of California, San Francisco. And, I have no financial connections to the tobacco industry or any of the organizations it supports directly or indirectly.

I'm here to urge the committee to recommend against the FDA authorizing the renewal of the MRTP. I think that the app -- the application has not met the legal standard of demonstrating that, as actually used -- and the as actually use is very important -- the snus product is actually caught appropriate for the protection of public health and reducing harm.

The application does not really adequately deal with the issue of dual use. A sizeable fraction of snus users -- somewhere probably between a third and two thirds, depending on the survey that you look at, are dual users. And dual use actually increases the risks of a variety of diseases above smoking alone. That point is not treated at all in the application or in the risk model.

The second problem is that the -- the question which was used to assess perception or -- or, pardon me. The question that was used to assess whether or not people

Commented [HTS1]: I don't know what word that is supposed to be, but "caught" doesn't seem to make sense.

understand what switching completely means, was very poorly worded. It basically asked about using snus and cigarettes on the same day. Many dual users do not use the two products on the same day. They use them on some days. And the standard definitions which are used for dual use are use of the two -- either of the two products -- pardon me -- both of the two products within the past thirty days.

Another problem is that the survey itself is not a representative national sample. It was a convenient sample of customers. As the FDA mentioned, I -- I didn't hear the whole presentation, but there was very high attrition. And so, in order to really assess whether or not the product would -- will be appropriate for the protection of public health, the -- the analysis needs to be based on a representative sample.

And so those are reasons that I strongly urge the panel to recommend against renewing the MRTP.

I also urge the panel to specifically tell the FDA that they should not exercise enforcement discretion, and allow the company to continue making the current claim while they revised their application in an effort to deal with these problems. The tobacco companies have really been given a free pass with the exercise of enforcement discretion for years, while the FDA thinks about these applications.

Finally, I -- I'd just like to comment that the previous speakers all came from organizations that as far as I know have -- have collaborated with, and often have some kind of financial connection to, the tobacco industry. And none of them even mentioned that. And I think it's very important that TPSAC and the FDA carefully assess direct and indirect connections with the manufacturers when assessing the independence and objectivity of the statements that you've heard so far this morning.

So, thank you for your time.

CHAIR DELNEVO: Thank you.

Next up is Denny Henigan.

MR. HENIGAN: Thank you. My name is Dennis Henigan. I'm Vice President for Legal and Regulatory Affairs at the Campaign for Tobacco Free Kids. I have no financial connection whatsoever with the sponsor or the tobacco industry.

I want to thank FDA and TPSAC for this opportunity to speak with you today. I want to address an issue that is relevant not only to the Swedish Match renewal application, but to all modified risk applications. And that is the role of TPSAC itself in these proceedings. In an October 2020 letter to then CTP Director Zeller, my organization and five other public health organizations expressed the view that FDA had relegated TPSAC -- TPSAC to a role in modified risk proceedings that is inconsistent with the letter and spirit of the Tobacco Control Act. And I believe that

conclusion remains valid today.

I start with the text of the statute. It not only requires FDA to refer every modified risk application to TPSAC, but also provides that not later than sixty days after referral, TPSAC, quote, shall report its recommendation on the application to FDA. Now, the final decision to issue or deny a modified risk order certainly rests with FDA. But it seems clear from this statutory language that no modified risk application may be acted on by FDA without TPSAC making recommendations on whether to grant or deny the application, and on the scientific issues necessary to make that determination.

To date, TPSAC has held five meetings to consider modified risk applications. FDA has yet to ask TPSAC to make a recommendation on the disposition of any of these applications. It also appears that TPSAC's role has increasingly been marginalized, as reflected in the number of

scientific issues which have been subject to votes by the committee, as opposed to simply general discussion.

In TPSAC's first modified risk meeting in April of 2015, which concerned these very General Snus products, TPSAC took votes on ten scientific questions. In its next two modified risk meetings to consider the ICO system and Camel snus products, TPSAC vote -- TPSAC took votes on nine issues and eight issues, respectively. But, in the last two meetings, in February 2019 in February 2020, which addressed three different products, TPSAC voted on only one issue.

So, it's apparent that TPSAC's role has evolved from being asked by FDA to vote on key scientific issues to simply being a discussion forum on those issues. And I didn't see any votes on the agenda for today's meeting either.

Now, this is in stark contrast to the role of other FDA advisory committees,

which routinely vote on the ultimate regulatory issue of whether a product should be approved. Earlier this month, for example, an advisory committee voted to recommend approval of an Alzheimer's drug as safe and effective.

I realized that the role of FDA advisory committees, in general, is subject to debate has revealed in FDA’s listening session on this subject. But the particular role of TPSAC in modified risk proceedings should give due regard to considerations unique to tobacco regulation, including the mandatory statutory role of TPSAC and the history of public health harm from tobacco products marketed with claims of lower risks to health than other tobacco products.

Since taking over as CTP Director, Dr. King has repeatedly and appropriately made clear that FDA decision making is to be guided by the science. He reiterated that again today. The best way to make that happen in modified risk proceedings is to ensure that

CTP's independent scientific advisors are given the opportunity to clearly communicate their collective judgments on the science to FDA and to the public at large, and that has not been happening.

Thank you so much.

CHAIR DELNEVO: Next speaker is Guy Bentley.

MR. BENTLEY: Good morning, everyone. I'm trying to be as brief as possible. I know it's been a long morning and a long day. My name is Guy Bentley. I'm director of Consumer Freedom at the Reason Foundation. And if you'd like any information about the sources of where we're funded, we publish all funders who wish to disclose their funding to us in the end of year issue of Reason Magazine, which we also publish.

At Reason Foundation, we're committed to ensuring that smokers who wish to quit -- quit using cigarettes have access to the broadest possible range of reduced risk

products, and information that can help them make the best decision to improve their health. To be granted and MRTP, as we've heard, the applicant must show that products in question significantly reduce harm, and the risk of tobacco related disease to individual tobacco users, and the benefit -- and benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products.

Since the applicant was granted these MRTP status back in 2019, the underlining science and epidemiology have remained unchanged, demonstrating that snus is significantly safer than combustible cigarettes, and that smokers who switched to snus exclusively will improve their health. The claims also are authorized by FDA remain true today, and provide consumers with accurate and valuable information about the benefits of using snus instead of cigarettes.

Access to accurate information about the benefits of switching exclusively from cigarettes to snus benefits public health today, and continue to do so if this MRTP is renewed.

As the applicant has demonstrated, the overwhelming majority of General Snus users, both understand the claims being made in the MRTP, and accurately perceive the messages being communicated. A significant portion of users transition to exclusive General Snus use, and a larger proportion of dual users that we heard about earlier do significantly reduce their cigarette consumption, which is also similar for what we see for FDA approved smoking cessation products, such as nicotine replacement therapies.

Furthermore, since the MRTP was granted in 2019, we see no evidence of General Snus reaching unintended audiences, especially youth who do not use tobacco products.

Critics of the original application

in 2019 -- one specifically heard earlier, Professor Stanton Glantz -- specifically wrote and hypothesized that the granting of the original MRTP would increase positive perceptions of General Snus amongst tobacco naive youth, and therefore increase use amongst tobacco naive youth.

But this hypothesis has not been borne out in the real world, as the product has actually been used and marketed. There has been no significant increase in the overall snus market, as we heard earlier. And even the smokeless tobacco market as a whole, amongst adults, it has been relatively flat in terms of use. And in terms of youth use, current high school use of smokeless tobacco -- of all smokeless tobacco products, including snus, fell from 4.8 percent in 2019, when MRTP was granted to, 1.5 percent in 2023.

And snus users are likely to be an even smaller portion of this category, and among smokeless tobacco youth users, uses are -

- is exclusively confined to white and Hispanic males. That applicant's conservative use of the MRTP authorization is likely to have severely limited its positive impact on communicating with consumers. But still, we do see benefits to those currently using General Snus in terms of their perception of the relative risk of using General Snus. The FDA could work with the applicant to further develop effective communication in order to reach the population that would most benefit while limiting the reach, so as not to appeal to unintended audiences.

One of the CTPs goals, outlined in a strategic plan, is to educate adults who smoke about the relative risks of tobacco products. If this MRTP renewal is rejected, it will severely undermine CTP's goal and further impede efforts to reduce the burden of smoking related disease.

We urge the committee to consider the negative ramifications of denying this

renewal. The science of relative risk is clear and overwhelming. The MRT's -- MRTP's impact has been positive, if small, and no identifiable harms stemming from the original authorization exist. Therefore there is no reason why it should not be renewed.

If this suite of products can't gain the overwhelming support of TPSAC and the FDA, the utility and validity of the MRTP as a pathway to communicate accurate information about reduced risk products should be reconsidered.

Thank you so much for your time.

CHAIR DELNEVO: Thank you.

Pam Ling?

DR. LING: Hello. Good morning. Good morning. I'm Dr. Pam Ling. I'm Professor of Medicine at the University of California, San Francisco, and Director of the Center for Tobacco Control Research and -- and then from -- and Education, and principal investigator of the UCSF Peace Corps. I have no financial ties

to tobacco companies.

Thank you for the opportunity to highlight a few important points from our two public comments, demonstrating that FDA should not renew the MRTP order for General Snus.

First, Swedish Match did not demonstrate that General Snus, as used by consumers are appropriate for the protection of public health. This means Swedish Match needs to present scientific evidence that these products, as actually used by consumers, will benefit the health of the population as a whole, weighing any potential benefit to users who might switch from cigarettes to snus against the harms to non-users, including kids, who may initiate tobacco use with General Snus, or those using it with other tobacco products, such as cigarettes, e-cigarettes, or nicotine pouches.

Our January 2019 comments showed that the scientific study submitted by Swedish match in 2018 to support its initial MRTP

application, and which it also relies on to support this request for renewal, did not demonstrate that the modified risk claim was communicated properly or understood by consumers. The wording used in that study to test whether consumers understand the claim asked, for general snus to put you at lower risk of disease, how many cigarettes can you smoke on a day when you also use General Snus.

The wording of the question is problematic because it implies using General Snus on some days, while continuing to smoke on other days, is compatible with complete switching. Only between 37 and 56 percent of the participants selected the correct answer, which is zero cigarettes.

The General Snus patterns of use study that Swedish Match submitted in December 2023 did not address these deficiencies, and includes several other studies design flaws. The study relies on a non-representative convenient sample of a highly selective

population of General Snus purchasers that does not represent cigarette smokers in general. The study was further biased by poor rates of follow up, and eliminated many respondents for unclear reasons.

Even in the sample of enthusiastic snus users, 12 to 14 percent of respondents co-used General Snus with cigarettes. And dual use and perceptions of the safety of dual use was not addressed in the Swedish Match study.

Less important the Swedish Match study completely ignored the key question of whether the authorized MRTP claim caused any cigarette smokers to switch completely, and whether that switching was counterbalanced by dual use, less cessation, or snus uptake among non-smokers.

Dual use is even more important now Philip Morris International is co-marketing Swedish Match General Snus with its nicotine pouches, Zyn. For example, the General Snus webs -- website suggests you purchase from the

northerner.com website, where they are co marketed as companion products to use in different situations, stating if you're craving tobacco, use snus. If you need a nicotine kick while you're at work or in school or in transit, use Zyn pouches.

Because PMI co markets General Snus products with Zyn, consumers are likely to be confused and believe that then is authorized to be sold in the US, despite the fact that FDA has not granted ZYN PMTK -- PMTA or MRTP authorization. Both Zyn and General Snus come in mint flavors that are popular with kids, facilitating further interchanging mint snus for mint Zyn.

In summary, continued marketing of General Snus with MRTP claims is not appropriate for the protection of public health. FDA should deny Swedish Match's renewal application, because one, Swedish Match did not demonstrate consumers understand they must use General Snus exclusively instead of

cigarettes to get their purported health benefits.

Two, the consumer perception studies Swedish Match relied on for both its initial MRTP application and the current renewal application were flawed. Three, Swedish Match presented no support for the claim that among the general population, existing adult users of tobacco products will switch completely to General Snus. Four, Swedish match studies did not address co use of snus with other tobacco products. And finally, Swedish Match's co marketing of General Snus with Zyn pouches is problematic and raises questions of public health, especially for youth.

Thanks very much for your attention.

CHAIR DELNEVO: Thanks, Pam.

Bonnie Halpern-Felsher?

DR. HALPERN-FELSHER: Hello, members of the committee. My name is Dr. Bonnie Halpern-Felsher, and I'm a Professor of Pediatrics at Stanford University. I'm a

developmental psychologist with -- with additional training in adolescent and young adult health. I have over 30 years of experience researching why youth use tobacco, with a focus on risk perception, decision making, product standards, and marketing, as well as tobacco prevention and education. I have no ties to tobacco companies.

The FDA should not renew the modified risk granted order for the eight Swedish -- Swedish Match General Snus modified risk tobacco product application for General Snus products, because as actually used by consumers, these products will not benefit the health of the population as a whole, which is the standard to be met here.

Swedish Match's July 17, 2023 MRTP renewal request relies, in part, on its argument that General Snus products are still not appealing to youth, claiming that marketing General Snus with the authorized MRTP claims that benefit to the population as a whole,

considering non users, such as kids, as well as users. However, these assertions have not been justified. They're not accurate.

In fact, the 2023 National Youth Tobacco Survey data showed that 800,000 middle and high school students have ever used smokeless tobacco products with 330 current defined as past thirty-day users. So, while smokeless tobacco use is certainly less popular than cigarettes, or e-cigarette use among teens, it's still happening. We still see young people using smokeless tobacco. And our own data even show that such use is increasing.

The National Youth Tobacco Survey data confirmed that dual use of smokeless tobacco along with other tobacco products is a significant problem, especially among kids. As such, smokeless tobacco use among teens is still something we, and the FDA, should in fact still worry about.

In its July 2023 renewal request letter, Swedish Match uses FDA's March 2023

authorization of the US smokeless tobacco companies, Copenhagen Classic Snuff, as a modified risk tobacco product as support for the authorization of General Snus as a modified risk product. However, they fail to mention, such as our own research published in the Journal of Adolescent Health in September 2023, showing that exposure to the Copenhagen Snuff MRTP claim actually increases interest in moist snuff among adolescents.

Specifically in our study, we showed that for California adolescents, they were randomized to view a Copenhagen Snuff image with or without the MRTP reduced risk claims. We found that adolescents exposed to the MRTP plan were less likely to perceive smokeless tobacco to cause, quote, a lot of harm. This will show that among adolescents who are past thirty day users have at least one nicotine product, which was put on the e-cigarettes, viewed the MRTP claim actually increased their willingness to try moist snuff.

These findings suggest that smokeless tobacco MRTP claims increased interest in using smokeless tobacco use among -- excuse me -- increased their interest in using smokeless tobacco for youth. And increased susceptibility to smokeless tobacco use among youth is likely to harm public health, especially since Swedish Match provided no evidence of MRTP claims increased the interest in switching the smokeless tobacco among adult users.

Swedish Match's MRTP request letter states that evidence annually submitted by the company since 2015 continue to demonstrate that there's no significant youth initiation of General Snus. However, that evidence has been redacted from the renewal request.

Further, Swedish Match contends that they provided evidence demonstrating correct consumer perception of the risks. However, the purported evidence from the post market studies annual -- annual reporting is also heavily

redacted.

As I published on before, while we do not believe that the tobacco industry should be allowed to enroll youth in their studies, I, along with other scientists from People for Tobacco Free Kids, we published a study in 2020 saying that there are safe and effective ways in which the FDA can conduct their own research or find others to do so to really look at the MRTP or PMT process with youth in its decision making.

So, in summary, it's really important to note -- to note that smokeless tobacco, and --

Oh. The other issue is co-marketing, as others have said, that we're very concerned that General Snus is also being co marketed with Zyn, as well. And that when things are co marketed, youth think that both are authorized and both are safe.

So in summary, FDA should not renew the Swedish Match MRTP order, because smokeless

tobacco and dual use of smokeless tobacco with other products is still popular among youth. Our own research mentioned today, as most other studies show, that teens exposed to MRTP claims for smokeless tobacco products actually increases their use -- their interest in using those products. There's evidence -- There's no evidence that youth correctly perceive or understand the risks associated with these products.

And finally, co-marketing mint flavor General Snus with mint and other flavored Zyn also presents a serious public health issue. We are very worried about the flavors as well.

Thank you very much.

CHAIR DELNEVO: Thank you.

Our last open public hearing speaker will be Diana Zukerman.

DR. ZUKERMAN: Thank you. Can you hear me?

CHAIR DELNEVO: We can.

DR. ZUKERMAN: Thank you so much. I'm Dr. Diana Zukerman, president of the National Center for Health Research. Our center is a nonprofit public health think tank that scrutinizes the safety and effectiveness of medical and consumer products, and we do not accept funding from companies that make those products. Our largest program focuses on cancer prevention and treatment.

Thank you for the opportunity to share my views today. My expertise is based on my current work, as well as my postdoctoral training in epidemiology and public health, and as a former faculty member and researcher at Yale and Harvard. I've also previously served as professional staff in the US House of Representatives and US Senate, and at the Department of Health and Human Services. And I'm a founding board member of the nonprofit Alliance for a Stronger FDA, which educates Congress about the need to financially support the essential work of the FDA.

The question today is whether General Snus should continue to be labeled as safer than other tobacco products. I will focus on the scientific evidence, which I personally found challenging due to lack of some key information. So, I will raise the questions that were not a focus of the FDA review. And I respectfully encourage you to try to get the answers to those questions today.

I'm glad to see that panel members and previous speakers have asked some of these questions already.

We all know that the risk of smoking include cancer, lung disease, and cardiovascular diseases, but equally important, most smokers start smoking as children or teenagers. And most of these diseases are diagnosed decades later, usually when the individuals are in their fifties or sixties, or even later. And so, that's more than 30 years later, often 40 or 50 years later, sometimes

even later than that.

And in contrast, the data being discussed today found, number one, a significant increase in serious -- several serious cardiovascular diseases. And these were diagnosed in studies that followed relatively young, white, men. For example, there Araji study, published in 2022, included nine million person years of study, which sounds very impressive, but it averaged 22 years of follow up. And that included some individuals that were followed for only five years. And that really messes up the data.

So those results indicate that some serious risks that are evident, are apparently evident at a younger age than are found with cigarettes.

Number two. There was no increase found in oral cancers, despite previous evidence that smokeless tobacco causes oral cancers. However, oral cancers usually develop in people over their fifties or older, and many

of the individuals in these studies are considerably younger than that.

So, my question is, whether the follow up for these individuals in any of these studies is long enough to draw conclusions about oral cancer. In addition, the information provided in previous research indicates that snus in Sweden differs from the snus that's sold in the United States. And of course, the people are also different and have other different health habits. And therefore the data provided on Swedish consumers may differ from the impact on US consumers. And I hope you will ask that question.

The bottom line is, how good is the evidence that using the General Snus sold in the United States is safer than smoking cigarettes in either the shorter term, meaning about 10 to 20 years, or the longer term, which could be 30, 40, or even 50 years.

Number two, how often do General Snus users also use other tobacco products or

switch to other tobacco products? Apparently, the answer is, they often do. So does the nicotine in General Snus make it more difficult to quit tobacco use, and instead results in continued use of snus and other tobacco products?

And last, can the information available be understood by teenagers or adults who consider using snus, if it has a modified risk claim, since that would be perceived as a seal of approval by the FDA.

All I can say is, I had trouble understanding it. I had trouble drawing conclusions, because there are so many unanswered questions.

Thank you very much for the opportunity to speak today.

CHAIR DELNEVO: Thank you.

(Pause.)

CHAIR DELNEVO: So, we're actually going to break now for lunch, but we are going to reconvene at 1:15, not 1:30, so that we have

sufficient time for discussion.

(Whereupon, the above-entitled matter went off the record at 12:26 p.m. and resumed at 1:21 p.m.)

CHAIR DELNEVO: Welcome back, everybody, from the lunch break. I want to orient folks as to what we're going to be doing. For the next hour or so, we're going to be facilitating discussion amongst the TPSAC members looking at questions 1 and 2 posed to us by FDA CTP.

We're going to try to shoot for dividing our time roughly up into thirds where we're going to focus on question 1 first, then question 2, and then we'll wrap up the discussion by having everyone at the table with the exception of FDA, making their own final comment about the Swedish Match MRTP renewal application. Then we'll have a break and then we'll have another presentation from FDA that's not specific to Swedish Match and then we'll have additional discussion after that.

And so, with that, if we can pull up the first question. So, question 1, FDA reviewed the literature and the Applicant's data and conducted internal analyses of the Applicant's data to describe characteristics of people who use snus. Patterns of tobacco use among people who use General Snus, and transitions from combustible cigarette smoking to exclusive use of General Snus. And so we're going to discuss the use behaviors of these modified risk tobacco products and any implications they might have. We will try our best to call on you in the order that people raise their hands. And so if anyone would like to start. Scout?

DR. SCOUT: All right. First of all, I guess I'd like to go on the record saying that I'm disappointed in one aspect of this meeting and that's the fact that we are being given "evidence" of a scientific meeting that honestly wouldn't pass the standards of any publication or training that we get at a

professional organization, because I just spent a lot of time during the beginning of the meeting trying to understand how many of the people for the public comments out of the 25 we were given in advance were actually connected to the tobacco industry. And as I can understand, only two out of the 25 public comments clearly had no connection with the tobacco industry. And everybody who did not claim they had a connection, we have a long history of the tobacco industry hiding their connections with these organizations.

And then we even have, you know, the number of people who spoke publicly who did fund things like, you know, Reason Foundation, saying that I had to look at their magazine in order to find out that they have $14 million in tobacco industry contributions just in the last year, which is more work for us. And other people just saying that it's above their paygrade whether or not they're paid by the tobacco industry.

So I would just like to say that I think we really want this to be a scientific meeting and we want it to be accessible to people. We have a problem right now. We talk about the regulatory barriers that the industry is facing. I also think we have a problem that the public health industry is facing in even being able to respond appropriately to these things and suss out who's actually representing commercial interests and thus giving us a sales pitch versus who is actually representing an independent interest and is not funded to have an opinion one way or the other.

So not only am I concerned about how hard it is to decipher that as someone representing the general public here, but also it's a concern that only two of the 25 comments in advance appeared to not be represented by industry. So I would like to really ask FDA if we can have a better process for disclosing how much of the information presented to the Scientific Advisory Committee is sales

information and has a significant conflict of interest and thus would not be allowable in any CE or CME presentation or any publication without that being disclosed.

And the optional part of it -- of the disclosure is something that clearly people are not taking advantage of. The only people who are, are the ones who don't have conflicts. So that's just a point I want to point out in advance. I think we've got some real barriers to the community that does not have a conflict of interest in being able to navigate this process, put in comments related to it, and decipher whether there are conflicts of interest on the existing comments.

With that said, as far as I can understand, if we are listening to the people who do not have conflicts of interest, out of the five people that I could discern did not have conflicts of interest, four of them were clearly very much against this proposal. The fifth was very clearly pointing out that there

were enough gaps in the data that, that was a position that was such a situation that they could not take a position because of the significance of the gaps in the data. And I would -- So we seem to have near uniformity from the nonconflicted points of interest on what the decision should be here. And I encourage us to take that into account as a scientific body.

If I look at the actual data, the strength of the data and the research, I would have to say that I'm also not sure if we could pass any kind of an NIH standard to get this funded if we had presented similar data to NIH about a project that we were interested in. Because if you first talk about the fact that is a convenient sample, that there was no effort made to even compare it with a full probability sample we had to even match the demographics from PATH to adjust or provide weighting to the convenience respondents so they more accurately represented the real

population being connected -- being affected by this issue. That, that's a significant challenge in the data.

The fact that we have such a high rate of attrition is also a significant challenge in the convenience sample. I'm particularly concerned that we have a high rate of attrition in the youth population, which we are particularly concerned about. And also with low SES. The idea that by wave four, we had -- it was predominately higher SES people, which to my understanding of smokeless tobacco and snus use is very discordant with the general population using snus, makes me very suspicious of the wave four information. And then you add in the fact that this -- what's being asked for is a continuation of this warning is again applying only to people who are solely using snus and had zero levels of, you know, combustible cigarette use. And by what I see from the data, that's only a quarter of the population that are using snus right

now.

So as I understand, we're currently being asked to continue warning a quarter of the population about something that's relevant to them. And then putting out a warning that is not relevant to the other three quarters of the population that snus is approaching, which also again makes it a concern. You add in the fact that we have from industry documents that it's not appealing to youth. There's no evidence thereof, things like that. And then you have from the nonconflicted presenters, information like we have a substantive increase in the number of youth between 2022 and 2023 on the National Youth Tobacco Survey reporting using snus use. And from one of our presenters talking about the fact that, that's 330,000 youth using snus right now, that appears to directly contradict the information given by the industry related to appealing to youth.

And then you also talk about the fact that while there is snus declines, in a

lot of the data presented, we also see from PATH data that there's snus increase -- snus use increase instead. So you add all of these things together and I cannot exactly see where we find substantive information to support the continuation of this warning, which would only again even apply to a quarter of the users and not actually apply to three quarters of the users.

CHAIR DELNEVO: Dona.

DR. UPSON: Thank you. Yeah and I echo Scout's concerns. As an associate editor for the American Thoracic Society, the studies would not be published. They wouldn't even be, you know, accepted to go out to reviewers. And so I have a lot of concerns about the data that we're looking at. And I'm wondering if there's some way for FDA to sponsor good studies that will answer the questions that we're interested in? Thank you.

CHAIR DELNEVO: Lucy.

DR. POPOVA: Let me step back and

kind of lay out a little bit of framework for which we can look at this. I was trying to understand what are the criteria for renewal? And in different places -- and what the study was supposed to do, and in different places, it's listed differently. So I went back and there's the -- in the presentation earlier, they talked about the draft guidance to the industry, which was never finalized.

I went back to the Tobacco Control Act itself. And in the Act, it states that the applicant, once they receive the order, they need to determine the impact of the order issuance of the order in the MRTP claim on consumer perception, behavior, and health. So this is the mandated thing where it's like you need to assess the impact the MRTP claim has on consumer behavior including uptake, dual use, and complete switch.

Instead the study -- and in the study documents again, some of which were really heavily redacted and I feel like as

members of TPSAC, we should have received them as early as they were submitted and nonredacted because we need to see those original tables. And none of the data were there except in big summaries -- which then were summarized as like making claims that the data couldn't support.

But the study objectives for like how do general snus users use tobacco and nicotine products? This is very different from what impact does the order have on behavior. So in that sense, I think it would be good to have -- for the FDA to clearly specify what are the criteria based on which we will evaluate the evidence. Right now the study basically, it's been presented as we are showing the evidence of absence of negative effect and evidence of a good effect, which is not the case. What we're seeing is absence of evidence.

CHAIR DELNEVO: So I do want to say -- take a moment and jump in myself with my own comment about this. And so I do think that --

and I'm hearing other folks say it as well -- the post-market surveillance study, there was quite a bit of disappointment in the execution of the post-market surveillance study. As a survey methodologist myself, I was disappointed to see how that was executed.

That being said, I do want to remind folks that, that post-market surveillance study plan was signed off on FDA. And so there might be recommendations that come out of here about strengthening the quality of post-market surveillance studies. And I think that, that's an important thing for us to remember is that this was also a plan that was signed off on. And that there are some answers we're not seeing is a function of the way that those -- that study was designed. And that there's shared responsibility in the sign-off of that particular post-market surveillance study.

DR. LEVENTHAL: I agree with Dona's suggestion that it seems worthwhile in order to kind of make the determine of APPH to do

additional analyses of a data set that might be able to more rigorously answer the question. And so the U.S. PATH study with now seven waves would provide a sufficient data source in order to in detail look at transitions and snus use and subsequent transitions and use of other tobacco products. And what would be of interest is cessation of combusted tobacco products, dual use, escalation, or declines in the frequency of tobacco use overall. And then also as a comparator, another product that is non-combusted. What are the switching rates for that product to provide a gauge overall of the impact?

And then relatedly, one thing that hasn't come up yet is use in the young adult population. And it would be useful to look in the most recent wave of PATH about that use. According to the data that I'm aware of, the last published analysis of PATH, or one of, I guess the few, 10 percent of young adults age 18 to 24 had ever used snus back in 2013/2014.

So looking at those estimates currently would be of use to the decision.

And then finally in just thinking about youth uptake, I think the presentations today focused on current use, which was low -- less than 1 percent, I believe, of snus use. But current use may not be the most sensitive indicator of risk of uptake of regular and potentially harmful tobacco product use patterns given that teens, you know, may have a slow escalation that crosses years. And so of note, I think the most recent NYTS reported that there was 3 percent smokeless tobacco ever use in their sample of high school and middle school students. But I don't believe the snus category was taken apart. So that seems like an additional analyses that could be done to address the question as to whether impact on switching versus impact on youth uptake and potential other beneficial or harmful consequences like dual use.

CHAIR DELNEVO: Dona.

DR. UPSON: Thanks. Just a follow-up to that. Is this something that CDC could do as part of their NMWR reports?

CHAIR DELNEVO: Ben is raising his hand with response or an answer or clarification.

DR. APELBERG: Yeah. I just did want to chime in. In the FDA Backgrounder, we do have estimates of snus use among adults and among kids from the PATH study and from NYTS. But keep in mind, that's the whole category of snus products. We're talking about specific -- eight specific products that have been authorized with MRTP. So I think it's really important to -- you know, as you guys are deliberating, to think about one, I'll say, it would be very helpful for us to hear from you all about recommendations for the ways to -- you know, better ways to design post-market surveillance and studies, but I think we have to be really cognizant of the fact that we're talking about a very small number of users.

Right?

I'm not sure it's really feasible to do a probability-based sample to like discover the few thousand users that exist out there. So I think to FDA, it was pretty logical to kind of recruit at the point of purchase. I mean I get that, that presents some challenges in interpretation and we'd really just love to hear your perspective on what, you know, this evidence that's been presented can tell us or can't tell us, I think getting us into the initial discussion. But I do think that's kind of just an important part of this to consider. You know, and so like for example, as large as the PATH study is, it's not really designed in a way to be able to estimate the impact of, you know, a particular -- a few particular sub-brands of a product that's not widely used.

Also note that the -- you know, that number 300,000 was mentioned, but I'm pretty sure that was referring to smokeless tobacco product use as a category, not snus as a

subcategory. So we do have those estimates in the -- in the background. I'll also just note that the APPH standard is actually the standard for the pre-market tobacco product application, appropriate for the protection of public health. The standard for authorization of a risk modification order is -- it also talks about population health, but it's the -- you know, it's that language around significantly reducing the harm to individuals, as well as benefitting the population as a whole. There's still both population health standards, but I just wanted to clarify that.

I'll just say that, yeah, it just would be really helpful for us to hear, you know, you all's perspective on like well, what do you feel like are the takeaways from these studies? Are there, you know, certain things that are -- we can be more confident in, in terms of like what it's telling us? Are there certain things that we can be less confident in and just sort of having that discussion would

be helpful. And then of course as folks are mentioning, you know, any thoughts about how studies can be designed in a better way moving forward, we'd also of course love to hear that.

CHAIR DELNEVO: Thanks, Ben. So a couple thoughts and reactions to what you said. So first, with regards to designing studies, I know others take objection to the fact that it was a convenient sample. Really it was a cohort that was recruiting specifically General Snus users. And I think that as a starting point was appropriate because we do have PATH and NYTS as population surveillance to help identify if there is unexpected up-tick in behavior for the product category as a whole. And then specifically if there's uptake of the product category, then you can look at the brands that are being utilized if there's high uptake.

So I think the data sources are complimentary and they fill gaps with each other. And to me, it was more the measurement

in the instrumentation of the post-market surveillance study and then -- and then the attrition. The attrition is a huge, huge problem because you're losing people. And so efforts at, you know, should there have been for example, replenishment after that first major drop off might be some of the things that FDA thinks moving forward for additional applicants that have MRTPs and need to continue to do post-market surveillance studies.

I also just want to remind folks that, you know, snus is a subcategory of smokeless and General Snus is the product we're talking about. And I think we need to be careful in not attributing things we might be seeing in a product category overall specifically to one brand when in fact, Camel Snus is the number one selling snus product on the market today. It's not General Snus at all. And it actually might be Grizzly Snus and some of the other brands as well. So I think we just have to be careful, because when we

talk about PMTAs and MRTPs, we're talking about a specific product and a specific brand. And we can draw inferences from larger categories, but I think also need to be thoughtful with those particular inferences.

Mignonne, on the phone?

DR. GUY: Yes, I'm here. Thank you so much. I appreciate it. I just wanted to add my two cents in here. I do agree with my colleagues about the rigor of the post-market surveillance study. In particular, I agree that the instruments and measures were problematic and implementation was also concerning. But when we think about -- when we consider this application as a mechanism, you know, watching the presentation from the applicant, I consistently honed in on a desire to communicate that this product can help to facilitate switching from other combustible cigarettes or transition from combustible to just quitting fully stop. And this is -- herein lies a little bit of a problem and I

don't know that it's as much an issue with the applicant or as much of an issue with the -- for the sort of how we're operationalizing these things as an FDA, which I'll get to in a second, but the data submitted by the applicant, it did not adequately address the dual use of combustible tobacco products or other noncombustible tobacco products such as electronic cigarettes. And we know that individuals that use -- that may use combustible tobacco products -- excuse me, combustible cigarettes and transition off of those, they may in effort to quit smoking or quit using those products, they may use multiple products, right, sort of over the life course of them trying to make these transitions. And we just don't capture any of that in these data.

And the notion of dual use or co-uses is particularly concerning if we're talking about not just combustible cigarettes, but other non-combustible tobacco products.

I'm thinking of e-cigarettes actually because we would see a quick transition over from combustible cigarettes to e-cigarettes before we'd see something like snus. But I'm concerned that any sort of dual use or co-use increases a variety of health risks and could this potentially exacerbate underlying health conditions that we already expect, as the evidence already shows, from individuals who are currently using or have used combustible cigarettes in the past. So I'm just not seeing a lot of compelling evidence that -- at this moment -- not to say that it cannot be produced in the future -- that we can actually issue a renewal with the data that's been presented.

And there's something else that was said that was a little bit problematic for me and perhaps it's not as big of a concern for my colleagues, but I'm thinking about the primary form of data collection being an online survey, which I have no problems with. I too am a survey methodologist and I understand and value

them. But I'm actually concerned about the lack of rigor given that there's like no verification in terms of understanding other products that may be used along the way. So it's kind of hard to assess or ascertain the potential use behaviors of the health risks fully if we don't have that additional information. And considering the fact that the sample is so small, you should be able to somehow conduct a study of this nature.

So yes, that's what I have to say for now. But I do think there's merit in having future discussions about strengthening the rigor and the quality of post-market studies, particularly in this one -- in this case. Thank you.

CHAIR DELNEVO: Risa.

DR. ROBINSON: Thank you. So putting the approach -- the questions and the approach aside, I thought the switching -- the study on the -- the slide on the switching was compelling at first. And then I -- if you look

at the numbers, only 16.7 percent actually switched completely whereas 33 percent-ish went to some day and 50 percent only reduced their cigarettes per day. So you know, that's on the order of 70 percent of that -- those respondents who did not achieve any reduced adverse health effect.

And so I'm wondering if that's the criteria, do we really have a modified risk product in comparison to any -- in comparison to just switching -- completely switching from cigarettes to no cigarettes based on any other cessation method?

CHAIR DELNEVO: Nancy.

DR. RIGOTTI: So I'm of several minds about this because I accept that the quality of the post-market survey was not what we would hope for. I mean I think we're asking for a level of specificity in answering a question that is just not -- I'm not sure it's achievable. I suppose it's achievable with enough money and enough sample, but that's

asking a lot for each single product. And it would make more sense if there was something for smokeless tobacco products that -- you know, if we had more like a standard for types of products as opposed to specific -- specific brands. Now I realize that's not how the law is written, so we probably can't do it that way. But that would seem to be a lot more sensible.

I agree with the statements here that the post-market survey design, I think was reasonable the way it was done and the way it was conducted. I do think that the results -- the analysis could be better and I'm wondering if FDA would have any capacity to after hearing all of this, maybe go back to the data that they have and at least try to do some more sophisticated analyses of especially the laws to follow up people.

So I think the question is just what is the level of evidence that we need in a regulatory setting as opposed to more of a

basic find the science setting. And I just wonder -- I don't want us to hold this to too high a standard. And I --

(Off-microphone comment.)

DR. RIGOTTI: I don't -- I wonder if -- I don't want us to have such a high standard. We need to figure out what the appropriate standard is for the level of evidence that we are asking for. And I think maybe that wasn't entirely -- you know, I think it maybe wasn't entirely clear. I think that -- I'm not saying that we should say okay, fine. It's okay. But I think that we should -- maybe the disagreements that we're having with the results we're hearing is because of that.

CHAIR DELNEVO: So -- and perhaps FDA can clarify, instead of having me paraphrase. But with regards to making a decision on an MRTP or an MRTP renewal, there are several pieces of the puzzle that must be considered, including, you know, is the modified risk claim accurate based on the

health risk of the particular product? And we're not spending time here today discussing that piece because my takeaway from FDA reviewing the evidence, reviewing the updated literature is that with regards to the specific product itself, it is a lower risk product and no new science has been introduced to change that particular assumption. And we're not talking about that because we've not been asked to discuss that piece.

So there's other components to it and that has to also do with how consumers perceive and understand the products, which is relevant to question 2. And then the last piece is what are the potential benefits and harms to the population as a whole, which is where question 1 and the behavior piece kind of comes in. Did I get that right? I see Jennifer's kind of nodding and Ben turned his mic on.

DR. APELBERG: Yes, I think that's fair. You know, I mean Dr. Popova talked about

the post-market surveillance requirements and the rest of that sentence that talks about, you know, why they're being conducted include to review the accuracy of the determinations upon which the order was based. Right? So it's like we're continually assessing. There's new information here. You know, do the determinations that were made prior, do they still hold or has something changed that would alter that, that way? And so I think you've captured it.

DR. JORDT: Yes, I'm actually quite concerned that we're not discussing the issue of health effects here and that probably the data from 2014 as still seen on their face value. I still think there are some concerns about health effects that were discovered recently. As I mentioned, the mucosal lesions and the link of snus with diabetes. So I think FDA would be well advised to look into these and develop approaches to monitor. Right? This cannot be expected to be monitored right

now, but maybe through PATH and other approaches, this can be monitored.

Yeah, I wanted to stress that I still have the feeling as if both the manufacturer and FDA sees these products as if they were cigarettes from that perspective. They are looking at lung cancer, nitrosamines, and other constituents. But these products have constituents that are not present in cigarettes with their own toxicological properties including flavors such as the wintergreen flavor, Methyl salicylate, or also they have like synthetic sweeteners in them like Ace-K where FDA has certain recommended values that people should not exceed. And it's been shown in both cases that smokeless products users in some scenarios actually exceed those -- the intake of these substances and the FDA recommended values.

Coming back to the actual data, if we take them as face value and the questions, I think there's a big discrepancy between how

people understand the risk. I mean in these questionnaires, we see that over the four waves of PATH, PATH was analyzed here, 80 percent of users on average say that yeah, they should not smoke any cigarette at all to have a benefit from using these products. However, then in their -- what we see in the actual behavior, it's less than 20 percent of users who exclusively use General Snus or even less, right? So there's a huge discrepancy about what people understand. In fact, they may not actually understand this after all. And what actually then the use behavior is.

And the third thing I'm concerned about, yeah, we just discussed it. The amount of products sold here is minimal in the United States if you compare that to Zyn for example, there's 40 to 50 times more cans sold than General Snus. I mean is there in fact a benefit for the whole population with these small sales numbers? It's really hard to say. Right? So I'm just concerned we're discussing

here -- spending a lot of time discussing a product that has as minimal market share. So thank you.

CHAIR DELNEVO: Maria.

DR. GOGOVA: If I step back and think about really what is the purpose of the MRTP claim, it's really to provide truthful, accurate information to adult smokers so that they can make informed choice. But I think it's very hard to say we have way more ways to do what they will do with the claim or with the information they receive. And when we are looking at the population, you know, there are many multiple factors, which people take into account to change behaviors. One of them can be motivation. One of them can be they're concerned about their health. And therefore I don't think that the claim alone can do all those kind of things. You know, it can provide the information, which can help them to change the choice.

And you know, when we talk about

this study with all the limitations, you know, I still see, you know, that there were several smokers who were able to completely switch from smoking to snus. We've heard about, you know, it's very small number of people in the large scale of tobacco consumers, but I think we should be thinking about like every life counts and can be potentially influenced by having the product available for them, having the information about regular-use risk potential.

And therefore I think what we need to be really focusing on is having more products in the marketplace that consumers can choose from, which to feed their preferences and can be satisfying. So whether the dropout is because they didn't like the product or you know, shared tobacco landscape was changing significantly. So we don't know really what happened to those people. But I think for those who stayed who we've seen from the attrition analyses, those people were committed to smokeless product. They were willing to --

trying to quit smoking. For them, this product works.

So I think we have to be balanced between whether we are expecting 100 percent change among all the tobacco consumers that potentially could see the claim or really only looking for those that the product really was working for.

CHAIR DELNEVO: Olivia.

DR. WACKOWSKI: So I think with respect to the youth issue, I think it's actually reassuring to see at least from the population level data that it hasn't really changed over this time period, which is I think consistent with what we would want to see in this situation. From the consumer study, I think that there are definite issues with the study design as have been mentioned. But at least among those that did participate, who appear to be true users of this product, there is at least some evidence that for some people, it did seem to help them move along in the

right direction. So is there some benefit to some people? Perhaps, yes. I don't know that we know from a population level impact that it's a huge impact, but it does seem to help some people.

I think one issue I have with the study in general is that we don't know the extent to which any of this is actually related to exposure to the claim. So that's a challenge. And with that in mind and you know, what we've heard about how it was quite limited, I think that's something that we need to think about this. Some of these movements could actually be a conservative estimate of what would have happened if they had more information.

CHAIR DELNEVO: I'm going to call on Dona in a second, but I want to also open the floor up to folks. We are going to continue discussion, but I'm also putting question 2 up there for folks if we can -- Feel free to still comment on question 1, but start bringing your

discussion for question 2 in.

DR. UPSON: Thank you. I agree that every time we can help anyone who uses combustible cigarettes to stop is a success. As a clinician every time I have one patient who will stop, you know, it makes my day. I don't know that we can say with certainty that the use of snus is what's helped those people stop smoking. A certain percentage of people stop smoking every year. Is this above that baseline? We don't know because there was no comparator. I'm not saying it's not true, but I don't know that we can say with confidence that it is.

CHAIR DELNEVO: Anyone want to start discussions off on question 2, consumer understanding and perceptions? Oh, I'm sorry. Risa.

DR. ROBINSON: I just want to make one comment about the applicant in the presentation claimed that the advertising wasn't meeting the -- wasn't meeting the

unintended audience, meaning youth. But yet, I have a question around why do we have the same percentage of youth users of snus than we do have adults? So it's like 0.5 percent -- 0.5 to 0.7 percent of youth and 0.4 to 0.8 percent of adults. To me, it seems like we have the same percentage of youth and adults using the product. And if that was the case, how are we claiming that we're not reaching the youth in the advertisement?

CHAIR DELNEVO: I'm not going to answer for the applicant.

(Simultaneous speaking.)

CHAIR DELNEVO: But when you're using at snus use in general, there are multiple brands that are on the market today. So we don't know specifically which one. And then prevalence for youth and adults is often calculated differently where for youth, it's any -- any use in the past 30 days and that includes experimentation. So just some context on measurement.

DR. ROBINSON: I was just wondering how -- like are we initiating snus in youth and then they're continuing on into adulthood because that really wasn't addressed. But I don't see how they didn't state that it's starting in adulthood and yet we do have prevalence in youth at the same rate as we do in adults. So I'm assuming that they're starting in the youth and they're continuing on.

CHAIR DELNEVO: Lucy.

DR. POPOVA: Well, let's talk about the understanding and perceptions. Again, as I mentioned, the TSA Tobacco Control Act specifies that it should be determine the impact of the order issuance, which means the claim on consumer perceptions. In this study, what it tells us is this sample of heavy users, what do they think? This is not in any way can be connected to the impact of the claim on their perceptions. We don't even know if they saw them. How much they've seen it, if they

were exposed or not. This could be their pre-existing belief. It could be an effect of the claim. We do not know.

So in that sense, none of the information presented answers the question of how the consumers -- the effect of the claim on the consumers. What we do know and this is the same information as before is there's some misperceptions among the users. And this has always been the case if you use a product, generally you perceive it to be less harmful. So nothing changed. So we're kind of like back where we were before, but no new information that can allow us to make any claims on how consumers perceive this have been -- can be drawn from this data.

CHAIR DELNEVO: Scout.

DR. SCOUT: Regarding consumer perception, I'm also very concerned. I think that the potential of where this is put and the placement and the potential halo effects. As we heard from one of our folks giving testimony

that did not have a conflict of interest earlier getting public comment that when you see -- when you see a warning like this, there is some evidence showing that youth in particular then extrapolate that warning to the full product class and apply it across the broad product class. So there's real concern I have that while their research was answering -- attempting to answer this question in a very narrow capacity there are really -- maybe placement effects that have a significant impact.

As well, we've heard several times -- and you know, we can see it ourselves going on the internet, that there is this co-marketing of this alongside Zyn. And considering that has had a rampant runaway effect with youth these days. All you have to do is finish -- visit any college campus and you'll understand that, that herd of horses has left the barn. And we're dealing with a whole new level of addiction that we're going to have

to try and sweep up after the fact with too few resources. That this co-marketing and the potential impact of being able -- of having this halo effect and the co-marketing in place could be potentially very dangerous.

As well just as a broader thing, I would also like to say that considering snus is the sole category of tobacco products that I know of that has a particularly targeted marketing campaign for the queer communities, it's particularly disappointing to think that the queer information was willfully not collected in any of the data provided here.

CHAIR DELNEVO: I do want to add one comment on the co-marketing and broadly speaking to the public health community for not actively engaging more in the open public comment period. Because we heard the views of one -- of researchers at one institution. And the co-marketing that was pointed at in the open comment letter -- the public comment letter pointed to the fact that the retailer

site, Northerner, which sells a variety of smokeless tobacco products was promoting both Zyn and General Snus. But Northerner also sells FRE, Lucy, Camel Snus. It sells a variety of products. And so to say that the company is co-marketing when a third-party online retailer is doing co-promotions, they're not the same thing. I mean there might be co-marketing.

DR. SCOUT: I'm not sure that alleviates the concerns of what the impact might be about having this warning in halo effect if co-marketing is occurring by any entity.

CHAIR DELNEVO: Annette.

DR. KAUFMAN: So I want to build on what you're saying Dr. Scout, because as I'm sitting here and I'm re-reading the messaging -- and I completely agree with all of my colleagues here, the label states General Snus. And I heard Lucy just say generally perceived as less harmful. So as we think about the word

"general", I'm not pointing fingers, but if something is marketed as General Snus and has an MRTP claim on it, amidst a power wall or amidst other marketing, this halo effect is potentially likely to happen.

CHAIR DELNEVO: Lisa.

DR. POSTOW: Yes. So I definitely agree with what I'm sharing here. I do want to point out that as we discuss the dangers of the halo effect and assuming the public -- assuming that the MRTP claims can be extrapolated to all of -- all snus products or all products in a certain category, I do want to point out that the health effects data is all snus products. And so just when we're discussing that, just keep in mind how important the distinction is.

(Off-microphone comment.)

DR. SCOUT: I was just bringing up, isn't our particular co-marketing about actually not even a snus product, but you know --

DR. POSTOW: Right. No, I think

that's a separate question. Yeah.

DR. SCOUT: Yeah.

CHAIR DELNEVO: Ben.

DR. APELBERG: Thanks. I just wanted to comment on a few things. One, I just wanted to clarify that like these products all have required health warnings that are the same health warnings that are on smokeless products, but what we're talking about here is a claim that's related to modified risk. So it's a claim of reduced risk. That's not a warning. They have separate warnings.

And I guess it would be helpful for FDA to hear the committee's perspective on the question of understanding -- I guess in the context of, you know, what the evidence is telling us around whether consumers -- the consumers who the company is communicating. They're targeting adult smokers or adult tobacco users, whether the understanding appears to be correct or there's inaccuracies or are there any concerns about

misunderstanding. So I think would be helpful to just have like further discussion there.

I think it's also -- you know, there's been a few comments about the halo effects, and it would be helpful to sort of think about that in the context of what the applicant communicated in terms of how they're actually presently marketing the modified risk claim. Like would that still hold -- you know, is that more of a concern if the claim is being marketed on the product, you know, directly next to another product versus what we were hearing, which is sort of a much more kind of controlled age-gated communication.

So, yeah, it would be helpful to kind of hear more of that. Like based on what we've got in terms of the understanding data. Is it in the direction we'd want to see it? Are there concerns that have arisen or something in the middle?

DR. SCOUT: Aren't they asking for an expansion of it as well --

FEMALE PARTICIPANT: Yeah.

DR. SCOUT: -- beyond the age-gated --

DR. APELBERG: Yes. I mean that's what they've talked about.

DR. SCOUT: But I think I'm talking about in the context of like what the post-market data are, you know, are telling us and how the company has communicated that they've marketed it to date. Just sort of having that context, I think would be useful.

CHAIR DELNEVO: Dona.

DR. UPSON: In terms of the health warnings, one thing I didn't see was the increased risk for heart attacks and strokes, which might have more impact, especially on older users than gum disease.

CHAIR DELNEVO: Adam.

DR. LEVENTHAL: I mean, in relation to these questions, nuances like where the MRTP claim is placed on an advertisement and then how do those affect perceptions, I'm not sure,

but it could have important effects, either, you know, to enhance accurate perceptions or lead to misperceptions or halo effects.

For instance, one of the things that I noted when reviewing some of the example marketing is the word "lower risk" was bolded, and that was the only bold statement. And so I wondered whether that type of presentation of the information could lead people to focus in on lower risk and not really read the rest of the statement as clearly. So, whether there could be requirements related to how the information is presented.

And one other point related to the -- I guess the website and the procedure that people need to be 21 and an existing nicotine tobacco product user, I was a little -- you know, I applaud the company for having some protections in place. I was confused as to why the gate included any nicotine and tobacco, if their target audience, wouldn't it be people who smoke cigarettes? Or would it also include

people who use other tobacco products, including e-cigarettes, you know, and nicotine pouches, and of course the other smokeless.

CHAIR DELNEVO: Olivia.

DR. WACKOWSKI: I think going back to the perception data that was shared at least in my read, I think it does show us some understanding of the direction that we would hope at least among the users, you know, most answered the relative risk question correctly, although in fairness, I think that was kind of an easy question to guess at. Most people did still perceive that there are risks for the different diseases. And in analyzing it two ways, there was generally an understanding that you should use snus exclusively to get reduced risks.

But I think again, the issue is, you know, we don't know to what extent this understanding is attributable to the claim or these people who were users to begin with already had kind of favorable and accurate

perceptions. And that might be, you know, because of the design.

CHAIR DELNEVO: Lucy.

DR. POPOVA: Very quickly another point I wanted to bring up is that the question about understanding of complete switching being necessary to reduce risk, this question was only asked of people who answered correctly to the previous question. So it wasn't asked of people who already had some misunderstanding. So we -- this further reduces our ability to generalize or to say okay, what is actual understanding of the need to switch completely.

And in our studies when we do it with general population of smokers, we see like much, much higher rates of misunderstanding that -- And it's not necessarily like how many cigarettes can you smoke to get the benefit, but more like if you switch completely -- if you use exclusively. And the people are having a hard time understanding that.

CHAIR DELNEVO: Risa.

DR. ROBINSON: Thank you. I want to make an observation about the warning label. It says, using snus instead of cigarettes puts you at lower risk. And it doesn't say using snus exclusively, instead of -- And I noticed that, that's the language directly from the FDA when comparing snus to cigarettes. But the language from the FDA when referring this General Snus to other smokeless tobacco products, they specifically say, and when used exclusively, instead of other smokeless tobacco products. So I feel like the word missing is exclusively. And for me personally, that would make things super clear.

CHAIR DELNEVO: Nancy or --

DR. APELBERG: Yeah. Can I just -- Yeah, I want to make sure I understand what the point is. The authorized claim -- you know, the claim that we authorize, it's not a warning label. It's a modified risk claim. This was what the company requested and so the company provided the MRTP application. Our initial

review of the application evaluated whether that statement was scientifically substantiated. And then there was consumer perception testing, so we evaluated whether people understood that. And then you know, determined whether the products immediately reduced the risk of disease and benefit the population as a whole. And that's how we sort of came up with -- That's how we ended up with the modified risk authorization. And so that authorization is for that specific claim that was proposed to be used in marketing by the applicant.

Other statements that FDA might have made in the -- in the review of the decision summary just reflects our evaluation of the scientific evidence. It's not a statement that, you know, the company is authorized to use in marketing. They would have to have had to request that through the modified risk tobacco product review process. So hopefully that just clarifies the distinction between the

different statements.

CHAIR DELNEVO: And because words matter, I'm going to re-read exactly what the authorized claim is. Using General Snus, instead of cigarettes puts you at lower risk of mouth cancer, heart disease, lung cancer, stroke, emphysema, and chronic bronchitis. So that is the reduced risk claim that General Snus was allowed to make.

DR. ROBINSON: May I follow up? Am I correct in that, that's only true if they exclusively switch and don't use anything else? Because I also heard others here say well, they switched for one session and use snus instead of cigarettes, but then they switched back to cigarettes. So is the health claim only valid if they exclusively switched, maybe using the 30-day use criteria?

CHAIR DELNEVO: So I'm going to ask Ben, was the intent of the modified risk statement to imply exclusive switching?

DR. ROBINSON: Right. Say exclusive

switching maybe based on the --

(Simultaneous speaking.)

DR. ROBINSON: Using the 30-day use criteria because that seems to be something that we gravitate towards.

DR. APELBERG: Well, they're two different things. I mean how you assess whether someone is -- like how you assess what products people are using and whether they're exclusive users or not, I mean that's like an assessment of behavior. This was a statement that was proposed. And part of that was an evaluation of consumer perception data. How do people interpret and understand that statement? And so that included in the original submission, evidence related to ensuring that people understood that if they dual used, they'd be at greater risk than if they just used the product exclusively.

So yeah, that is baked into the statement. But that's all based on our evaluation of the consumer understanding of

that claim. And so that actually was debated and deliberated on in a prior TPSAC meeting when we were meeting to talk about the authorization. I remember a lot of discussion around different language, instead of or completely switch or other kinds of terminology, you know, and people had a lot of different ideas about it. But what we try to do is just look at the scientific evidence that is really looking at like -- And that was an experimental study where, you know, individuals were shown the product with the claim and then asked, you know, a series of questions about it regarding their understanding.

But then in the post-market context, you know, the purpose of this study partially was to just continue to ensure that people generally understood that the product has risks, that it's not risk-free. I mean these are all tobacco products. They're all harmful products. That it's less harmful than cigarettes and that using it exclusively would

pose a lower risk than if you used in dual use.

CHAIR DELNEVO: So we can't go back in a time machine, but if I'm -- So because of the concern of dual use though, the intent of the risk claim is supposed to capture complete switching. Is that right? The language says instead of cigarettes.

DR. APELBERG: Yes. There's different language that you could use to imply. Yeah.

(Simultaneous speaking.)

CHAIR DELNEVO: Maybe better language if it's renewed. If people understand instead of doesn't mean today I use General Snus, tomorrow I use cigarettes. That's not complete switching. It technically is definitionally correct.

DR. APELBERG: Yeah.

CHAIR DELNEVO: You did use it instead on day one, but on -- you know, on even days you used one product and on the odd days, you used the other.

DR. APELBERG: Yeah. Well, I think that's why it would -- itself would understand the Committee's perspective on the understanding data that we have like post-market. You know? I think what Olivia talked about was helpful sort of context for thinking about what we can take away from that.

CHAIR DELNEVO: Nancy.

DR. RIGOTTI: So, you know, when I look at the wording of the modified risk statement, it seems to me that I get it -- I get what it's saying, that it implies complete switching. I can also see where you could, you know, sort of see it a different way. And I think the question would be that, you know, what is the FDA going to want to require of modified risk statements, data about that in order to accept modified risk statements. That's not really a question of is this okay? You know, will we -- will we renew this one? But would, you know, the next time a product comes along, how much level of detail because

understanding -- health communication science is really complicated as I understand it. And to make sure that something is really as crisp and as well understood as possible. Is that what's being asked of the manufacturers do that level? Because it didn't seem like that's probably what happened five years ago.

DR. APELBERG: Yeah. I will just say actually following this discussion of the Swedish Match applications, we're going to have a session -- a short session on consumer understanding and operationalizing it. And I think we can get into a lot of the specifics there. I will just say, you know, it's not -- we're not -- we have not articulated that there is certain language that's the right language to use because we know for sure that it's, you know, more well understood. What we require is that a company propose language and then test that language. And it's the scientific evidence we're evaluating through that testing to ensure that people comprehend it in a way

that's going ensure that they understand it accurately and are more likely to use the product in a way that can benefit them. So I just -- I'll reiterate that.

And I do agree though with you that it's not really the task at hand to kind of revisit whether that claim was the right claim or there should be a different claim. And that was the claim that was authorized and it just would be helpful to know if there is concern now for some reason that people don't understand that or is it just -- or does the evidence before us suggest otherwise?

CHAIR DELNEVO: Nancy.

DR. RIGOTTI: So I was sort of getting to that, and I think that we can't -- I guess the question is would the recommendation be to go back to the company and the manufacturers and say you need to make it better before we would renew this. I think that would be the question. And if we did, then we'd have to be clear on exactly what it

would take.

What I'm hearing here is that we are not -- I think we've been able to say that it doesn't look like the youth are picking this up in a big way. At least they're not picking up smokeless in a big way and probably not this specific brand, but we don't have the data that it's not the specific brand. But do we need that level of data in order to feel like the modified risk categorization is okay? And do we need -- We can't, as Olivia pointed out, we can't say that it's the statement that is changing the behavior. But the behavior looks like there's something happening. Is it really that much? Is it really that valuable? Who knows. But it looks like it's not going in the wrong direction.

And so if we want to get that level of detail, then we need to probably make it clearer to the manufacturers that that's what they need. It makes their job a lot more expensive, but presumably they're in business

and maybe they can afford it. And it just means that the process of getting this regulation will be more difficult and more expensive. But if that's what we think we need in order for us to feel that we're protecting the public, then that's what we're talking about. But if we don't need that level of detail, then in a very broad sense, at least certainly when I came in after reading the materials and after hearing the presentations, I thought it was, you know, reasonable -- much -- it wasn't perfect. Maybe some more analyses could help. But I thought it was, you know, not as bad as some others are interpreting it here.

CHAIR DELNEVO: So in the interest of time and getting some saturation with the kind of comments and Nancy with your -- it sounded like that would be your final comment. Is that your -- Is that your final comment here?

DR. RIGOTTI: Can I leave then?

CHAIR DELNEVO: No. You can't leave, but I won't call on your again. If you wish to add something again later on, you may. But with that, we're going to start to go around the room. I hope Annette you're okay. I'm going to call you on first, we started with that end of the table. Any final comments you wish to make regarding questions 1 and/or 2 or broadly about the application that we are considering?

DR. KAUFMAN: Yes, but you keep starting with me and I'm not ready. Hold on. So I think related to the behaviors, the question 1, I think all potential patterns were not examined. So I think there's more nuance that needs to be examined related to question 1. And then related to question 2, is this what you're asking for, Chris, like a -- Okay. Related to question 2, I share Dr. Leventhal's comment around the emphasis on lower risk and how that may affect perceptions. But I also agree with Lisa around the general

sense that snus is less harmful than cigarettes in general.

I just also want to point out and I know we're going to talk more about this, but the assessment of knowledge is not the same as the assessment of perceptions. And I saw in the write-up that that was very muddy. And so questions related to knowledge are separate from questions related to beliefs about harm of a product. I'll stop there.

CHAIR DELNEVO: Thank you. Andy.

DR. BAILEY: Yes, I just want to make a general comment here and there's been some questions about the renewal. But I would argue that really if you think about Swedish Snus, it's quite possibly the least harmful tobacco product that, you know, has ever been on the market, I think. And so we've got to, you know, keep that in mind. It's a small market share too and there are small sample sizes, I think that come into play that makes some of the details a little bit more difficult

to get to. But if we think about this product and the history of Swedish Snus and the harm level of it very low obviously, if this product can't maintain modified risk status, I don't -- you know, I don't know if any of them can. That's my comment.

CHAIR DELNEVO: Amy.

DR. MADL: I just have a general comment with respect to the product General Snus. It's I think been really well demonstrated it's a significant reduced harm product. And one thing that really kind of struck me in the presentations that were provided is that when you're looking at a modified risk claim and other types of products like classic snuff is that communication is given to broader channels. And when you look at the reduced harm of General Snus, it's greater when you're looking at known human carcinogens like NNN, NNK.

So I think there is an opportunity here for FDA to consider some even-handed

guidance to the applicant in channels to communicate those reduced risk communications to consumers. And really give smokers an opportunity for reduced harm nicotine products.

CHAIR DELNEVO: Maria.

DR. GOGOVA: So I think I believe that the consumer have rights for truthful and accurate information. And we should be able to reach out to that audience and communicate. At the same time, I also believe that, you know, currently the post-market surveillance studies had some limitations, but I think it doesn't disqualify the knowledge that the General Snus is significantly less risky than conventional cigarettes. And even from the studies, although we cannot really -- relative to the impact of the claim, we see that there are some smokers who are completely switching to General Snus. And I believe, you know, we should really be thinking about how we can reach the target audience without creating consequences so the consumer have more information available

for them to make informed choices. And then for the post-market surveillance, I think we should be thinking, you know, how to tailor the post-market surveillance studies to really get to the question that we need to get and not making it so burdensome on the manufacturers that they will never try to apply for MRTP. And therefore we will have no products, nor information to communicate to the tobacco consumers.

CHAIR DELNEVO: Thank you. Taryn.

MS. WATSON: Thank you for the opportunity to be here. I have some homework and information to relay back to my IHS colleagues. But just from -- just my comment initially is just looking more closely at data contributions at the IHS level and how we can provide more feedback and looking closely at marketing efforts among American Indians and Alaska Natives. Thank you.

CHAIR DELNEVO: Dee.

DR. KITTNER: I agree with Scout's

recommendation that the public commenter should be required to disclose tobacco industry ties and potential conflicts of interest. I saw no new information today that would cause me not to recommend a renewal. The extremely low rates of nitrosamine levels, low levels of use among the youth in particular from what we've been able to see.

However, I would not recommend expanding the use of the claim. Particularly the request to point of sale and social media and digital platforms, I would find to be problematic given all the concerns raised here by my colleagues here around the data that have been discussed. And the co-marketing and the halo effects that have been discussed and other concerns.

And if possible -- and I'm also concerned about dual use and the switching. Right? And for us to have the most benefit, we want people to quit completely. Certainly to completely quit combustible tobacco use. And I

guess I'd like to really encourage FDA to work with the applicant to change the language of the claim to be clear. And clarify that we're talking about exclusive use or completely switching so that consumers really understand how they're able to gain the best public health benefit.

CHAIR DELNEVO: Lisa.

DR. POSTOW: Yes, so I agree with my colleagues about clarifying the exclusive use aspect. Generally speaking, I'm -- it's unclear to me what the threshold is for the FDA to determine that something is reduced risk. And then whether the public has the same understanding of what that threshold is as the FDA. So I think in this case, I don't really have an issue with it, but I could imagine cases where the FDA's threshold might be different than the public's understanding of what reduced risk is. And I think that's just something to think about for the future.

Regarding the expanded use, I'm

actually going to disagree with Dee here. If the FDA feels that the MRTP claim is in the benefit of public health, then it should be easier to get that information than it looks like it is from what they're doing here. People have to put quite a bit of personal information into the website in order to see the claim, which personally, I would never do that. So anyway -- So, yeah.

CHAIR DELNEVO: Lucy.

DR. POPOVA: I want to say thank you to the FDA for all the work they've done putting all the materials together and comments and all that. And also to the company because they're the first one doing this a few years back and now the first renewal. So in that, it's -- you know, we're all in this together. And now I'm going to give you some things to consider and maybe make clear and improve the process.

In terms of health's actual claims, going back to we do know that this is very low

risk if this is used by nonsmokers who never smoked. Since we've had a lot of studies now kind of looking at the switching patterns and biomarkers and all of that, I think moving forward, we do need to take this into consideration. Do we have enough evidence and scientific base to say yes, switching completely will actually benefit you. Because right now, we know if you never smoked and use it, this will be better than smoking.

In terms of the studies post-marketing surveillance, I think we need to make very clear what are our research questions? And then design the studies around that. If it's -- we're looking at impact, it's a different study. If we're looking at patterns of transition and cohort, it answers different questions. FDA needs to be very clear in what study is going to be done, what research questions they're going to answer. And then communicate that not to just companies, but to the public and to us. And we can provide that

feedback early on, rather than four years later when the study has been done and we're like well, this is not -- doesn't give us the information we were looking for.

And in terms of what Ben was asking in terms of what studies can we do, how can we better do it? I think that again, when I raise a research question, this is what the study should be done. If we need to know how the claim affects perceptions and behavior, this is like a study of marketing campaign. This is when we put, you know, FDA does marketing, you know, prevention campaigns and all of that. You look and see how is exposure related to outcomes? It's very simple. So we need to -- This is going to be a study designed and there's a lot of literature on how to evaluate real world communication efforts, instead of just doing lab studies, which -- the experiments, which are done at the early stage.

And for the -- We didn't talk too much about expanding the marketing, but I agree

that smokers should have that information. And Swedish Match is part of PMI. PMI has a huge database of smokers. They could devise a study where they -- I think direct mail to smokers would be very appropriate. They can send -- They do send coupons. They have all that information. Why can't they track that information, create a study to show okay, does this claim track? Do people buy it? Do people not buy it? They can have very sophisticated designs. They probably are already running those studies, just not sharing them with us.

But anyways, there's a lot of things available out there to do this properly and to see real world impact of this modified risk claim. But for right now, the evidence presented, it's just not sufficient to say one way or another. Like we don't have really any new evidence compared to where we were five years ago.

CHAIR DELNEVO: Adam.

DR. LEVENTHAL: So, based on the

evidence reviewed today, the claim as written appears to be accurate in terms of the health effects. So no new data coming out to suggest one way or the other. Now in terms of, you know, allowing the MRTP claims and its impact on public health and kind of both sides of the coin, I do agree with Dee that to mitigate the adverse impact on youth uptake and young adult uptake, which we didn't have much data presented today on, limiting the channels of marketing to venues where people who don't currently use combustible tobacco products are unlikely to see. So like for instance stores that you have to be 21 and up to enter, you know, the website gating, those would be ways to protect against that concern.

CHAIR DELNEVO: Sven.

DR. JORDT: Yes, I concur with several of the other panel members in that the language of the reduced risk claim needs to be more precise. Stating that -- yeah -- you should not smoke at any time. Right? You

cannot just use these interchangeably, that you really have to, yeah, quit using cigarettes. But also that you should consider not using other nicotine products because the risks associated with other products such as e-cigarettes and others is not really clear.

In terms of yeah, having hidden the statement in several layers of web forms with a lot of information, I think that's in fact counterproductive. So being able to present this claim in other context would probably help. I still remain concerned a lot about the dual use and I hope the rephrasing of this claim might help with that if that's possible. And if this MRTP renewal is approved, the FDA needs to expand its monitoring of health effects towards other biomarkers, other indications such as mucosal lesions linked to diabetes and other factors. We already have ten years of user data and we'll have -- if this is five years or if this extends for ten years, that should be possible. Thank you.

CHAIR DELNEVO: Risa.

DR. ROBINSON: So I do agree that we have a reduced exposure product here as assessed on the bench top. I think on a population level, the data are less clear. And that's mainly around the messaging with using the words "instead of" versus "exclusive use instead of".

I'm also concerned about youth initiation. As my colleague Scout here mentioned that on college campuses if we expand the advertising, we might have an up-tick in more college students initiating this type of use. That's all. Thank you.

CHAIR DELNEVO: Scout.

DR. SCOUT: I remain very concerned that the strength of evidence provided to us would not pass NIH study section to get funded. There's just so many things that have been brought up; concerns about the exact wording, on how this was presented to people, no research on dual users, concerns about the

attrition, which I understand while the original study was approved, the attrition rate was obviously not approved. And considering this is a set of industries that are absolute magicians in getting people to continue doing things, it's kind of amazing that they couldn't get them to take a third survey. I mean, give them a free cappuccino maker if they go through all three.

Post-weight, there are actual renumerations so that they are incentivized to get through all of -- I'm sorry, four waves I guess it was. Also concerned about the fact that there was nothing like imputation, other laws to follow, strategies put in place in order to minimize that. They didn't match the referent population that they had from PATH with any kind of indication. So the fact that we have high SES population at wave four makes me really dubious about the value of any of the information that's even coming out of that.

And you add on the fact that we're

talking long gestation periods for some of these outcomes that are part of the evidence base that this is less -- lower risk makes that suspect as well. And then add on the fact that the warning currently is only accurate for about a quarter of the users. And for three quarters of the users, it's an aspirational warning. And yet 100 percent of the users are going to be reading that and presumably thinking that, that is a science base that they can react to.

Then if we look at the actual wording of it, I am certainly concerned that it's not well understood the way it's currently put out that we didn't have information on modified risk claims for youth. That we have now heard for the first time here that there was a bunch of redacted information with youth in these applications and we have no access to that whatsoever. That absolutely makes me concerned as well.

So I think not even counting what

the placement effects of these claims might be that may not be within Swedish Match's purview to look at, but maybe it's really in FDA's purview to look at that we need to understand more about the halo effects here, particularly when it's put next to things that are having runaway success in different populations. So ultimately, I judge this to be a claim with a gargantuan asterisk next to it that is not publicly conveyed and we're expecting that the population will somehow guess all of the caveats at the end of the claim.

CHAIR DELNEVO: Nancy, do you have anything to add?

DR. RIGOTTI: I think I would add that I think that if it's reasonable to consider expanding the ways in which it could be marketed, although I have some concerns about the point of sale because it's going to be sitting next to other -- it's not going to be sitting next to cigarettes. It's going to be sitting next to something else.

DR. UPSON: I agree that we weren't presented with any data to negate the claim from what it was before and with the concerns for the wording. And if the wording of the claim is changed, I think a great deal of care needs to be taken, I think for this population of many people with lower education and lower socioeconomic status, they may not understand what the use of "exclusive" means in this context. So I think it's important to change the wording, but with great care.

I remain skeptical of studies that are done by the industry or done by anybody who has a biased interest in the outcome, so I would really encourage FDA to do their own studies or to get funding for other people to do the studies. And I agree that we have a big concern for dual use and of initiation of nonsmokers of our youth. And so I would be careful about expanding where the claim can be stated. And it might be reasonable to do it in other places, but again, we have to be careful

where youth are going to see that. Thank you.

CHAIR DELNEVO: Olivia.

DR. WACKOWSKI: In terms of the data we looked at, I think that there's some -- some evidence that there may be some benefit -- minimal benefit so far, but I think we also haven't seen any compelling evidence that there's been harm or unintended consequences.

In terms of the perception data, I think as we said, you know, we're missing some critical information about potential claim exposure or connection to that, although at least some of the consumers that, that data was obtained from, if they were consumers for two years, potentially would have seen some of it. But as has been mentioned, it's you know, pretty varied. With that talking about sort of the claim expansion, I think it's reasonable to consider other channels. If nobody ever sees the claim, then you know, we really don't have a purpose to have it. But as others have said, I think we need to be careful about which

channels those are to limit youth exposure.

CHAIR DELNEVO: Mignonne.

DR. GUY: Thank you. Regarding the data presented, I'm not going to belabor the previous comments, but I continue to have concerns about the rigor of the study and potential health risks associated with use of other tobacco products other than cigarettes. I am also concerned about the potential for confusion on the part of consumers as my other colleagues have expressed about the MRTP claim.

I agree that FDA and the manufacturer both have to be very, very clear about the -- about exclusive use at this table, using that term. But also knowing that we have to modify that language and ensure that it's acceptable to the individuals that are actually using these products. I think about the gentleman who spoke earlier about the folks who use it are from -- I thought he said Appalachia, but I can't remember and truck country, potentially individuals with lower

levels of education, lower levels of health literacy, things of that nature. So we have to be very clear that we're -- very clear about the language that we're using for the populations that are using the products.

And for those reasons, I agree with my colleagues that I wouldn't recommend expansion of disseminating the MRTP claim to the point of sale on social media at this point in time. This is not something, you know, that we want to roll out into all sorts of domains without having adequate data to substantiate the safety of doing that -- the act in and of itself and then have to pull back with putting out fires as we often do within the tobacco control domain. That would be it.

CHAIR DELNEVO: Thank you. There are over 28 million people in the U.S. that smoke combustible cigarettes. And on the continuum of risk, this product as far as a tobacco product is concerned, not tobacco and nicotine, but as far as a tobacco product is

concerned is on the opposite end of that continuum of risk.

Has the MRTP for General Snus helped us realize what its potential could be? No, it's really hard to evaluate the low sales perhaps due in part to the very conservative marketing approach used by the company, which makes that a little challenging. Did the General Snus MRTP promote youth uptake? The data seemed to suggest no, so that's I think a good thing.

Did the General Snus product produce switching like we would hope? It's unclear. It's hard to tell in the data. And so I ask FDA if they can, do some more robust analyses, perhaps stratified analyses by the use of other tobacco product types, I think would be important. I remain concerned that maybe some of the changes we're seeing are just secular changes or what we know about people that use a variety of tobacco products is they use a variety of tobacco products. And so it could

be the e-cigarette that helped that combusted cigarette smoker transition off of the cigarette and not the General Snus product. We don't know. Hopefully FDA can take a closer look at that.

The post-marketing studies in general, I think need to be designed a little bit better and a little bit stronger. And then the last comment I'd like to make is ask FDA to consider also reevaluating their proposed product standard for smokeless tobacco which they made a number of years ago. This particular product would meet that product standards. The companies are capable of producing smokeless tobacco products with very low levels of NNN. And perhaps that is something worth considering reevaluating at this point. And with that, I'm going to let Ben have the last word.

DR. LEVENTHAL: Can I say just one more thing just very briefly? Sorry.

CHAIR DELNEVO: Only if I

acknowledge you, Adam. No. Adam, yes, of course.

DR. LEVENTHAL: All right, thanks. I was going to say one thing -- one recommendation is if there is a renewal of the MRTP, all FDA-related communications could help provide context to provide information to avoid halo effects. So kind of reinforcing that an MRTP renewal does not necessarily mean less harmful than other products. And it's specific to this product, this brand.

DR. APELBERG: Great, thanks. You know, I'll just say really -- at FDA, we really appreciate the Committee taking the time and you know, really putting in the effort to prepare and to, you know, to really consider the evidence and all the various questions that were raised today. You know, we're going to have the transcript to be able to go back to, to really dig deeper into everyone's comments and feedback. And so we just really appreciate the time and effort that's gone into the

discussions today. So just thanks.

CHAIR DELNEVO: And with that, we're going to take a ten-minute break. And when we return, we're going to hear another presentation from FDA.

(Whereupon, the above-entitled matter went off the record at 2:51 p.m. and resumed at 3:04 p.m.)

CHAIR DELNEVO: Okay, we're into the home stretch. I would like to introduce our next speaker, Alex Persoskie from FDA, who's going to talk to us about consumer understanding across MRTPAs.

DR. PERSOSKIE: Okay, hi everybody. Clicker. I'm just going to see if I know how to use this. Okay, just testing that out. My name is Alex Persoskie, I am a supervisory social scientist in the division of population health science in CTP's office of science, and I'll be giving a general overview of CTP's evaluation of consumer understanding in modified risk tobacco product applications, and

the goal is going to be to tee up the Committee's discussion of four questions that we're seeking your input and recommendations on.

So this presentation is not a formal dissemination of information and does not represent agency position or policy. First, I'll start by going over some relevant regulatory background to set the context for the discussion of consumer understanding and explain why consumer understanding matters. Second, I'll describe modified risk labels, labeling, and advertising, including explaining what these are and what types of content we've seen on them in MRTPAs up to this point. Third, I'll present a potential framework for assessing consumer understanding of MRTPs. Fourth, I'll describe some psychological constructs that are relevant to assessing consumers' understanding of modified risk information. Fifth, I'll go over some considerations about measurement of these

constructs, and then last I'll introduce the questions that we have for the Committee.

So first, the regulatory context and background. When an applicant submits an MRTPA, FDA's scientific review includes evaluations of many types of information. We need to characterize the product itself, which depending on when it originally came on to the U.S. market may or may not have previously gone through an application pathway such as PMTA. We have to identify the modified risk information that the applicant proposed to market the product with, substantiate that the modified risk information is accurate, and evaluate the overall health risks of the proposed MRTP relative to the comparison product, which might include health effects that are not described in the modified risk information itself, but would still affect people who used the product.

We need to evaluate consumer understanding of the information, which is the

focus of my presentation today, and we need to evaluate the MRTP's impact on the population as a whole, including people who currently use tobacco products and those who do not, and we need to conduct an environmental assessment. In our reviews, we consider all available scientific information that we can, including information provided in the application as well as other information such as that submitted in public comments or published in the scientific literature, if we're aware of it.

When Congress passed the Family Smoking Prevention and Tobacco Control Act, or Tobacco Control Act for short, and the President signed it into law in 2009, they made several findings, including that tobacco product advertising and marketing have historically been directed to attract young people to use tobacco products, and advertising had portrayed the use of tobacco as healthful, including to minors. Congress also found that among people who currently use tobacco

products, marketing products as modified risk when they do not in fact reduce risk could lead people to continue using the products rather than quitting or reducing their use of tobacco. A primary example of this was that many smokers mistakenly believed that light and low tar cigarettes caused fewer health problems than other cigarettes, which reduced their motivation to quit smoking. Congress also found that advertisements in which one product is claimed to be less harmful than another product had been misinterpreted by consumers, even in the presence of disclosures and advisories intended to provide clarification.

Given such risks, Congress concluded that there was a compelling government interest in ensuring statements about modified risk products are complete, accurate, and relate to the overall disease risk of the product, and that FDA was the appropriate regulatory agency to evaluate modified risk tobacco products, including evaluating the consumer impact of

labels, labeling, and advertising that contain information about modified risk. They tasked FDA with reviewing tobacco products sold or distributed for use to reduce risks or exposures, and they stated that prior to marketing such products, it is essential that manufacturers be required to demonstrate that such products will meet a series of rigorous criteria and will benefit the health of the population as a whole, taking into account both the users of tobacco products and persons who do not currently use tobacco products.

When it comes to consumer understanding of MRTPs, the Federal Food, Drug, and Cosmetic Act, as amended by the Tobacco Control Act, lays out a general standard for what needs to be demonstrated. The standard, which is in section 911 H1 of the FD&C Act, states that the HHS Secretary shall require that any advertising or labeling concerning MRTPs enable the public to comprehend the information concerning modified risk, and to

understand the relative significance of the information in the context of total health and in relation to all the diseases and conditions associated with tobacco use.

That brings us to the role of consumer understanding in modified risk tobacco product applications. Consumer understanding is a standalone statutory requirement that must be met to receive a modified risk granted order, or MRGO. We also need to evaluate consumer understanding because it is one factor among many that can influence peoples' use of tobacco products, including initiation, cessation, using products more versus less frequently, and switching between different types of tobacco products. For example, people may have misperceptions about the health harms and addictiveness of cigarettes and other tobacco products. Prospective studies suggest that lower perceptions of risk among adolescents are associated with greater likelihood of initiating cigarettes. Perceived

risk and vulnerability also predict smoking quit attempts and cessation among adults in longitudinal studies. That means consumer understanding plays a role in the health effects of authorizing the marketing of an MRTP.

Let's now get into modified risk labels, labeling, and advertising, including what these are and what types of content we've seen on them in MRTPAs up to this point. Briefly, I want to explain this term LLA, which might sound a bit odd or redundant. We use this term LLA because it is written in section 911 of the FD&C Act. Basically, labels include displays on containers or packages, here is an example of the front and back labels from a Camel Snus MRTPA that was discussed in a TPSAC meeting back in 2018. I'm using Camel Snus as an example here, because they had all three types of materials.

Labeling is more general, and includes labels as well as other materials that

can come along with a product. Again, from the Camel Snus MRTPAs, here's a part of a consumer engagement handout that was proposed to be used by company representatives when engaging consumers in adult-only facilities and at retail. And then advertising isn't explicitly defined in the Act. Advertising might sometimes be discussed in terms of its intent as being directed to attract people to use tobacco products, or its effect of expanding the size of the tobacco market by increasing consumption of tobacco products, and there are many types of advertising channels and media as listed here. Also shown is an example of the outside and inside of a direct mail advertisement.

So a modified risk LLA contain modified risk information, in other words, information that represents that the product presents a lower disease risk, is less harmful than another tobacco product, or contains or presents a reduced level or exposure to a

substance or is free of a substance. Typically, in MRTPAs we've received up to this point, the LLA has included information about the reduced risk or exposure, including statements that the product is lower risk, or presents less exposure to a substance than another product, as well as information about how to use the product to get the risk or exposure reduction, such as a description of use patters or use instructions. In some cases, the LLA has also included general product information to explain what the products are, information sometimes referred to as balancing information to put the modified risk information in context, for example statements that the best choice for one's health is to quit all tobacco products, and information sometimes referred to as disclaimers that says what the modified risk information does not mean.

As suggested previously on the LLA slide, modified risk information may be

included on labeling or labeling that come with a product once a consumer has purchased it, and it may also appear in advertising such as direct mail, email, point of sale, print and digital media, that consumers can view even if they haven't purchased or otherwise come into contact with a product yet. Different types of LLA can be designed for targeting and tailoring to various potential audiences, for example certain advertising channels can be used to directly target potential consumers who currently use the comparative product, or who are over the federal minimum age of sale of tobacco products, and advertisements can be tailored to appeal to particular groups through imagery or other characteristics. This slide shows snippets from example advertisements from some previous MRTPAs. The one on the left is from an email ad for General Snus, and the one in the middle is a print ad for IQOS, and the one on the right is a print ad for VLN cigarettes. Here you can see the modified risk

information, other information about the products, branding, and images of products and packages.

Let's now move into a potential framework for assessing consumer understanding of MRTPs. This slide shows one potential way of breaking down and thinking about adequate consumer understanding of MRTPs. As a reminder, section 911 H1 says that modified risk LLA must enable the public to comprehend the modified risk information and understanding its relative significance in the context of total health, and its relation to all tobacco-related diseases, but it does not give the specific ways in which FDA should assess this. Based on the ways we have approached this provision in the past, this slide reflects a potential framework that breaks consumer understanding into three components or buckets. We're seeking TPSAC's early input on this potential framework as part of the discussion questions that will follow this presentation.

This potential framework includes, on the left, understanding the specific risk reduction or exposure reduction that the LLA describe, in the middle, understanding that the proposed MRTP does confer health risks or harm and is more harmful than non-use, and understanding the risks relative to cessation with or without the use of FDA approved cessation therapies, and then on the right, understanding how to use the proposed MRTP to reduce one's risk or exposure.

So let's now look at each component in more detail. This first component of the potential framework is about whether the LLA would enable consumers to understand that the MRTP poses less risk of the outcomes it talks about, particular diseases, health effects, harms, or exposures. For example, for LLA with information about reduced risk of diseases A, B, and C, would consumers understand that the product presents lower risk of these diseases than the comparative product?

This second component of the potential framework is about whether the LLA would enable consumers to understand the extent of the health risks and harms that the MRTP does still confer. This includes many diseases and harms including addiction. This gets to the absolute levels of health risks, which for a young person who doesn't use any tobacco products implies a comparison with non-use, and for someone who currently uses tobacco products would imply a comparison with cessation of all tobacco use. Also, it would be important to ensure that current tobacco users understand the health risks and harms of using an MRTP compared to quitting all tobacco through the use of cessation therapies that have been shown to be safe and effective.

The third component of the potential framework is about whether the LLA would enable consumers to understand how they have to use the MRTP to reduce their risk of disease, harm, or exposure. In what we've seen to date in

MRTPAs, this has mainly involved switching completely from the comparative product to the MRTP and no longer using the comparative product, but one application was for very-low-nicotine combusted cigarette products, and also had the stipulation that people needed to substantially cut down on their overall cigarette smoking.

We've seen various phrasing across different MRTPAs, and researchers have been conducting generalized work to evaluate whether people understand various phrases and different potential ways of getting across to consumers the idea of complete switching. Not all such phrases might be readily understood by consumers, and people might misinterpret them in particular ways, and so it's important for FDA to evaluate the information on a case-by-case basis in applications.

Let's now talk about the constructs and information we have considered in the past when evaluating consumer understanding. In

terms of how we have operationalized consumer understanding, our view has been that understanding is multi-layered, and there are multiple overlapping ways of conceptualizing and measuring it. Given the focus on risk in MRTPAs, in the past we have been interested in comprehension of risk-related information at a surface level, and also understanding of that information at a deeper level, including consumers' understanding of its significance and meaning for their overall health. As shown in the figure here, labeling and advertising have characteristics that influence their understandability, such as readability, and then once consumers view the labeling and advertising, research can use various methods to probe consumers' understanding in different ways. This can involve probing their basic comprehension, their knowledge, and their perceptions of risk.

So as I just suggested, evidence on consumer understanding can generally come from

two main sources, and I wanted to give a quick overview of these before going into each one in more detail on subsequent slides. First is the LLA itself, which we examined to determine whether it appears understandable, and the second is research in which consumers view proposed modified risk LLA and answer questions about the LLA, the product, and their risk perceptions, to evaluate whether representative members of the public actually understand it. We call these types of studies tobacco product perception and intention studies, or TPPI studies, for short.

TPPI studies can be conducted by the applicant or by other researchers. They can be submitted in the MRTPA itself, or they can be referenced or provided to FDA in public comments. They can also be published in the scientific literature, and we can become aware of them that way, however general findings from the broader scientific literature may not be informative for a particular application, given

that each application is product-specific, and has specific modified risk information that may or may not be similar to the wording that was tested in a study. As far as study designs, TPPI studies can be qualitative, such as in-depth interviews or focus groups, they can be quantitative surveys, or they can use mixed methods.

Each study design has strengths, weaknesses, and utilities, so we generally suggest applicants consider using both qualitative and quantitative methods when conducting TPPI research. For example, qualitative study designs can be useful to develop different presentations of modified risk information in ways that can be later tested in quantitative studies, and quantitative study designs can provide numeric estimates of the proportions of the study population who have an acceptable understanding. As noted here, in 2022 FDA published a guidance for industry on principles

for designing and conducting TPPI studies, which provides the agency's current thinking on the design of such studies.

Okay, so getting into each type of evidence, we start with the labels, labeling, and advertising itself. In past reviews, we have considered the extent to which the information on the LLA, on its face, would appear to promote the public's understanding of the product's risk. So first, does the information appear to be accurate and not misleading? For example, is the proposed information exceedingly broad in its reference to reducing tobacco-related diseases or harm? Does the information purport that the product's risks are lower than can be substantiated? Depending on the facts, this could be misleading on its face. Second, does the information appear readable, clear, and comprehensible to people even if they do not have a high level of formal education? We have looked at factors such as reading level scores,

but we're more concerned with overall apparent clarity and salience of the main ideas. Third, does the information explicitly describe how one needs to use the product in order to reduce their risk, harm, or exposure?

In terms of evidence from TPPI studies, we consider a variety of outcomes, collected from participants either while they're viewing the modified risk LLA or after they finish viewing the LLA. In other words, some measures of consumer understanding give participants the opportunity to view the modified risk LLA while they are completing the survey items or questionnaires, whereas for other outcomes, participants view the modified risk LLA for a period of time and then complete questionnaires without referring back to it. We can generally lump the consumer understanding outcomes into three categories, shown in the circles here. I'll go into more details about these on subsequent slides, but these include recognition and recall,

knowledge, and risk perceptions. We view these as falling on a continuum in terms of the depth of understanding that they each show, with some outcomes reflecting a shallower or more verbatim understanding, and other outcomes reflecting a deeper understanding.

We want to note that each construct gives us a different type of information about consumer understanding, and together, different constructs may complement each other. Recognition and recall, for instance, reflect surface level understanding and are a low bar and first step for evaluating whether people really get it. A few examples of items from published studies are on this slide. Since recall items usually ask participants to provide an open-ended response, they also could be influenced by other factors such as education, age, or health literacy. Another note regarding recognition and recall measures is that participants cannot review the modified risk information while completing the

questions, and so the items are in part capturing the memory of the claim, and not just comprehension of it. Also, whether questions include cues can affect results such as the likelihood of participants responding 'don't know.'

The next construct, knowledge, goes a bit deeper and asks people to spontaneously interpret the modified risk information and push on what it actually means in a way that relates to real world use and health effects of exposures. These questions can be quantitative or more qualitative in nature. The final construct, risk perceptions, refers to people's judgements about the likelihood or severity of health effects from using tobacco products. Given that the key information consumers need to understand that concerns risk, risk perceptions are an important construct to assess when evaluating consumer understanding. There is significant published literature on tobacco risk perceptions, and they generally

break risk perceptions out into two types.

Absolute risk perceptions are judgements about the health risks of using the product in an absolute sense, such as whether a consumer expects certain product use pattern to cause health harms. When evaluating consumer understanding in an MRTPA review, it can sometimes be challenging to judge the accuracy of absolute risk perceptions, as there can be a lack of consistency in how respondents interpret and use response scales no matter how they are labeled, and that's the case for both verbal and numeric labels.

Relative risk perceptions are judgements about the health risks of using the product compared to the health risks of using another product, such as the comparative product, other tobacco products in the same category, or FDA approved cessation therapies. For both absolute and relative risk perception measures, we recommend being specific in terms of the health harms and the use patterns, for

example, assessing the perceived health effects of partially versus completely switching to the MRTP. You can see how these added levels of specificity effect question wording in the examples on the right side of the slide.

The last topic we'll talk about today before getting into the questions is measurement considerations, some of the study design and questionnaire features that we have considered when evaluating consumer understanding evidence. As mentioned before, FDA put out a guidance that discusses principles for conducting TPPI studies, and this presentation draws on what is in that guidance.

Our first recommendation in the final TPPI study guidance is to use an experimental design in which participants are randomized to a control group that does not view the modified risk LLA, or an experimental group that does view it. Then, participants answer questions about the LLA and product's

risks. This type of experiment can help demonstrate whether and how the modified risk information influences consumer understanding. Moving onto some considerations for the scales used to assess consumer understanding, which are on the left hand side of the slide, FDA recommends including more than one type of measure or scale, and insuring that items aren't too easy and that they have objectively correct answers so that they can be scored for accuracy, otherwise it's difficult to interpret the results and whether they reflect sufficient understanding.

On the right side of the slide, we have some things to consider when assessing risk perceptions. We recommend that risk perception items be worded as specifically as possible, that helps ensure that we know what underlying belief the item is capturing, and that all participants are thinking about the item similarly. This also helps us evaluate whether people's perceptions are accurate, for

example, we recommend specifying the use conditions in risk perception items, things like duration of use and frequency of use, such as every day, dual use, exclusive use, et cetera.

When measuring any psychological construct, including recall, recognition, knowledge, and risk perceptions, it is critical to ensure that the measures are valid, given that the constructs are not directly observable. Validity means that a measure is a meaningful reflection of consumer understanding, that is, people who understand the risks and the modified risk information better will score more highly on the measures than will people who understand the modified risk information less well. We describe this further in the TPPI study guidance that I mentioned previously. When evaluating the validity of measures of consumer understanding, we consider factors such as face validity, meaning the extent to which the measure appears

on its face to tap into the construct and lack bias in terms of how it is written; we consider whether the items were cognitively tested to determine whether people similar to the study population correctly interpret what the items are asking and how to express their responses, we also consider whether the items were previously used in published literature that demonstrated their validity by finding expected statistical associations with validated measures of other constructs, and we consider whether the applicant conducted their own such validation research on the items.

So lastly, before jumping into the questions that we have for the Committee, here's some additional miscellaneous considerations. First, FDA's evaluation of consumer understanding and MRTPAs has been focused on the adequacy of people's understanding after viewing the modified risk LLA. We have not applied specific predetermined thresholds in terms of the

percentage accuracy that we need to see on given questions. We have taken a holistic view that considers everything we know about the product, the LLA, the research, and the potential consequences of any potential misunderstandings that we see, if any. In addition to assessing the sufficiency or adequacy of people's understanding, we have also considered whether viewing the modified risk LLA improved people's understanding, such as by correcting some of the entrenched preexisting beliefs that people may bring with them.

Related to this, we acknowledge that people have preexisting beliefs and perceptions about tobacco products, and that they bring these with them when they view modified risk LLA, for example, many U.S. adults perceive that all smokeless tobacco products and snus are equally as harmful or more harmful than cigarettes, and we recognize that such beliefs can sometimes be resistant to change through

exposure to new information in modified risk LLA. Relatedly, we recognize that people may respond differently to LLA when they view the LLA a single time in a brief, single session experiment or survey, compared to consumers who view LLA repeatedly in the real world as they come into contact with the full marketing campaign. Lastly, we are cognizant that different types of misunderstandings can have different implications across different groups, and we have tried to take that into account. For example, if someone is not an intended user of an MRTP, for instance if they are under the federal minimum age of sale of tobacco products, we would be more concerned if they underestimated rather than overestimated the harmfulness of tobacco products.

So I want to quickly give an overview of the four questions before jumping into the discussion. The first question that we have for the Committee is about this potential framework that I mentioned a moment

ago. So we presented a potential framework for conceptualizing what aspects of consumer understanding should be demonstrated in MRTPAs, and we want to know what the Committee thinks of this potential framework and whether you would suggest modifications. The second question is about the fact that most studies of consumer understanding involve presenting the LLA to participants as part of a controlled laboratory experiment, whereas in the real world, consumers could be exposed to LLA repeatedly and in various advertising formats, and we'd like to know whether the Committee expects consumer understanding to differ between real world and experimental settings, and if so, how we should be accounting for this in study designs and evaluations of experimental studies, and then more broadly, what does understanding in the real world look like, and how could CTP and applicants monitor this understanding as part of their PMSS?

The third question is that there may

be unique consumer understanding considerations for the intended and unintended users of an MRTP, and so should consumer understanding be assessed differently for this various groups? What are possible red flags that indicate consumers are misled or not understanding, and how could those red flags be measured? And then the final question, consumers bring with them preexisting beliefs that affect how they interpret claim information and how they answer survey questions, so how, if at all, should FDA take these preexisting beliefs into account when assessing and evaluating consumer understanding of claims? So I'll go back to the first one, and then turn it back over to Dr. Delnevo.

CHAIR DELNEVO: Thanks, Alex.

(Applause.)

CHAIR DELNEVO: Just one kind of clarifying question is, this is going to hopefully inform future MRTP applications, is that right?

DR. PERSOSKIE: Yeah, I think that's right, I think what we're looking for is to really -- kind of building off of what we had talked about earlier, which was in the context of the single application, sort of more broadly, the approach that FDA is taking to evaluate consumer understanding, what is the perspective of the Committee on that, are there different things we should be considering? And that then can be used to inform not just us, but also the regulated industry and kind of the types of evidence that we're looking for and how we might go about that evaluation. So yeah, it's really like more programmatic in terms of the approach that we're taking around this topic for MRTPs.

CHAIR DELNEVO: And I guess a related question is, there are renewals in the pipeline, right? Like this is the first, but there are other products as well, maybe the next one is coming up too soon for the manufacturer to potentially incorporate some of

those things, but could there be, maybe it's just a comment, that there's an opportunity to pivot for the remaining products to incorporate some of these kind of best practices that folks are going to be discussing today.

Scout, I know you need to leave soon, so --

DR. SCOUT: Thank, yes, I appreciate it, I'm sorry, I do have another federal thing I have to leave for immediately. But to quickly kind of say responses to the questions, first of all, discussion question number one, yeah, I think another piece should be -- is adding and understanding the broader impact of this MRTPA aside from just in that item, but in the real world scenario where we're bombarded with a lot of information.

So what are the contextual, what are the placement impacts, different things like that I think should definitely be considered, and then that really rolls into discussion question number two, yeah, I think we should be

using real world scenarios instead of laboratory scenarios to understand people's conceptualization in understanding this. Things would be like VR experiments or VR scenarios that people can be immersed in, like what if you're in a convenience store and you're seeing these different types of risk factors, is something that could be very simple, and then how can you monitor it in the future? Presumably they're going to have layers of these that continue to stack on top of each other, so I would actually consider as you do the later testing, add the previous ones in that actual scenario, and then occasionally go to an offshoot study where you go back to the previous one and figure out whether it's still having the impact it is intended, and then also explore, as the future one emerges, whether in the layering of all these different warnings, people are understanding the graduated risk successfully.

Next one, number three. Yes,

definitely for the various populations we have to understand. Some examples would be that youth obviously have different types of reactions to risk scenarios, and we understand that you know, the tobacco industry already put out youth warning labels that look like they were warning youth away, that were actually market tested to realize that they enticed youth, we also would anticipate then populations where there's problems with the government, like the queer population or the Latine population, that we might have a different kind of reaction to government warnings or government perceived warnings on labels, so definitely needs to be populations assessed.

And then for number four, I think you obviously need to assess preexisting beliefs before you do any kind of research, and then if you make the research a little bit more like clinical trials with an intervention and a non-intervention comparison, I think that would

ultimately make it stronger. And I understand that there's concern that all these things offer a greater regulatory burden for the tobacco industry, but we are dealing with the public health burden of lite cigarettes to this day, so unfortunately I have little sympathy for the regulatory burden the tobacco industry caused us to need this level of oversight with all possible future risk information. With that, sorry, got to go.

CHAIR DELNEVO: All right, so let's spend some time talking about discussion question number one, what do folks think about the potential framework with these three components, is there anything missing or would you suggest any modifications? Olivia.

DR. WACKOWSKI: I think the framework is good, I think it makes sense, I think it's pretty consistent with what has been viewed so far. I think if we want to consider potential additional things to think about, it might be relevant to assess understanding of

who the intended audience of the claim is, do adult smokers perceive that the claim is for them, do youth who are exposed to the claim perceive that it is not for them, do they perceive that it is for adults who use cigarettes? So I think that might be something relevant to assess, and you might see differences based on claim language. You know, if the claim has switching completely language, that might be more of a clue about who the intended audience is then, just use instead of. Thank you.

CHAIR DELNEVO: Lucy. We might have a ping pong between the two of you, was my prediction.

DR. POPOVA: Well I was really excited that this was included, and I commend the team on developing the framework and asking these good questions. I appreciate that there were -- it kind of went straight from understanding to operationalization, but then there was a little bit of conceptualization

buried in there, and I think conceptualization should be up front. So what do we mean by understanding? And this is kind of, you guys got to that part, was is it just comprehending, meaning I understand what this claim says, but I don't agree with it, or do we want people to agree and believe, which is where we're talking about persuasion.

And this goes to different levels, and not just -- and if we go deeper, there's more than just superficial belief, where like, I know smoking causes cancer, versus -- Delnevo, his work done, where the deep knowledge which is do you know if you get lung cancer diagnosis you have less than three years to live? And do you know how it would feel to tell your kids you have cancer?

So like that kind of stuff is very different, different level of understanding. And I think just going back and just inserting conceptualization earlier might be really helpful, just in that -- and it might be fine

that we are actually limiting it to just superficial, because you're not going to get, with these claims, exposure, maybe on the website, kind of self-exposed, we probably won't get to that deep level of understanding at all, but we do need to know what affect do those claims have? And for that, we have -- and I think this framework fits nicely to see, okay, how do we measure all of those things, because we might not need a criteria on which we need to match, but we do need to have good measures to see what those claims do.

DR. RIGOTTI: I guess one thought I had was, would you ask the questions in a way that made it clear that the risk or the behavior being described affects me, as opposed to affects people?

DR. KAUFMAN: Well, Alex might want to chime in --

DR. PERSOSKIE: Sorry, yeah. I believe that was on one of the slides, but I didn't really focus on it. But yes, yeah, for

risk perception measures, it's generally recommended that you ask about a person's own risk, because they might recognize a risk for other people but not themselves. No, no, yeah, I did not focus on it.

DR. KAUFMAN: There's a lot of kind of best practices for survey methodology on assessing harm perceptions of products, but my question is, this first bullet says risk or exposure. Could it be also risk and exposure, possibly, depending on the modified risk tobacco product and the claim that it's making? And then I know on an earlier slide, Alex, on the second bullet point you mentioned cessation, and on the first slide you sort of threw in nicotine replacement therapy, and I'm wondering what the thoughts are of FDA around assessing perceptions of modified risk tobacco products compared to medicinal, over-the-counter pharmaceutical products for cessation?

CHAIR DELNEVO: Piggybacking on that for a minute, Annette, is there's also just

general misperceptions about nicotine and health risks, and that would be -- we see that also in the NRT space as well, is a resistance to using NRT because of misperceptions about the dangers of nicotine. So I think that's a good point.

DR. KAUFMAN: Yeah, so maybe how does NRT fit into this framework? Or does it, because you're the Center for Tobacco Products, you're not SEER, but it's very relevant I think when talking about these products.

DR. PERSOSKIE: Yeah, that's an important consideration for sure, because we want to make sure people aren't using MRTPs instead of using the products that have been shown to be safe and effective.

CHAIR DELNEVO: Risa.

DR. ROBINSON: Yeah, I'm wondering, maybe you've already done this, but have you brought in a focus group of users just to kind of understand the language that they're using and kind of where they're coming from?

DR. PERSOSKIE: Are you asking about research specifically done by FDA? There's a lot of literature and research out there on, yeah, talking to people about -- and also done by applicants who have submitted MRTPAs, they have sometimes included that those qualitative phases in either developing their modified risk LLA, getting some like initial kind of qualitative responses to it, and also there's been cognitive testing of different items that ask people about what they think about products as well, to make sure that people were able to answer the questions in a way that would accurate reflect what they really think.

CHAIR DELNEVO: We're going to actually move onto the next question. So in most studies of consumer understanding of modified risk LLA, participants viewed the LLA as part of a controlled laboratory experiment whereas in the real world they would have been exposed repeatedly and in various advertising formats. And so we're being asked to consider

would we expect the consumer understanding to differ between the real world and experimental settings? If so, how should we account for this in study designs and what does our understanding of the real world look like, and how could CTP and applicants monitor consumer understanding as part of a post-market surveillance following an authorization?

DR. POPOVA: Sure, I can kick us off. I think it is reasonable to expect that there will be differences, and this is the same thing if we would think in terms of how we test messages, like smoking prevention messages where we have experimental studies at the early studies, we see effects on those are usually bigger effects than when we release a campaign in the real world. People see it, it gets messier, the effects are generally smaller. And there's a lot of literature on how do we evaluate campaigns in the real world versus in the lab and how to do that, so just building up on all of that, and I would say measure the

amount of exposure, and see how that relates to the actual, how it's marketed. So if it's only marketed very small, but you have a lot of exposure, where's it coming from? Or vice versa, if there's a lot of marketing happening, but people are not reporting exposure, what's happening here?

And then how this exposure relates to people who see very little, what's their belief, how this differs with people who are really heavily exposed. Kind of CDC's standard is like 12 exposures in like four months to see, okay, do we have that level of exposure in the real world, and how that effects, and then, very importantly, it would be good to also measure, not just, this is called the one way flow, but there's also a two-step, or a two way, where not only do you get information directly through this message, but you talk to people. You see other people may be posting on social media, and so this need to be taken into account, and this interpersonal conversation is

happening that will change beliefs and perception as well, so accounting for that. And again, it's just this is the way campaigns are evaluated in the real world and the same approach could be used here for evaluating this real world impact of modified risk statements.

CHAIR DELNEVO: Yeah, I would say also along those lines, I mean it really is just about doing broad surveillance, and so for example, in the path study, just asking participants in path, just documenting just the general level of exposure to these types of messages that are out there, so that you have some context, right, from a generalizable sample, versus a more kind of in-depth focus that you might see in a post-market surveillance study looking at consumers of those particular products. So I agree with Lucy that you're going to get exposures, they're going to be different in the real world, and so being able to monitor exposures in the real world I think is an additional

ancillary piece that needs to happen in a robust survey or surveillance sort of way. Mignonne?

DR. GUY: Yes, thank you so much. First of all, I'd like to applaud the FDA for considering this deductive framework and for presenting the questions to our Committee, because I think they're really important and could have tremendous implications for improving communications and messaging to the public. One of things that I wanted to ask, or delve a little bit deeper about before Scout did the mic drop and left, was, I'm curious about specific populations, right?

Because part of the issue that we have right now -- and I don't think this is a surprise, these are data that are published and we can see, is an erosion of trust in various entities on the part of the consumers or the general public. And we see there's a greater erosion of trust and distrust for certain types of messaging across different populations, and

I'm thinking specifically within black populations, because that's what I focus on. How -- and part of this has to do with all of this sort of white noise and the other noise that's happening within the broader public related to messaging and hostility towards these populations -- or perceived hostility towards these populations coming from various entities.

My question for you is how can we account for or address this broader context? It's delving a little bit deeper into what Scout was saying, and I realize that it's slightly digressing from the typical conversations about methods and things of that nature, but I'm really shifting more into the real world and how individuals consume information, but it's not in a vacuum, right?

They're bombarded with multiple types of information, yes, about these types of products that we're focusing on specifically, but we have to account for the broader context

of the types of information they're receiving more broadly that may be relevant or targeted towards specific populations. I hope that was clear, and if it was not, feel free to ask questions.

CHAIR DELNEVO: Does anyone have any additional -- because we're starting to delve into things that are, we're now talking populations, and we're getting -- it's kind of hard to kind of isolate the thoughts around single discussion questions. So Olivia, did you have something to add to question two? And if anyone else has something to add to question two, then we'll move on to question three, and then when we get to question four, everything is open for discussion, but I want to make sure we get through the questions.

DR. WACKOWSKI: I just wanted to piggyback on Lucy and Cris' comment about exposure measurement, I think it's important to measure exposure to these messages and could also be relevant in real world studies to

measure these same consumers' exposure to other messages that might sort of conflict with what the message is saying, because that might ultimately also impact their perceptions. So whether it's exposure to tobacco prevention ads or campaigns or cessation messaging might also ultimately impact their perceptions.

CHAIR DELNEVO: Annette?

DR. KAUFMAN: Just one last comment in terms of the question, and Olivia as you were talking it made me think that perhaps what is ultimately needed in addition to what's listed here is pre and post and continuity and the types of questions that are asked over time. So if an MRTP is going to be released in January, the assessment of knowledge, understanding, perceptions, and all the other constructs that you want to get at must be addressed and assessed in the same population level that needs to carry pre and post release of the MRTP claim, or MRTP.

CHAIR DELNEVO: Just to clarify,

Annette, are you suggesting that before an MRTP is made and the manufacturer can use it in their marketing materials that there are some baseline measures that are obtained prior to that?

DR. KAUFMAN: I think that would be ideal, right, because then you would be able to understand how the exposure in the real world, once the claim is out in the open in the real world, you'd be able to track if any impact is happening on the population level.

CHAIR DELNEVO: Risa?

DR. ROBINSON: Thank you. In my mind, one of the differences between experiment and the real world is whether they actually read what you're providing them. So in an experiment they're going to read it because you're asking them to read it, right, in the real world if you give them a big thick pamphlet like comes with your medication, what's the chances that they actually read that? That's my comment.

CHAIR DELNEVO: Maria?

DR. GOGOVA: And also I would like to hear your perspective, like how to disentangle the comprehension of the claim, whether it's truthful, accurate, and not misleading from the perception, which is influenced by many other factors, like we're talking about a preconceived notion of a product not being less risky than conventional cigarettes. It's the peer pressure, it's the motivation of the individuals, it's the attitudes and beliefs. How can we take these into account when we are talking about real world situations? So maybe it's not the misperception of the claim as much as the internal beliefs of the individuals which will impact how they will, you know, explain the claim to themselves.

CHAIR DELNEVO: So in the context of those post-marketing surveillance studies, I think it would be a good recommendation for the manufacturers when they're designing their

studies to include relevant covariates that are known to be associated with either uptake or quitting, so that they can be controlled for in the analyses.

We'll move on to question three, but that doesn't mean that folks can't come back to one and two. So as covered in the presentation, there may be some unique consumer understanding considerations for the intended and unintended users of an MRTP. Should consumer understandings be assessed differently for various populations and what are possible red flags that indicate consumers are misled or not understanding, or how those red flags be measured.

So I'm going to jump in there. So A, with regards to B, I think monitoring sales data and continuing to monitor brands that are being used by various populations and looking for upticks, unexpected upticks in initiation and adoption of certain products, and if they're for the right groups I think makes a

lot of sense. And then just a comment with regards to populations, you know, earlier on -- and I understand the distinction between naïve users who more often than not are youth, right, and then current users of tobacco, but I also want to remind folks that youth are also current users of tobacco and so could potentially be audiences for some of these messages if in fact it helps move them down or risk containing or quitting altogether. They're not mutually exclusive groups, and I think we have to remember that. Lucy?

DR. POPOVA: I want to caution against measuring differently for different populations, because then you won't be able to compare directly and see are we even further in increasing our disparities if we have measures that cannot be comparable between the two? For red flags, I would say make sure we do qualitative research, because that's when a lot of stuff you never even thought about comes up, and then misperceptions that people have are

really interesting, and you can just show them the message if they're never seen it, start by just asking, what have you seen communicated about this product out there, and then you'll hear some things that they say which is not anywhere, but they come up with this information. Then when you show, they often misperceive, so that qualitative research is really valuable for identifying those misperceptions, and then later on you can plug those in and do surveys and just standard stuff.

And also make sure doing social media monitoring, because that's where, discussions on Reddit in particular, users oftentimes come up in there, and like on YouTube videos where they talk about how to make a product less risky, for example, or whatever, evading regulation or other things, so social media is a good source of information on that.

CHAIR DELNEVO: I'll move on to

question four. So consumer and study participants bring with them preexisting beliefs that affect how they interpret claim information and answer survey questions. For example, the majority of the public believes that smokeless tobacco products are equally as harmful or more harmful than cigarettes. How, if at all, should FDA take preexisting beliefs into account when assessing and evaluating consumer understanding of proposed MRTP claims? Maria?

DR. GOGOVA: I think it can be a useful tool to really ask before you even expose the consumers and participants in the studies to question their preexisting beliefs, because it can help you to put the actual data into the context, you know is it because of the claim or because they have their preexisting beliefs? The same is about believability, if people believe the claim, you know, you might be seeing they're understanding questions or responses, so I think it's useful to

contextualize the actual results.

CHAIR DELNEVO: And I think some of the ideas, both in Alex's presentation and also brought up by the folks here today, you know, methodologic approaches, you know, obtaining a baseline before the MRTP claims are out there in the wild would be an important thing and would help address, at least, this concern that there are preexisting beliefs, and then randomize -- I don't have a star six on mine. Or, as in Alex's presentation, split sample randomized experiments, where participants, half see the MRTP claim and half that don't, and so you know, even if you don't have baseline data, those that didn't see the MRTP claim can be used as a proxy for what some of those baseline beliefs might be. And so I think methodologically there's some approaches that can be used. Olivia?

DR. WACKOWSKI: Yeah, I agree with those comments that Cris just made. The only thing for like a brief experimental study, I

always consider not necessarily asking preexisting beliefs before exposure to the claim, because you don't want to prime them or influence how they're going to answer the questions right after, but I think if you have that in the control group then you have that proxy for it, and certainly in sort of the population level studies you have a lot of time in between the assessments, so, yeah.

CHAIR DELNEVO: Recognizing that it's been a long day I'm actually going to turn to FDA and ask, have you gotten some useful information from these four discussion questions, or shall we just keep trying to discuss?

DR. APELBERG: We've conferred. Yes, no, this has been really helpful, insightful. Like you said, it has been a long day, but I think it's been a lot of, you know, the sort of topics you guys are raising are things we've been considering ourselves. So yeah, it's helpful. I don't know Alex or Erin

if there's anything else specific you wanted to touch on?

DR. PERSOSKIE: Okay, I'll say one thing. So one thing, this wasn't necessarily really like the motivator for the question here, but I feel like one thing that maybe gets somewhat or maybe got a little bit lost in the discussion for the related to consumer understanding for the Swedish Match application was just how surprised a lot of the U.S. public would probably be if they heard kind of the epidemiologists and the medical, people who are medically trained and are able to view the epidemiological data. I know there is some disagreement about other things that maybe are not captured or the timeframes of studies, but is it, like should we be looking at, like, how big is the gap between what the average potential user for the product thinks, or current user, or dual user of the product thinks about its risks, and what someone who is an epidemiologist or another kind of specialty

who focuses on tobacco research, what they think, and should that have some sway in kind of how much we think it could benefit someone? If we think there is this big gap, basically.

CHAIR DELNEVO: So are you talking about providers, potentially, as a population that you might want to follow up on? Or did I misinterpret that?

DR. PERSOSKIE: Well, not necessarily.

CHAIR DELNEVO: I mean we've done a study showing people the IQOS ad with and without the MRTP claim, and the MRTP claim changed providers' willingness to endorse the use of the product to someone who smokes cigarettes who is not willing or able to quit, right? And so potentially, right, the population targets for some of these MRTP messages might extend beyond the consumers themselves. Is that what you're getting at, or no, am I getting it wrong?

DR. PERSOSKIE: I was getting more

at -- so, presumably the modified risk information could seem to have like more potential to change what a consumer thinks because they're already so far in one direction in terms of their perceptions of a product, and then what say, an epidemiologist who has studied it extensively would say, and in the case where there is that really big case, what should we kind of give that, should that influence kind of how we evaluate the MRTPA? Kind of the potential, because you might think there's more potential there for like long term consumer benefit to having access to, you know, clear information about how the product risks compare, or should that play a role in our evaluation?

DR. RIGOTTI: So I'm not sure I understand your question, but let me try. Which is that -- so using this example, if the public thinks that smokeless products are as bad as smoking cigarettes, but the MRTP claim is that they're less harmful than using

smokeless, that a particular brand is less harmful than other smokeless tobacco products, is, so does it matter that they overestimate the harm of tobacco, of smokeless? Because as long as they think it's less than smokeless, then it's going to be less than cigarettes, even if they're incorrect about the cigarettes. So that's where I'm confused what you're asking.

DR. ELLIS: So I'm a visual person, so just bear with me. I picture basically like a bell curve of some kind, and if you've got people really far, like in the negative, like they don't even have a neutral belief, they have a belief that smokeless is like equally or more harmful than cigarettes, and we're trying to see the effects of a claim that is so far outside their preexisting conceptualization of what that product is like, should we take that into account, and if so, how, when we are evaluating whether a level of understanding is adequate?

DR. RIGOTTI: I see. So you would have a bigger job, because you're going from a negative to an even more further along, I guess.

DR. ELLIS: Yeah, the claim would have a harder job, but for us, you know, we're mostly focused on, what do we do in those situations, how do we, if at all, take that into consideration?

CHAIR DELNEVO: Risa?

DR. ROBINSON: I'm wondering, is it possible to develop -- there's a continuum of risk, right? Or have you already articulated that continuum of risk, and is it possible to present the user with that continuum and have them say what do you currently believe, and now what do you believe after the advertisement, and then report the delta, and then that delta becomes the outcome measure as opposed to the absolute where you want to bring them, and then you could at least see people moving along the continuum as a result of the advertisement.

CHAIR DELNEVO: Lucy?

DR. POPOVA: This goes back to my earlier point about the need to clearly conceptualize what are you talking about when you talk about understanding, because this, you're talking about persuasion, and change in beliefs, which is different. And that one statement is likely not going to get you there, multiple exposures to the statement might, but it needs to come from different sources, there's a lot more needs to be done. With tobacco, persuading how harmful cigarettes are, we've been doing this for a long time, and we're still -- my argument is like, even though people always say like they're very harmful, very harmful, but they still don't have that very deep understanding. And so in that sense, it may be worse -- do measure it in different ways. Do they understand it, kind of like Alex was talking about, is there understanding, is it comprehension? Do they understand what the statement says? Do they agree with it, is a

different story completely, and moving their agreement and belief is going to be, probably not going to be as one exposure.

And then another thing I wanted to point out is like, we keep focusing on the modified risk communication, but it's really -- we always measure in comparison to cigarettes, and so emphasizing the risks of cigarettes, that might be another way of kind of reducing, so it's not just two things. It's like you bring up the perception of cigarettes even if perception of risk of smokeless stays here, you can have a bigger discrepancy. And so we can work in two directions and measuring both should be useful, because we also don't want them to think like oh, this is less harmful, but where does the perception of cigarettes go as a result?

CHAIR DELNEVO: Olivia?

DR. WACKOWSKI: I agree with all those comments, especially the difference between sort of the understanding of it on its

face as belief of it. I think we also just need to be thoughtful of our expectation of the ability to change the belief, not only based on the number of exposures but who the claim is coming from and that impact on the believability of it, as well as the fact that they're seeing it with the warning label information, and that, you know, to some extent that might feel contradictory.

Also, I was going to say earlier that in terms of study designs, I think potentially including the use of some open-ended questions that could even follow up some close-ended questions could also be another way of understanding perceptions a little bit more in some cases. The issue with the switching completely kind of wording in claims, we talked a lot about that being a sort of difficult language and difficult to communicate, but it's also difficult to measure, to find the right measure for that I think is really challenging too, and I think the applicants have a first

stab at it, but if FDA can provide guidance on good ways to do that as well, I think that will be helpful.

CHAIR DELNEVO: I think the suggestion for cognitive testing of the messages as well is super important, and not just of the messages but then of the survey questions that are asking about the messages are going to be important, and having different population groups kind of captured in that I think is also important. We know that individuals who are receptive to harm reduction and switching often do quite a bit of research on their own before, right, and so they tend to be more knowledgeable about the products and then also less likely to have incorrect perceptions about the risks of the products and nicotine, and so you're preaching to the choir to that group, but then understanding and making sure that the other populations of interest also understand the questions, I think is important. Sven?

DR. JORDT: I think it's a specific challenge if consumers need to, yeah, have to compare two products, but both have an MRTP, right? So for example, how do they compare a very low nicotine cigarette now with General Snus, right, where both have claims they are healthier than let's say cigarettes, right, because the VLN you say you smoke less, but then you're probably less addicted, however then with General Snus, it has more nicotine, you probably will use it indefinitely, right? So I think there are specific challenges here, it will be difficult to really overcome if consumers have to compare products where both have an MRTP.

CHAIR DELNEVO: All right, keeping an eye on the time, I'm not going to have us go round robin for final comments, but I am going to let anyone that hasn't yet spoken or feel that there is something additional that they want to say about these four discussion questions, I want to give everyone a chance to

make a final comment. Yes.

DR. MADL: I wanted to say something with respect to the first question, just in terms of consideration of potential additional characterization or contextualization, just to piggyback on a previous comment of reduced exposure, reduced risk, or the combination of the two. And when you have a product that has lower exposures to potentially harmful constituents, like what are those constituents, are they carcinogens, and how does that compare to combustible cigarettes? I'm from California, we have that language in our labeling in the state when we have products that contain carcinogens or reproductive or developmental toxicants to specify what the chemical is and what the hazard is. So some additional characterization or contextualization on exposure and what the potential risk is of that exposure might be helpful.

CHAIR DELNEVO: Annette?

DR. KAUFMAN: So I think a suggest would be to keep it simple and keep your eye on what the goal is of the study, or of what you need to know, and the questions need to map onto what information you need. So whether that is specifically knowledge, or whether that is specifically risk perception, not couching that and being accurate or inaccurate, it is a perception, not knowledge, and also product harm. And product harm could be accurate or not accurate, depending on how you want to frame it, but assessing the questions that asses those things need to map onto what information FDA needs to make a decision.

CHAIR DELNEVO: Any final comments? Going once, going twice. I'd like to give FDA a chance to make any final comments before we adjourn the meeting.

DR. APELBERG: Thanks Cris. I just really want to thank everybody here today for sticking with us to the end. It's been a long day, but it's been a really productive one.

We've had a lot of fruitful discussion both with regards to the Swedish Match renewal and the specific evidence presented there, but then also with regards to this broader conceptualization of how FDA has been thinking about consumer understanding. So just a big thank you to the Committee for all your work here, thanks to the applicant for doing the work that went into the preparation and your presentation, big thank you to our CTP staff for all their work, the work that's already happened and will continue to happen around MRTP. We appreciate the open public commenters and of course the attendees, both here in person and online.

So we're really pleased that we were able to come together to have this meeting. As Brian mentioned, we haven't had a TPSAC meeting on MRTP in quite a number of years, so it's really, we're excited that we're able to get back together. It's been really productive, and we look forward to just continuing to

engage with the Committee around these types of topics. So once again, thank you to everybody who participated and safe travels home.

CHAIR DELNEVO: Thanks Ben. I want to also thank the Committee members, our consultants, Swedish Match for their presentation, the individuals making the comments during the open public hearing, FDA, and a special thanks to Sirena and Janice for taking care of the Committee. And with that, the meeting is adjourned.

(Applause.)

(Whereupon, the above-entitled matter went off the record at 4:17 p.m.)