UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR TOBACCO PRODUCTS

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TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

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September 14, 2018
8:00 a.m.

FDA White Oak Conference Center
Building 31, Room 1503
10903 New Hampshire Avenue
Silver Spring, MD 20993

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M E E T I N G

(8:00 a.m.)

DR. MERMELSTEIN: Good morning. If anyone is on the phone, if you could please mute your phone. We're getting a lot of extraneous noise from that, thank you.

Good morning, I'm Robin Mermelstein, Chair of the Tobacco Products Scientific Advisory Committee. Thank you all for joining us today in the continuation of our discussions. I'm going to make a few statements and then we will introduce the Committee members.

For topics such as those being discussed at today's meeting, there is 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 me, as the Chair, so we look forward to having 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 topics at hand take place in the open forum of the meeting. We

are aware that members of the media may be anxious to speak with the FDA about these proceedings, however, FDA will refrain from discussing the details of this meeting with the media until its conclusion. Also, the Committee is reminded to please refrain from discussing the topics during the breaks.

Thank you.

MS. COHEN: The Center for Tobacco Products of the Food and Drug Administration is convening today's 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, healthcare professionals, a representative of a state government, a representative of the general public, ex-officio participants from other agencies, and three industry representatives. With the exception of the industry representatives, all Committee members are special government employees or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this Committee's compliance with applicable federal conflict of interest laws and regulations is being provided to participants

today in today's meeting and to the public.

The purpose of today's meeting is to discuss modified risk tobacco product applications submitted by R.J. Reynolds Tobacco Company for six products: Camel Snus Frost, Camel Snus Frost Large, Camel Snus Mellow, Camel Snus Mint, Camel Snus Robust, and Camel Snus Winterchill.

Accordingly, this meeting is categorized as one involving a particular matter involving specific parties.

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 screened 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. William Andy Bailey, Willie McKinney, and David Johnson are participating in this meeting as non-voting representatives. Dr. Bailey is acting on behalf of the interests of the tobacco growers; Dr. McKinney is acting on behalf of the interests of the tobacco manufacturing industry; and Dr. Johnson is acting on behalf of the interests

of the small business tobacco manufacturing industry. Their role at this meeting is to represent these industries in general and not any particular company.

Dr. Bailey is employed by the University of Kentucky, Dr. McKinney is employed by Altria Client Services, and Dr. Johnson is employed by National Tobacco Company. Thank you.

DR. MERMELSTEIN: We're going to introduce the Committee members. Again, I'm Robin Mermelstein. I'm a professor at the University of Illinois at Chicago. And we'll go this way today.

DR. OSSIP: Good morning, I'm Deborah Ossip, and I'm a professor at the University of Rochester Medical Center.

DR. WANKE: I'm Kay Wanke at the Office of Disease Prevention at the National Institutes of Health.

DR. KING: I'm Brian King. I am a Deputy Director of the Office on Smoking and Health at the U.S. Centers for Disease Control and Prevention.

MS. BECENTI: I'm Alberta Becenti. I work with the Indian Health Service, public health advisor.

DR. BAILEY: Andy Bailey, University of Kentucky.

DR. JOHNSON: David Johnson, National Tobacco,

representing the small tobacco manufacturers.

DR. McKINNEY: Good morning, I'm Willie McKinney. I'm the Vice President of Regulatory Sciences for Altria Client Services, and I serve as the Tobacco Manufacturing Industry Representative for this Committee.

DR. HOLMAN: Good morning. Matt Holman, Director, Office of Science at FDA's Center for Tobacco Products.

DR. KITTNER: Deirdre Kittner, Deputy Director in the Division of Population Health Science at CTP, and I'm also the technical project lead for these MRTPAs.

DR. WACKOWSKI: Olivia Wackowski, assistant professor at the Rutgers School of Public Health.

DR. BLAHA: Good morning. Michael Blaha, Director of Clinical Research, Johns Hopkins Ciccarone Center for the Prevention Heart of Disease.

DR. BIERUT: Good morning, I'm Laura Bierut, Professor of Psychiatry at Washington University in St. Louis.

DR. WEITZMAN: Good morning, I'm Michael Weitzman, professor at the New York University School of Medicine.

DR. DUFFY: Hello, I'm Sonia Duffy, and I'm a professor at Ohio State University.

MS. COHEN: Caryn Cohen, Designated Federal Officer for

the TPSAC.

DR. MERMELSTEIN: And do we have any Committee members on the phone this morning?

MS. HERNDON: Yes, this is Sally Herndon. I am the government representative on TPSAC. I am the head of Tobacco Prevention and Control for the Division of Public Health in North Carolina.

DR. THRASHER: This is Jim Thrasher. I'm a professor in the Arnold School of Public Health at the University of South Carolina.

DR. GIOVINO: Hi, Gary Giovino, professor and chair at the University of Buffalo School of Public Health and Health Professions.

DR. KOZLOWSKI: Lynn Kozlowski, professor at the School of Public Health and Health Professions at the University of Buffalo.

DR. MERMELSTEIN: Okay, I believe that's it for our Committee for today. We're going to start with an open public hearing session.

Both the Food and Drug Administration 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's important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with the Sponsor, its product, 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 the meeting.

Likewise, FDA encourages you, at the beginning of your statement, to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationship at the beginning of your statement, it will not preclude you from speaking. The FDA and this Committee place great importance in the open public hearing process. The insights and comments provided can help the Agency and this Committee in their consideration of the issues before them.

That said, in many instances and for many topics, there will be a variety of opinions. One of our goals today is for

this Open Public Hearing to be conducted in a fair and open way where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore, please speak only when recognized by me as the Chair. Thank you for your cooperation.

We're going to now begin with our first speaker. Each speaker will have no more than 6 minutes for their comments, and we'll start with Dennis Hennigan for the Campaign for Tobacco-Free Kids.

MR. HENNIGAN: Madam Chair, members of the Committee and FDA staff, let me first clarify that I am not Matt Myers. I'm much younger than Matt Myers. Matt was a little under the weather today, so the Committee has allowed me to pinch hit for him, and I appreciate it very much. I am the Vice President for Legal and Regulatory Affairs at the Campaign for Tobacco-Free Kids, and I have no financial relationship with the Applicant.

So thank you for this opportunity to address the Committee as it considers this modified risk application for Camel Snus products.

Before turning to several key issues regarding the application, I'd like to address a threshold issue which I

think deserves attention, and that is the relationship between this proceeding and another important FDA initiative on smokeless tobacco.

Over 18 months ago, FDA published a proposed rule to limit NNN in smokeless tobacco products to a limit of 1 µg/g of tobacco on a dry weight basis, and the Agency estimated that in the first 20 years there will be 12,700 new cases of oral cancer avoided by this rule and 2200 oral cancer deaths would be prevented.

Now, the public comment period on this rule closed over a year ago and in our judgment this rule should have been issued in final form by now. Yet, FDA is now considering a modified risk application for a product that, according to FDA's briefing document, would not meet this standard. I suggest that it may not be a wise use of Agency resources, including TPSAC's resources, to consider granting a modified risk status to a product that appears to violate a product standard that FDA believes would save thousands of lives. Instead, I would urge FDA to issue the final NNN rule and require Camel Snus and every other smokeless product seeking modified risk designation to demonstrate that it meets this standard.

But on the assumption that FDA is prepared to go forward

with this modified -- to consider this modified risk application, there are several issues that TPSAC must evaluate with particular care and they have been posed by the questions that have been advanced by the FDA staff.

Under the relevant statutory standard, Reynolds has the burden to show that the product will significantly reduce harm to individual tobacco users and will benefit the population as a whole, taking into account both users and nonusers of tobacco products.

On the issue of individual harm, there is no doubt that smokers will realize a health benefit from use of Camel Snus only if they completely switch to the product. However, the high levels of powerful carcinogens like NNN and NNK in Camel Snus cast some doubt on the degree of health benefit realized even from complete switching. And although comparisons are difficult because the route of exposure to these carcinogens is obviously different for snus versus cigarettes, FDA's briefing document found that the Reynolds data "did not demonstrate a potential for reduced exposure from the six Camel Snus products as compared to cigarette smoke." So this is a key issue which requires careful attention by the Committee.

On the issue of population-wide effects authorizing these

modified risk claims, TPSAC is faced with a cluster of key issues. Let me highlight a few of them.

First, although Reynolds puts great weight on the Swedish experience, not only are the products different, but there are key cultural and market differences between Sweden and the U.S. that casts doubt on the utility of the Swedish data. Indeed, when TPSAC considered the Swedish Match modified risk application for Swedish Snus, it determined that the Swedish data did not provide relevant information on the likelihood that U.S. smokers would switch to snus.

Second, snus and other smokeless products have a track record in the U.S. and everything we know about their use in this country indicates they are not likely to have a beneficial population-wide effect even if advertised with modified risk claims. The studies show that smokeless users in the U.S. are more likely to switch to cigarettes than smokers are to switch to smokeless products. And studies also show a persistent pattern of dual use in the U.S. including dual use of these products which may actually sustain smoking. Indeed, Camel Snus has been marketed as a dual-use product in the past, allowing smokers to use tobacco where smoking is prohibited.

Finally, there is nothing in this application that

addresses the impact of modified risk claims on youth or the likelihood that those claims will lead to greater youth initiation of tobacco products. Moreover, Reynolds' marketing plan does nothing to ensure that these reduced messages will reach only adult smokers and not kids.

At a time when FDA is faced with an epidemic of youth usage of e-cigarettes, indeed the Commissioner acknowledged this epidemic this very week, and e-cigarettes being another tobacco product widely touted as less hazardous than cigarettes, TPSAC should be deeply concerned about Reynolds' failure to address the potential impact of its intended modified risk messages on young people.

DR. MERMELSTEIN: Thank you, Doctor.

MR. HENNIGAN: And thank you again for the opportunity to address the Committee.

DR. MERMELSTEIN: Thank you.

Our next speaker is Nicolas John from R Street Institute.

MR. JOHN: Good morning, my name is Nicolas John, and I am the Northeast Region Manager of the R Street Institute, a Washington-based nonprofit public policy research organization dedicated to free markets and real solutions.

Before I begin, I'd like to thank this Committee for

affording me the opportunity to present written and oral testimony. I would also like to thank the Reynolds American panel for their comprehensive presentation at yesterday's session.

My primary focus is promoting access to harm reduction tools for people who engage in risky behaviors. More specifically, exploring ways that tobacco harm reduction strategies can reduce the thousands of smoking-related deaths the United States continues to experience annually has been a major focus of our research. It is in light of that prior research that we urge the Food and Drug Administration to grant Camel Snus the status of a modified risk tobacco product.

Responsible for 480,000 deaths a year, cigarette smoking is the leading cause of preventable death in the United States.

While nicotine replacement products are available for those who wish to quit, they have not been terribly effective at transitioning smokers to complete cessation. Between 25 and 35% of smokers relapse within 6 months.

Alternative risk-reduced products represent a new and likely more attractive option for people who are either unsuccessful in quitting using traditional nicotine replacement or who might not otherwise quit smoking.

Unfortunately, in 2017, the study found that 89% of U.S. adults believe that smokeless tobacco was as harmful as combustible cigarettes. It is unrealistic to assume that even when an overwhelming majority of our population believes that smokeless tobacco products carry the same risks as combustibles, we will ever see the full potential of the benefits these undisputed reduced risk products carry. Nobody would switch from a product they are used to and want when they believe the risks are no different.

The best available research indicates that snus compares favorably to both combustible cigarettes and conventional snuff. Analyses of toxicant concentrations in snus products compared to conventional snuff uniformly demonstrate a significant reduction in concentrations of harmful chemicals in snus products.

It is also worth noting that in several studies both Swedish snus products and Camel Snus products were the comparators.

Warning labels have the ability to set the record straight. Studies have consistently shown that warning labels affect smoking behavior relative to change and quit attempts. Specific warning labels which detail toxicants further

reinforce the negative health risks associated with combustible tobacco use. Health warning labels are also a vital source of information and have the potential to reduce disparities in access to knowledge.

This is why it is so important that products such as Camel Snus are assigned labels that clearly state the lower risk compared to combustible cigarettes.

In light of the FDA's recent proposal to begin a dialogue that will eventually lead to cigarettes with reduced nicotine content, the levels that are considered non-addictive, it is necessary that the FDA approves products that can serve as acceptable alternatives to current smokers.

Thank you very much for your time.

DR. MERMELSTEIN: Thank you.

Our next speaker is Gregory Conley from the American Vaping Association.

MR. CONLEY: Good morning. My name is Gregory Conley, and I am fortunate enough to serve as the president of a nonprofit health advocacy group called the American Vaping Association, which advocates for sane and sensible regulation of primarily vaper products with the aim of maximizing the number of smokers that voluntarily choose to switch to reduced harm products.

I am here today because any action that the FDA takes on a product that has decades of epidemiology behind it with regard to permission to make truthful health claims that will have a long-term impact on the chances of a vaping company coming to the FDA with science but not decades of epidemiology and seeking to make a health claim. We stand today in full support of R.J. Reynolds' application because decades of epidemiology show that snus, when you disconnect the act of using tobacco, from lighting something on fire and inhaling it into your lungs, that is so much less hazardous than smoking, that even when you make baseless assumptions about excess risk, even when you make assumptions about gateways that aren't truly shown in the evidence, you still end up with a clear net public health benefit from telling the truth.

Now, myself and others were disappointed when TPSAC looked at the evidence on IQOS, the extensive clinical trials and biomarkers of harm, and still came to the conclusion that there's simply not the evidence to say that the product gives reduced harm to smokers who completely switch.

Some quotes from the IQOS hearing during the decision part of the day: "I don't think I'd be able to, in good conscience, say that this really has been demonstrated to reduce harm."

"The evidence showing impact on disease is lacking." "Have the studies actually shown disease is actually lower in the people who switch?"

Well, you had some doubts about IQOS, you didn't have decades of epidemiology on a similar product to look at, but here today the answer to all three of those questions, "Can we in good conscience say you should switch?" "Is the impact on lower disease, has that been shown?" The answer is yes. Can anyone today look at the Camel Snus products, look at the decades of epidemiology on similar products, look at the biomarkers and the animal studies presented by Reynolds and say that it is not true that a smoker who switches to Camel Snus significantly or greatly reduces their risk of lung cancer, can you in good conscience say that? Yes.

Can you in good conscience say that a smoker who switches completely to Camel Snus will lower their risk of oral cancer? Yes, absolutely you can say that.

In good conscience can you say respiratory disease and heart disease will decrease if a smoker completely switches to Camel Snus? Yes, you can, in good conscience, say that. And I won't bore you with the others, but less health risks. Fewer carcinogens. Less harmful, less risk.

Can you, as scientists, look at the evidence today and in good conscience say Camel Snus will benefit smokers who completely switch? The answer is yes.

Now, very briefly, I would like to address the FDA's report that came out earlier this week and it led to Bloomberg running a story saying oh, the FDA just showed that a substitute for cigarettes is no better than smoking, and that was based purely on product characteristics.

If you think of the hierarchy of scientific evidence, at the bottom of the pyramid you have epidemiology; we have the epi here. In the middle, you have clinical and preclinical studies; we have that here.

But the FDA moved to the very top of the pyramid, simply looking at product characteristics with no regard to what actually gets in the blood and what gets exposed to the user and concluded, based off of normal higher levels of metals and NNN and NNK, levels that were present in Smooth snus years before and the epidemiology on those products at the time, the levels of NNN and NNK were higher, don't show an increased disease risk.

So the FDA decided that just because this product is somewhat, just a little bit different from prior iterations

from Sweden, that somehow we can't possibly say that these products will lower disease risks. It simply does not make sense. And this idea that Reynolds needed to kill more mice in order to show the difference between what we know, the causes and harms of cigarette -- that cigarette smoke brings to rodents when tested, we already know that, saying they should -- needed to kill more mice, look at more and more certainty in the questions that are before you.

Can you, in good conscience, say that Camel Snus reduces lung cancer, oral cancer, respiratory, heart disease risks among smokers who switch? I won't bore you by repeating myself too much again, but yes, you can, in good conscience, say and agree with all the claims that R.J. Reynolds seeks to make today.

Thank you very much.

DR. MERMELSTEIN: Thank you, Mr. Conley.

Our next speaker is Greg Wilson from Altria Client Services.

MR. WILSON: Good morning, and thank you for providing me the opportunity to speak here today. I'm Greg Wilson, Managing Director of Regulatory Affairs for Altria Client Services, which provides regulatory affairs and other support to the

Altria family of companies. Those companies include Phillip Morris USA, the maker of Marlboro cigarettes; U.S. Smokeless Tobacco Company, the maker of Copenhagen, Skoal, and Bruton; John Middleton, the manufacture of Black & Mild cigars; Nat Sherman's, a premium cigarette and cigar business; and Nu Mark, an innovation company that makes products like MarkTen.

As evidenced by our different tobacco companies, we manufacture a wide portfolio of products spanning the continuum of risk, including products that we believe have the potential to reduce tobacco-related harm for adult smokers who are interested in alternatives to cigarette smoking. However, encouraging those smokers to switch to less risky products requires truthful and accurate communications from FDA and other stakeholders about relative risk.

Although I'm not here this morning to express any opinions on the merits of the Reynolds application, I would like to take a couple of minutes to talk about the importance of truthful and accurate communications to consumers.

Despite longstanding efforts by the public health community and others to persuade people to never start or quit if they do, millions of adults will continue using tobacco products. There are currently about 40 million adult cigarette

smokers in the U.S. Based on data from the FDA PATH Study, more than half or 22 million of those smokers are interested in satisfying but less harmful alternatives to cigarettes. For these consumers, appealing reduced risk products may offer a promising opportunity to reduce the harm associated with tobacco use, particularly cigarette smoking.

A strong public health consensus was formed that not all tobacco products present the same risks. Public health authorities, including FDA, agree that there's a continuum of risk for nicotine delivery with cigarettes at the highest end of that spectrum. The continuum recognizes that the harm caused by tobacco results from combustion and that noncombustible tobacco products have an important role to play in reducing that harm.

But smokers can't be expected to switch to less harmful alternatives if they don't have full and complete information including about the relative risk of any particular product, and the current regulatory system is preventing smokers from being told the full truth about relative risks of different tobacco products.

That imbalance in information is having real consequences as evidenced by the fact that there's currently widespread

misunderstanding among smokers as to whether there's a difference in risk among tobacco products. This is a case, even though the science is clear, that noncombustible products are safer than combustible tobacco products. Many smokers, though, still believe that the noncombustible tobacco products present the same or greater health risks as combustible products.

For example, our analysis of the FDA Path Wave 1 data shows that 45% of current smokers incorrectly believe that e-cigarettes are as or more harmful than conventional cigarettes. Further, almost 90% of current smokers incorrectly believe that smokeless tobacco products are as harmful or more harmful than cigarettes.

These misperceptions do have ramifications. For example, data from the 2010-2011 wave of the tobacco use supplement of the current population survey demonstrate that many long-term cigarette smokers try to quit smoking by switching to other combustible tobacco products, suggesting a lack of awareness of the continuum of risk. Moreover, some consumers switched from smokeless tobacco to cigarettes in order to quit using smokeless.

To help end the confusion and begin moving adult smokers

down the continuum toward less risky products, it's critical that they receive truthful and accurate communications about relative risk. Of course, the Tobacco Control Act gave FDA a wide range of tools to effectuate the law's central purpose which, of course, is to reduce the harm associated with tobacco products. One of those tools is Section 911 which creates a pathway for manufacturers to pursue the marketing of tobacco products with risk reduction or other modified risk claims with, of course, the sufficient scientific substantiation.

But the MRTP pathway is lengthy and it can take years for a manufacturer to receive an authorization from the time they begin preparing their application.

In the meantime, there's a more immediate option. FDA and other stakeholders like the CDC can begin communicating truthful and accurate information to adult tobacco consumers. These communications are not only critical to correcting misperceptions about relative risk, but could encourage cigarette smokers who will not quit tobacco use to switch to less harmful products.

Thank you.

DR. MERMELSTEIN: Thank you.

Our next speaker is Alex Clark from Consumer Advocates for

Smoke-Free Alternatives Association.

MR. CLARK: Good morning. Thank you for the opportunity to speak with you today. My name is Alex Clark, and I am the Executive Director of the Consumer Advocates for Smoke-Free Alternatives Association. We are a 501(c)(4) nonprofit consumer organization with more than 200,000 members from all walks of life, nearly all of them former smokers.

Our disclosure is included in the written comments you should all have a copy of. It's also available from the website at CASAA.org. My salary and travel expenses are authorized by an all-volunteer board of directors who have no financial stake in the industry.

I'm here today to express CASAA's support for R.J. Reynolds Tobacco Company's MRTP application for Camel Snus. We strongly believe that consumers have the right to accurate information in order to make informed decisions about their lifestyle choices. Accordingly, Camel Snus marketing should truthfully inform consumers of the relative low risk associated with using this smoke-free tobacco product, especially as it compares to smoking.

In addition to speaking on behalf of our members, I'm here as someone who benefits from using snus. By way of background,

I first learned about Camel Snus in 2009 when I was searching for a smoke-free product to use in public transportation. Although I was using nicotine gum at the time as a bridge between cigarettes and as a means to cut down smoking, I wanted an alternative to the gum's uncomfortable side effects like sore jaws, bleeding gums, hiccups and heartburn. I also wanted a product that would more closely replicate the nicotine delivery of a cigarette.

Having used smokeless tobacco in the past, I also knew I wanted a tobacco product that didn't require accessories like cups or bottles for spitting. A quick Internet search brought me to Camel Snus as a convenient and less messy option and most important, a smoke-free option.

I also searched for expert opinion about the risks associated with using snus. I, like many others, believed that using smokeless tobacco meant I would likely be trading lung cancer for oral cancer, but I wanted a better understanding of just how big that risk was. My review was brief and by no means diligent, but I concluded that using snus would at least not increase my risk of developing a tobacco-related disease.

Unfortunately, my first experience with Camel Snus was lackluster at best. While the flavor was enjoyable and I was

mitigating the discomfort of using nicotine gum, I believe the product suffered from two not insignificant design flaws.

Number one, even though this is a smokeless tobacco product, the nicotine delivery did not match my expectations. It was difficult to imagine snus replacing a 40-plus-cigarette-a-day habit was possible.

Number two, although using Camel Snus is simple and discreet, disposing of used pouches always requires a trip to the trash can. Under normal circumstances this might not seem like a big deal, but on any flight longer than an hour it means potentially multiple trips down the aisle.

While the latter issue is easily solved by carrying a separate receptacle, the former is obviously more complicated, barring reformulation which, under the current regulations, requires navigating a costly and arguably prohibitive approval process. Some additional value of switching to snus must be communicated to people who smoke.

I can only wonder if my decision to abandon snus would've been different if marketing materials truthfully communicated the lifesaving potential of switching completely. Instead, it took four more years to completely switch to smoke-free alternatives, including vapor products and snus.

I made the decision to start smoking in 1991 as a means to managing stress behind the wheel of a car. I was not deceived by tobacco companies about the risks of smoking. To the contrary, I stole cigarettes from my dad and preyed on retailers who relax on checking IDs. I do not consider myself to be a victim.

Conversely, when I made steps towards changing my self-destructive behavior, I was kept in the dark about all of the tools at my disposal. To some extent, I believed my dependence on cigarettes was prolonged due to a congressionally mandated ban on messaging about safer alternatives to smoking.

We believe it is appropriate to include, with slight alterations, comments made by Dr. Carl Phillips on CASAA's behalf to TPSAC, regarding a previous and notably different MRTP application.

They are as follows: FDA has the potential to do even better than approving this MRTP application specific to Camel Snus. We do not begrudge RJRT marketing advantage that might come from being allowed to market Camel Snus as safer than smoking. They are, after all, undertaking the monumental effort and cost required to make such a claim. Compared to the status quo, there is no apparent downside for consumers from

warning that one brand of smokeless tobacco products is lower risk than they previously thought, even if they fail to learn that messaging generalizes to other products in the category.

Additionally, we understand, of course, that the MRTP process can only deal with the particular products in this application. Nevertheless, in an ideal world in which the government is devoted to improving the welfare or even just health of its citizens, the ability to communicate relative risk would be extended to all Swedish and American-style dip and chew products.

The same lack of evidence for the oral cancer risk or dental diseases applies to these products as of the evidence affirmatively supporting the claim that they are substantially less risky than cigarettes.

Thus, the greater good, in terms of government ethics, public health, and the real interests of the citizens who the regulation is supposed to benefit, would be served by generalizing the proposed postmarketing statements.

Thank you very much.

DR. MERMELSTEIN: Thank you.

Our next speaker is Guy Bentley from the Reason Foundation.

MR. BENTLEY: Good morning, members of the Committee. My name is Guy Bentley. I'm a research associate at Reason Foundation, and thank you for giving me the opportunity to present all evidence in support of RJRT's application for modified risk status for its line of Camel Snus products. Reason Foundation's nonpartisan public policy research permits choice, competition, and a dynamic market economy as the foundation for human dignity and progress.

On the basis of the evidence submitted by the Applicant, as well as previous clinical and epidemiological evidence concerning the relative risks of snus, we believe snus can play an important role in reducing the death toll from smoking, but it can only do so if smokers are fully and accurately informed about its relative risks.

Granting this application would allow the Applicant to make modest and truthful marketing statements about the product giving consumers accurate information so they can make an appropriate and important decision.

There are approximately 30 million adult smokers in the U.S. Cigarettes are responsible for close to half a million deaths per year and smoking is still the leading cause of preventable death in the United States.

In order to reduce the incidence of smoking-related deaths, FDA Commissioner Scott Gottlieb outlined a new approach to tobacco and nicotine regulation last July. While recognizing that nicotine is highly addictive, Commissioner Gottlieb also recognized that the delivery of nicotine is on a continuum of risk with cigarettes presenting the most risk and abstinence presenting the least.

As well as outlining measures to reduce nicotine levels in combustible cigarettes, Commissioner Gottlieb then states that importance of embracing products which present substantially less risk than cigarettes and can help smokers switch, but this strategy can only be achieved if smokers are actually informed about the potential alternatives to smoking.

We believe the evidence presented by the Applicant indeed shows that Camel Snus falls on the reduced risk side of the continuum and that smokers who switch exclusively to these products will dramatically reduce their risk of death and disease compared to continued smoking.

When examining the market for nicotine products, choice in the market is more likely to be welfare enhancing if it is voluntary and based on adequate information. If purchasing decisions are driven by either the seller's deceit and/or the

buyer's ignorance, a form of market failure will result from an information asymmetry. There is ample evidence to suggest there is a significant information asymmetry in the market for smokeless tobacco products.

As has already been commented on, several national representative surveys show that most U.S. adults equate the risk of snus to the same or more harmful risk than that of cigarettes.

Granting modified risk status to Camel Snus provides -- would be an important step in correcting such an information asymmetry.

Now, the Family Smoking Prevention and Tobacco Control Act requires that an MRTP application demonstrate that such products -- and demonstrate that such products as is actually used by the consumer 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 the users of tobacco products and persons who do not currently use tobacco products.

We believe the Applicant has sufficiently demonstrated that Camel Snus meets these requirements, and the evidence presented shows that smokers who completely switch exclusively

to these products will reduce their risks of developing lung or oral cancer, respiratory diseases and heart disease.

Now, FDA in its briefing paper to this Committee has raised some objections, highlighting that although Camel Snus has significantly lower levels of harmful and potentially harmful chemicals, that there are, in fact, high levels when it comes to cadmium, NNK, NNN, and nicotine in mainstream cigarette smoke.

But importantly, FDA rightly notes that Camel Snus products and cigarette products are drastically different in their product design and use versus smoking. Users may not be getting the same levels of HPHCs for each type of product, as indicated above, because actual exposure levels are influenced by factors such as user behavior, for example, the amount of product used by day, the route of administration or ingestion versus inhalation, the rates of absorption, and metabolism.

Exposure to smokeless tobacco, such as the six Camel Snus products, and cigarette smoke occurs via different routes, oral versus inhalation. "Consequently, there may be differences in HPHC bioavailability and target tissues. The carcinogenic effects associated with user exposures to carcinogens from each of these products, given the oral routes of exposure and the

fact that smokeless tobacco products are not combusted, it is possible that the carcinogenic potential of these Camel Snus products is lower than that of cigarette smoke."

And just say that it is potentially lower, but thankfully there is an abundance of real-world epidemiological evidence to show that it is, in fact, lower.

In Sweden, thankfully, we have real-world decades long experience with which to test such claims, snus being -- the Camel Snus products under review being largely similar to the Swedish snus used, used in the Scandinavian countries. Snus has been shown, beyond any reasonable doubt, to be the biggest single contributory factor to Sweden's record low smoking prevalence and the lowest level of tobacco-related mortality among European men. Smoking prevalence in Sweden fell from 18% in 2007 to 7% in 2017, a 61% reduction.

Despite FDA's cautious treatment of HPHC exposure in Camel Snus, their own briefing paper provides a realistic, if still somewhat pessimistic, assessment of evidence surrounding smokeless tobacco. For instance, FDA says in its briefing paper that the evidence on smokeless tobacco risks from the U.S. literature is generally consistent with the Swedish literature in terms of finding lower risks of disease

conditions including lung cancer and COPD.

DR. MERMELSTEIN: Thank you, Mr. Bentley.

MR. BENTLEY: Thank you so much.

DR. MERMELSTEIN: Our next speaker is David Abrams from New York University College of Global Public Health.

DR. ABRAMS: Thank you for this opportunity. My name is David Abrams. I am a professor at NYU of Global Health. Previously, I headed the Truth Initiative's Schroeder Institute for Tobacco Research and Policy Studies, and before that, I was head of the National Institutes of Health Office of Behavioral and Social Sciences Research, OBSSR. I have 42 class-years of experience in every aspect of tobacco control and nicotine use from basic science to public policy.

I am here to support the efforts to truthfully inform and fully inform the public and smokers that they can reduce their risks for smoking-related disease if they switch completely to a noncombustible form of tobacco such as snus or e-cigarettes.

In the United States, over half a million smokers per year die before their time and over 60 million more suffer unnecessarily from the chronic debilitating disease and costs of combustible lethal tobacco smoke.

There is a public health consensus that combustible

tobacco products are far and away the drivers of the vast majority of morbidity and mortality. Smokeless tobacco, especially low nitrosamine snus, is dramatically less dangerous.

The epidemiology from the Swedish experience and from some U.S. experience shows clearly that the modified risk statements are true. Smokers who switch completely to smokeless tobacco can reduce their risks of lung cancer, oral cancer, respiratory disease, and heart disease. But the public does not know the full truth and the whole truth and nothing but the truth. In fact, what they know is not only misleading and wrong, it's been going in the wrong direction for the last few years and getting worse. This is a big deal from the bigger picture point of view because every year we wait, half a million smokers are dying. So if not now, when do we begin to implement harm reduction strategies that we know may save smokers' lives?

In the National Cancer Institute's survey for the FDA, only 12% of Americans say they believe some form of smokeless tobacco is less harmful than cigarettes. That's a shocking gulf between what the public thinks and the evidence.

These MRTP ads represent a meaningful first opportunity to

break the ice and help smokers begin to understand the whole truth. In fact, in consumer protection law, omission of truthful information is not only regarded as deceptive, in some cases it's fraudulent to withhold or prevent the truth from being communicated to the public. But this is an important start in providing smokers with truthful information and products with some appeal. And it will start to educate smokers that combustion is the source of harm from smoking and not nicotine or non-combusted products while not harmless. I implore you to rise above the level of the critique of the acute and sometimes picky truths that we do in science when we're in the weeds. There are always doubts in science. The greater risk of unintended consequences is doing nothing and withholding truthful information from the public.

Today's vote is an opportunity to take a first step in advancing public health and committing in practice, not just in words, to harm reduction. We are at a turning point in smoking control. Your decision, FDA's decision, is not just about the details of this application, it's about the much bigger public health picture and the consequences of telling the whole truth to the public.

Commissioner Gottlieb and Zeller's vision for a

comprehensive regulatory system, including reducing nicotine in combusted products, hinges on the fact that there's a vital step in needing to migrate smokers to less harmful products. This is a two-faced process; you cannot have one without the other.

The Tobacco Control Act has set up the MRTP pathway to help move smokers to less harmful alternatives, but the bar is extremely high and it's very easy to be caught up in the details of risk. If this application before you for a product with decades of epidemiology, one that everyone agrees is much less harmful than smoking, the careful communication about relative risk cannot get through this pathway, then I fear you will actually be declaring this whole pathway unviable.

The continuum of harm in theory, and as stated by Mitch Zeller for almost a decade prior to being Commissioner, will become meaningless if you never ever implement a practical MRTP application because the bar is too high and we focus like angels on a pinhead on the problems and risks and not the unintended prevention of benefits.

Like Everett Koop did in the AIDS epidemic, we have an opportunity to get out this information and save lives, accurate information that enables people to make better

choices.

DR. MERMELSTEIN: Thank you.

DR. ABRAMS: This is the time for a Koop moment. Let's be brave and take some risks.

DR. MERMELSTEIN: Thank you. Thank you, Dr. Abrams.

DR. ABRAMS: And if we are wrong, there is postmarket surveillance --

DR. MERMELSTEIN: Thank you.

Our next speaker is Scott Ballin, health policy consultant.

MR. BALLIN: Good morning, I'm Scott Ballin. I've spent much of my professional life working on issues pertaining to tobacco and health with a particular interest in FDA, was the vice president and legislative counsel for the Heart Association and authored the petitions to the FDA seeking to bring tobacco under its jurisdiction.

I concede to the idea that we needed to pull the tobacco executives up before Congress, swear them in, and ask them tough questions including whether nicotine was addictive. Many of you elderly people in this audience may remember that important hearing.

I've been working in this area ever since, including

authoring several white papers on tobacco and nicotine harm reduction and for a number of years now, my focus has been to encourage stakeholders to engage in civil dialogue including here at FDA. I've worked for the University of Virginia on what I'll refer to as the Morven dialogues and consulted to the Food and Drug Law Institute for several of their tobacco conferences over the last couple years.

Last July 2017 FDA Commissioner Gottlieb and CTP Director Zeller, recognizing that the tobacco and nicotine role has drastically changed and is at a major crossroads, announced a new vision about where the Agency should be headed.

It focuses on ensuring that children and adolescents do not have access or use tobacco products or nicotine products, but equally important, ensuring that adult smokers have access to lower-risk consumer acceptable forms of nicotine including products like snus. I believe that both of these goals and objectives can be achieved in tandem.

I also believe that collectively, as governmental agencies, researchers, NGOs, innovators, manufacturers and consumers, we need to modernize our thinking about what should be a more rational and flexible regulatory framework that can serve our public health goals not only today but into the

future.

One important way is to focus on the regulation of tobacco and nicotine in alternative products based on the continuum of risk, which has gotten a lot of discussion recently by the Commissioner and Director. In spite of progress, the deadly combustible cigarette kills 480,000 Americans each year and costs this country an estimated 300 billion a year in healthcare cost and lost productivity. There are approximately 40 million, 40 million adult smokers who need attention and help.

It is unfortunate that many in the tobacco control community and in government continue to talk about all tobacco products as being equally harmful. Such antiquated, inaccurate, unscientific statements are misleading, at the very least.

While tobacco is often referred to as this nation's single most preventable cause of death, if one segments out combustible products versus noncombustible products, the equation drastically changes with smokeless products, NRT, and e-cigarettes falling much lower down the scale.

I think it's time to start having constructive dialogues about how to expeditiously implement the continuum of risk

approach.

Second, as part of the regulating of tobacco and nicotine products based on that continuum of risk, it's critical that we better educate the public and consumers in thinking -- in addition to thinking, too, that all tobacco products carry the same risk, the public also believes that nicotine causes cancer. We've done a horrible job of educating the public in many areas and confusion continues to reign. It's time for all stakeholders to work cooperatively, to correct these long-term informational deficiencies. We have known for almost 20 years that noncombustible, low TSNA smokeless products are 90% lower than this from the deadly cigarette, yet little information has reached the very people that could benefit from such information, the addicted cigarette smoker. The labeling of products and the marketing in terms of relative risk, as in the case of snus, is one way of correcting that misinformation.

Third, I think we need to push for continued civil dialogue and engagement, something that Commissioner Gottlieb and Mitch Zeller have also talked about and something I have long advocated. This engagement should not only be taking place at the FDA on a more regular basis, but in the private sector, as well, such as at the SONT, the Food and Drug Law

Institute, and the University of Virginia's Morven dialogues -- just several examples. These dialogues serve as forums for allowing a spectrum of stakeholders to come together and talk about important and often controversial issues relating to science and policy.

And, finally, let me conclude by saying that it has been almost 20 years since the Institute of Medicine issued its landmark report entitled "Clearing the Smoke." It's time for there to be more robust discussions of how we can collectively move forward.

We're in important crossroads, as the Commissioner has said. Collectively, we can and should do more to prevent a new generation of youths from taking up smoking and tobacco, but equally important, we need to make significant lower-risk products available to the 30 million adult smokers.

Let me conclude, also, by saying that we should not have to wait another 5, 10, 15 years to do what we should've done and started 20 years ago. Allowing noncombustible smokeless products, which I refer to as smoking replacement products, SRPs, to be labeled and marketed with truthful and accurate information would be a major step forward and I hope that you will take the appropriate steps to make that happen.

Thank you.

DR. MERMELSTEIN: Thank you.

Our next speaker will be Mark Greenwald, and he's representing the University of California Center for Tobacco Control Research and Education.

MR. GREENWALD: Thank you. Appreciate the opportunity to appear before this Committee. I'm Mark Greenwald. I'm a lawyer here in Washington with 18 years of experience in tobacco control issues. This presentation was prepared by Lauren Lempert of the University of California at San Francisco who was unable to be here because of illness. At her request and with FDA's permission, I'm presenting it in order to make it part of the record, and I am not representing the Campaign for Tobacco-Free Kids.

The information is a summary of conclusions reached by researchers at the University of California at San Francisco, Stanford University, and Georgia State University, who submitted a detailed analysis for the record in this proceeding.

Under Section 911 of the Tobacco Control Act, in order to receive an MRTP order, Reynolds must demonstrate that Camel Snus, as actually used by consumers, both significantly reduces

the risk of disease to individuals and also benefits the health of the population as a whole. Scientific analysis of this application by the researchers, as detailed in the written comments, concludes that Reynolds did not meet either prong of the statute.

Accounting for how Camel Snus is actually used by consumers is an essential part of a legal standard. Although Reynolds' modified risk claims are premised on the assumption that smokers will switch completely to Camel Snus, Reynolds' own research, as well as independent evidence, shows that complete switching or exclusive use of these products is actually extremely rare. Rather, it's much more likely that Camel Snus users will be dual or poly users of tobacco products and will continue to smoke cigarettes or use other tobacco products along with snus. Evidence supporting these statements is detailed in the epidemiology section of the researchers' comments.

Looking at whether Camel Snus significantly reduces health risks to individuals, Reynolds argues that because exclusive users of Camel Snus are exposed to lower levels of dangerous toxicants, they will have reduced risk of harm from lung cancer, oral cancer, respiratory disease and heart disease.

However, Reynolds' own studies show that even if Camel Snus is used exclusively, users may be exposed to greater levels of some dangerous toxicants, including TSNAs and heavy metals.

Systematic exposure to tobacco toxicants is a function of the chemistry of the product, constituent delivery and bioavailability and user characteristics, and Reynolds has not adequately addressed these factors. Also, Camel Snus has higher levels of NNN and NNK than -- snus and much higher levels than Swedish snus. Moreover, dual or poly use, the most likely outcome for most users of Camel Snus, could increase users' exposures to these dangerous toxicants and thereby increase their risk rather than reduce it.

Looking at the second prong of the legal mandate, when determining whether a product benefits the health of the population as a whole, FDA must consider, among other things, the impact on nonusers, including youth and young adults. However, Reynolds did not address the appeal of Camel Snus to youth or the impact of its marketing claims on youth.

It also did not consider the role of flavors on youth usage and the flavored Camel Snus products are more likely to attract youth and young adults than unflavored products. It's

also important to consider the constituents in the flavorings, not only because they impact abuse liability, but also because they may increase toxicity.

The researchers' analysis shows that Camel Snus marketing is likely to result in initiation and dual use among nonusers, especially youth and young adults.

Section 911(h) requires Reynolds to demonstrate that the proposed advertising and labeling for Camel Snus enable the public to comprehend the information concerning modified risk and to understand the relative significance of that information. However, the experimental design of Reynolds' study failed to demonstrate that its marketing would effectively communicate the modified risk information in a way that consumers could understand.

The researchers also cite flaws in Reynolds' population health model. For example, the model considers mortality but ignores morbidity associated with use of Camel Snus, and underestimates the likelihood that Camel Snus will delay smoking cessation, omits the impact on nonusers, especially youth, and does not consider the additive effect of dual and poly use.

The researchers conclude that Reynolds did not meet the

statutory requirements for an MRTP order and urge TPSAC to recommend that its application not be granted.

Thank you.

DR. MERMELSTEIN: Thank you.

Okay, the Open Public Hearing portion of this meeting has now concluded, and we will no longer be taking comments from the audience.

Yes, okay.

MR. MITCHELL: I'm confirmed as a speaker?

DR. MERMELSTEIN: Yes, you are. I'm sorry, we didn't have you as being present. So go ahead, Mr. Mitchell. You will have your time now.

MR. MITCHELL: Good morning. Thank you for the opportunity to address this important deliberative meeting. I'm Jack Mitchell, Director of Health Policy for the National Center for Health Research.

NCHR conducts and scrutinizes research that can be used to provide information for health professionals, patients, and policymakers. We take a scientific and patient-centered approach to monitoring the safety and effectiveness of drugs and medical devices. We accept no funding from any manufacturer or sponsor of medical or tobacco products and

therefore I have no conflicts of interest to report.

I'd like to start by commending Commissioner Scott Gottlieb's important public announcement this week that the Agency, after an extensive undercover inquiry, recently had issued more than 1,000 warning letters and 131 fines regarding e-cigarettes and vaping to industry manufacturers and retailers.

Dr. Gottlieb has given manufacturers, according to the New York Times, including one vaping firm owned by RJRT, 60 days to come up with a credible plan to keep e-cigarette and vaping products from consumers under the age of 18. Dr. Gottlieb intimated that if the voluntary effort is insufficient, the Agency will consider reversing the regulatory delay that FDA earlier announced.

These proposed regulatory proposals include the use of flavors in e-cigarettes and vaping products. While you're not considering e-cigarette products today, the bar has now been raised concerning all aspects of tobacco and nicotine use among young people.

In the industry, advertisements that claim to warn consumers about the dangers of addictive nicotine should be viewed with skepticism and those claims should be cautiously

and carefully vetted by scientific experts with no conflicts of interest.

All the Camel products under consideration by this Panel contain flavors that will attract young consumers. That was the deliberate intent of the flavors utilized by cigarette manufacturers prior to the flavors being banned from combustible cigarettes in 2009. I know that was the intent because I was a senior official in the FDA landmark investigation into the tobacco industry 20 years ago and I uncovered many such confidential documents outlining the use of flavors in advertising to attract youthful smokers.

Now these flavors are being used to create another generation of addicted smokers. Any claim to the contrary defies common sense in the industry's own decades-long trail of internal documents and strategies. Clinical scientific research suggests that compounds that give e-cigarettes their flavor are toxic with some ingredients being worse than others. The effects of these flavors in tobacco is not yet well known or adequately studied.

The FDA's written pre-meeting review of the Reynolds data stated that these flavors in smokeless tobacco may act as so-called permeation enhancers, thus increasing the overall health

risks associated with these products when compared to other smokeless tobacco products that do not have the same flavor ingredients. The FDA's review also noted that their products may contain two and a half to seven times the amount of nicotine compared to cigarette smoke. The American Heart Association has concluded that nicotine may contribute to smoking's negative effect on cardiovascular health. There's also more arsenic, cadmium, and NNN in the Camel smokeless products compared to other tobacco products. This will increase user exposure to carcinogens and other toxicants that may subsequently increase the risk for cancer, heart diseases, and other negative developmental effects.

In fairness, the Sponsor offered explanations late yesterday as to why they believe such increases are not significant or meaningful, but the Committee and FDA will have to judge those claims on their merits and by themselves.

FDA also concluded that the evidence that cigarette smokers switch to Camel Snus use is very limited. Instead, the dual use of smokeless tobacco and combustible cigarettes was common in the studies produced for FDA's consideration and dual use certainly, as you know, is not the same as switching entirely from combustible cigarette smoking.

The Sponsor, according to FDA, did not provide evidence from population-level studies to assess the likelihood that U.S. cigarette smokers would switch to smokeless tobacco products in any meaningful cohort, or to Camel products specifically. For example, one study showed that the incidence of switching completely from cigarettes to smokeless tobacco is only slightly more than 1%.

As many of you know, the rate of smoking in the U.S. was significantly reduced in recent years until the recent increased use and popularity among young people of e-cigarettes, vaping, and new smokeless tobacco products. We urge you to consider the impact of renewed tobacco and nicotine use on our young people in light of the FDA's newly expressed, this week, urgency and determination to contain it and what we must do to reduce these disturbing trends.

I thank you very much for your time.

DR. MERMELSTEIN: Thank you very much, Mr. Mitchell.

Okay, I believe that we are now actually concluding the Open Public Hearing portion of the meeting, and now we will no longer take further comments from the audience.

As a Committee, we're now going to turn our attention to our task, which is to consider the data that we have heard over

the last day and today, as well as the public comments. And we're going to move, I think, right now to Dr. Kittner's discussion of the questions that are before us.

DR. KITTNER: Good morning. Again, my name is Deirdre Lawrence Kittner, and I'm going to go over the questions that FDA is posing to TPSAC. I'm going to skip over the disclaimer, as you all heard it yesterday.

Just as a reminder, RJRT is seeking orders under Section 911 or Risk Modification Order for each of its six Camel Snus products.

To authorize a product, the Agency must find that the product is 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 of tobacco products and those who do not currently use tobacco products. While evaluating your responses to the questions, please keep the 911(g)(1) standard in mind.

Just so the Committee knows, you have some summary slides in your packet. I'm just going to skip over those and go straight to the questions.

Today we're asking TPSAC to focus on the lines of evidence

as they relate to these topics: the scientific substantiation of the modified risk information, consumer perceptions and understanding of the modified risk information, and the likelihood of use of the proposed MRTPs, including the likelihood that users and nonusers will use the products. Based on the data presented, we would also like the Committee to discuss any groups or users of concern, such as youth or non-tobacco users.

Here are the questions we are posing to TPSAC. The modified risk information in the ad executions include RJRT's key claims about the reduction in disease risk as a result of completely switching from cigarettes. So Question 1 specifically asks you to evaluate the evidence related to the reduced disease risk.

Discuss the available scientific evidence and vote on the extent to which the available scientific evidence substantiates the following modified risk information in the Applicant's advertising: Smokers who switch completely from cigarettes to Camel Snus can significantly reduce their risk of lung cancer, oral cancer, respiratory disease, heart disease.

Question 2: The Applicant’s advertising also contains modified risk information that describes a reduction in harmful

constituents in Camel Snus versus cigarettes, and modified risk information that is not as specific as the information presented in Question 1, for example, does not reference reduction in specific diseases or the need for complete switching. All of these statements are being evaluated as part of the MRTPAs. We're asking the Committee to discuss the available scientific evidence and vote on the extent to which the available scientific evidence substantiates the following modified risk information in the advertising:

a. Camel SNUS contains less of the harmful chemicals than cigarettes.

b. Smokers who use Camel SNUS instead of cigarettes can significantly reduce their health risks from smoking.

c. Switching to snus means less risk for you.

d. No smoke equals less risk.

Question 3: In addition to evaluating the proposed modified risk information for scientific accuracy, FDA also evaluates consumer understanding and perceptions of the modified risk information in the advertising. The Applicant plans to communicate all of the information together. The first page has less specific information while the second and third pages have more specific modified risk information and

additional information RJRT refers to as balancing information.

We're asking the Committee to -- next one, please. Thank you. We're specifically asking the Committee to discuss the potential implications of the proposed modified risk information including the nonspecific modified risk language, as described in Question 2.

We would like for you to consider the following questions:

a. Can the nonspecific modified risk information be misinterpreted?

b. Is there sufficient evidence that consumers would understand the nonspecific modified risk information?

c. Is there sufficient evidence about the impact of the nonspecific modified risk information on the likelihood of use?

d. Is there sufficient evidence about the impact of the nonspecific modified risk information on poly tobacco use or partial switching?

The final question will provide an opportunity to discuss the potential users of the six proposed Camel Snus MRTPs.

a. What is the likelihood that cigarette smokers will switch completely to the six Camel Snus products?

b. Are there other groups of potential users,

particularly unintended users, youth and former cigarette smokers, for example, of concern?

We look forward to the discussion.

DR. MERMELSTEIN: Thank you.

Okay, we are going to, as a Committee now, discuss and go through the questions in order of how they are presented. So remember, again, this is an application for modified risk claims and there are key ones.

So what we want to think about now are the evidence that we've heard and thought about and how accurate we feel the statements are in terms of smokers who switch completely from cigarettes to Camel Snus can significantly reduce their risk of a variety of diseases. So let's take these one by one. Let's start with the lung cancer.

Debbie.

DR. OSSIP: This is a question for the lung cancer consideration, but it's robust, I think, across the -- all of the first four questions. I would like to get a very clear understanding of how the six products under consideration compare to the products, smokeless tobacco products, that were used in the large trials that were cited with disease endpoints, NHANES, CPS-I and II. The first question is, were

they equivalent? And then the second is, if they were not equivalent, in what areas were they not equivalent? For example, the TSNAs, the heavy metals that appear to be elevated in Camel Snus relative to the other products.

And then specific questions about flavorings, and I want to distinguish between flavorings and flavors. Flavorings, just to be clear for those here, represent the ingredients that are used to create what's perceived as a flavor. So if, for example, a mint product had been used previously, it doesn't necessarily mean that that had the same flavoring composition.

So it would be helpful for me in considering how to weigh that evidence for these specific products since these specific products were not included. One is the basic question: Were they equivalent? And then the second is: If not, how are they different? And then the third is some judgment about does that matter what the implications are at those differences.

DR. MERMELSTEIN: Okay, this is a point for Committee discussion and unless there's some specific comments from the FDA.

DR. KITTNER: The only comment that I have right now is that the epidemiology evidence that we have is not specific for the products under consideration, so we look forward to hearing

the discussion.

DR. MERMELSTEIN: Right.

Yes?

DR. McKINNEY: Part of the question was very specific for the product and I think that to really get an answer to your question, we should invite the Sponsor to answer that question briefly. For you to have the information that you require for the discussion.

DR. MERMELSTEIN: Which part of that, about flavorings? I believe we have the answer about the data about the epidemiology and no, there are a variety of products used in prior epi studies and, you know, that included some that were similar and those have changed over time. So I think that we know that there's a large variability in the epi studies.

DR. SHIFFMAN: I think we can address both and I think we can do it really quickly. Very quickly.

DR. MERMELSTEIN: Very quickly.

DR. SHIFFMAN: So there are two questions. One is how do these products compare particularly in terms of toxicants, if you will, and I'm going to ask Dr. Marano to address that. If you can let us have the slides, we'll just show you -- we'll do without the slides. Dr. Marano, use hand buckets.

DR. MARANO: What we also know about the products that were in the epidemiological studies is that they had much higher toxicant levels than what are current toxicant levels in Camel Snus. In addition, they were also consumed in much higher quantities and much more frequently than Camel Snus today. So the toxicant levels were much higher, including TSNAs, cadmium, arsenic, B[a]P.

DR. SHIFFMAN: So, sure, the epi is based on more toxic products than what Camel Snus is today. In terms of flavors, a lot of the issues that get raised are the conjecture that flavorings would be penetration enhancers. We'll ask Dr. Dan Heck to address that again, very quickly and without slides.

DR. HECK: I think the most direct evidence we have that speaks to the notion that flavors may enhance permeation, we've seen in our in vitro studies where we looked at all six flavors and size variants side by side under identical conditions and looking at the cytotoxicity which reflects the permeation of HPHCs into the cells and causing the cytotoxic effects. Again, we saw no difference whatsoever among those flavor variants.

And, again, as Dr. Marano said, you know, the epidemiology reflects the entire variety of products, flavored, unflavored, and the different types of smokeless products. And as a

family, those certainly cluster in a very, very low risk level compared to smoking and that's the essence of the proposal.

DR. MERMELSTEIN: I think it would be realistic to say that there is a broad variety in the epi data and that to test it specifically on these products would probably be an untenable thing at this point, for decades, in populations.

DR. OSSIP: So my question is more -- thank you. My question is really just how to weigh that evidence in evaluating the current products, what caveats or considerations there may be in the generalizability of those data to these six products.

DR. MERMELSTEIN: Dr. Bierut.

DR. BIERUT: One of our colleagues on the phone yesterday brought up this discussion which is we've had these general surveys and surveys have their strengths and benefits; the strengths of them are they're large population-based studies, but we know in the self report we're going to get a wide variety of different products reported there and those surveys are quite old. Some of them, you know, we're talking about products, I'm sure that we're going back to the '60s, '70s, '80s.

And so we have to kind of think we have this epidemiologic

data which is summarizing information over decades and how do these products, do we think these products are -- I think the phrase our colleague stated yesterday, no worse than the products that existed in the '60s, '70s, '80s or are they equivalent or potentially better than those products. And we have to kind of go with the generalization of how do we think these products really measure up to those previous products.

DR. MERMELSTEIN: I think that across the different diseases, that there's more data on some and less data on others and that's another thing that we consider with each of these diseases separately. There is a substantial amount of data on lung cancer as well as data that showed among for complete switchers, even. So we had some nice graphs that we could look at that looked at data and relative risks and showing a great reduction for the complete switching. For some of these diseases there was more data than others, so I think that's something that each -- that everyone can consider as well.

Other questions or thoughts from the Committee about the specific relative risks?

DR. GIOVINO: This is Gary.

DR. MERMELSTEIN: Gary.

DR. GIOVINO: I sent an email request. Is it okay to talk?

DR. MERMELSTEIN: Go ahead, we got it.

DR. GIOVINO: So yeah, I think the epi studies were done on products that were considerably dirtier, including chewing tobacco, so that just adds to my sense that they were of greater health concern, but snuff also being bad enough.

I want to go back to something that Dr. Heck said. In the in vitro studies, I need -- the concern is that, you know, companies are always adding new chemicals, flavorings to products and my guess is that the flavorings that are in Camel Snus weren't in the studies from decades ago and to the extent that permeation enhancement is a concern, you said that there were no differences across flavors in the in vitro studies. My concern is did you have a non-flavored control group? I can't recall from the -- from your document, so I thought I'd just ask.

DR. MERMELSTEIN: I will ask Dr. Heck to answer that.

DR. HECK: No, we did not. These were the products as actually marketed and as proposed in the proposal.

DR. GIOVINO: So how do you rule out the possibility that the current flavorings are not permeation enhancers if you

don't have a non-flavored control group?

DR. HECK: Well, just with respect to the differences in flavors among this family of products, we saw no differences whatsoever, suggesting that any differences among these products are inconsequential.

(Off microphone comment.)

DR. HECK: And as we saw relative to smoking, the -- all six products manifested only about 3 to 5% of the toxicity of cigarette smoke tested at an equivalent level of nicotine.

DR. MERMELSTEIN: Thank you.

DR. GIOVINO: Yeah, thank you.

DR. MERMELSTEIN: Dr. Kozlowski on the phone.

DR. KOZLOWSKI: Thank you. Just commenting generally about this issue, I think if you look at the CPS data, there's a massive difference in all-cause mortality, 18% in smokeless users, compared to something on the order of 200% increased mortality in cigarette smokers, 18 versus 200 or even more. That's made up of these diseases largely so much more than others.

So oral cancer would be a relatively minor contributor to that all-cause mortality; lung cancer, respiratory disease, heart disease, major contributor. And I think there has been

evidence presented that there is significant reduction in risk. The biggest question is about oral cancer, but I think it's important to think of what we mean by significant reduction in risk. For lung cancer, it's a massive reduction in risk; for respiratory disease, it's a massive reduction in risk.

I think for oral cancer, there is evidence that it's a sizeable reduction in risk and there are a whole bunch of other health conditions that if we could reduce risk by 20% we'd consider that an important risk reduction. So my general view is that there is evidence of significant reduction in risk based on products that are either at least as toxic or more toxic.

Thank you.

DR. MERMELSTEIN: Thank you, Dr. Kozlowski. Although I do believe, just as that one comment, the oral cancer, and I can be corrected, was one area that there were no data on complete switchers, so that one we just had a little less data on to evaluate.

Dr. King.

DR. KOZLOWSKI: But there were data on people who were -- I think it's the Henley study, the -- there was evidence of a reduction.

DR. MERMELSTEIN: Yes, correct. Correct.

Dr. King.

DR. KING: Yeah. So I would agree with the assessment that there's variability in terms of the different, you know, disease outcomes. You know, obviously looking at -- and I think that the Applicant realizes that as well. If you look at the different executions, there's actually one that removes, you know, specific disease outcomes. So I think that there's relatively broad consensus of variability, you know, in terms of the science.

That being said, I think epidemiologically there's a lot of things that we need to consider here. As an epidemiologist, there were several factors related to these studies that give me some pause. I think generalizability is a big issue and these studies were old and they were among men and I suspect that in terms of the racial, ethnic and other variability there probably wasn't quite a lot. And I think that in terms of the generalizability of the studies, that's something to importantly consider and also in the context of the shifting landscape. And we know, from not only the epidemiology of use but also from industry documents and other resources, that products have evolved over time.

So this notion that we're somehow supposed to be tied down to using these older epidemiologic data to generalize it broadly to an evolving product class and an evolving landscape of users is something that I'm not entirely comfortable with.

That being said, I also think it's important to make distinctions between morbidity and mortality and these studies are mortality and as was noted yesterday through the FDA comments, we're virtually devoid of data on morbidity. And as was mentioned during the public comments earlier today, we know that there are 60 million people that are living with smoking-related disease which, of course, we know if the overwhelming cause of burden in disease and death, but there's also many smokeless tobacco users that are living with disease as well. And so I think looking at the broad context of morbidity and mortality, as well, is important. And also I think it's important to look at significance.

And before I was in the government and transferred over to this realm of my career, I used to teach an epidemiology section in a medical school and I would always warn the students against statistics untouched by the human mind and that notion is that we can't just look at significance and that carries a very weighty definition, but you have to look at the

magnitude of the association as well as other factors that are in existence.

And so I really encourage us, when we're looking at these data, that just because something is statistically significant it may not necessarily mean it's significant in a broad array of other things and it's really important that we look at not only is it significant but what is the broader importance in terms of the various disease and -- or risk on the broad population as a whole.

And so that's where I'm really struggling when we start to parse these out, but I think it's an overall implication for us to consider is what is that actual science and is it really generalizable to today and that's something that I think this Committee needs to consider very strongly.

DR. KOZLOWSKI: This is Lynn Kozlowski. Can I make a comment?

DR. MERMELSTEIN: Go ahead, Lynn.

DR. KOZLOWSKI: I want to emphasize, I was not talking about statistical significance in my remark, I was making the point that if you had -- you've got some cases here which there would appear to be a huge reduction in risk and other cases where it might be a reduction on the order of 20%, 30%. In a

lot of other contexts, that would be considered an important reduction in risk. So I'm not speaking about statistical significance.

DR. KING: And that was not in direct response to that, just to --

DR. MERMELSTEIN: Okay.

DR. KING: -- clarify that the language that we're being asked to assess is significant and so that's important in this context.

DR. MERMELSTEIN: Okay. Other thoughts about these disease -- Debbie.

DR. OSSIP: I wanted to, first, take a look at the wording, the proposed wording and following up to some extent on what Dr. King said. "Smokers who switch completely from cigarettes to Camel Snus can significantly reduce their risk of" and there are some considerations that I have in this. One is that the issue that's been raised of when is it appropriate to say significantly, when is it not appropriate to say significantly.

"Reduce," is -- is there a direct comparison between switch, those who switch completely and those who continue smoking?

And then the third is "their risk" which is a very personal kind of statement and I do have some concerns that that may -- and perhaps this goes down under consumer perceptions, although it's a little bit hard to consider this in the absence of that. Can we make a claim about whether it reduces a particular individual's risk?

We don't have data on some of the specific populations like youth, like children, who really do need to be considered in that much of the uptake products that are newly -- or having refreshed marketing campaigns impact youth. So I have some concerns about making that a very individual kind of comment that says, to me, as a smoker, that I can reduce my personal, individual risk and I don't know, it's possible that it's biologically plausible that it's a term, whatever, but I don't know that we have data to support that for every person reading this their particular risk will be reduced as opposed to more of a population-level statement.

DR. MERMELSTEIN: Okay. I think some of that distinction we can get to later with the comment down below about less risk for you where it is more personal, perhaps.

Dr. Thrasher.

DR. THRASHER: Yeah, thanks. This is just a question for

clarification around process. So are we talking right now or providing all of our comments and questions that have to do with all four of the disease outcomes or will there be an opportunity to present questions and comments after we vote for each one?

DR. MERMELSTEIN: No, I'd like to discuss all four and then we'll vote on each -- then we'll vote separately, but I think a lot of the discussion does overlap for each of them. So if you have any comments about just the broad Question 1, that would be appropriate now.

DR. THRASHER: But that there will be an opportunity to ask follow-up questions after we vote on Question 1 around lung cancer; is that correct?

DR. MERMELSTEIN: Well, it probably would be better -- I'm not sure what you're asking, Jim. If you're asking --

DR. THRASHER: What I'm asking is are we going to have all the discussion right now and then vote --

DR. MERMELSTEIN: Yes.

DR. THRASHER: -- on each of these different items --

DR. MERMELSTEIN: Yes.

DR. THRASHER: -- or are we going to vote and then have opportunity for discussion and vote, etc.?

DR. MERMELSTEIN: I'd like to have discussion right now about all (a) through (d) of Item 1 and then we'll vote on (a) through (d).

DR. THRASHER: Okay.

DR. MERMELSTEIN: So we won't vote --

DR. THRASHER: Okay, thank you.

DR. MERMELSTEIN: -- and discuss and vote and discuss.

DR. THRASHER: But I do have a question and it's really around oral cancer and heart disease outcomes. And one question is for the Applicant around why they decided to remove oral cancer and heart disease from the third execution, and then I would also like to ask FDA to clarify some of its comments around how -- for these two particular outcomes it's more challenging to interpret the risk reversal after switching to exclusive snus use because FDA does make comments about these two that are different from the evaluation of the evidence around respiratory disease and lung cancer.

DR. MERMELSTEIN: Dr. Shiffman or --

(Off microphone response.)

DR. BORGERDING: We believe that the products that were part of the epi were much more toxic than Camel Snus and that the epidemiology shows compared to cigarette smoking that Camel

Snus has less risk for these four disease endpoints and the advertising is about communicating relative risk to cigarette smoking.

When we were developing the ads, though, we were mindful, at a previous TPSAC meeting, that there were concerns about the absolute levels of risk, the fact that there was some risk for these two disease endpoints. So given the state of that discussion, we felt that it was prudent to have three different executions, one that would focus on all four disease endpoints and one that would focus just on the two.

DR. MERMELSTEIN: Thank you. And then a comment from the FDA.

DR. THRASHER: Thank you. Can FDA respond to my other question?

DR. MERMELSTEIN: Yeah, we're getting --

DR. KITTNER: Yes, we're asking Ms. Cate Corey from our Division of Population Health Science to respond.

MS. COREY: This is Cate Corey, epidemiologist. My understanding is that your question is about our comments on, perhaps, in the backgrounder, related to oral cancer and heart disease and the risk reversal after quitting being a little bit more complicated?

DR. THRASHER: That's correct.

MS. COREY: Um-hum. And so therein as we heard and discussed over the past day, for lung cancer and respiratory disease, the magnitude of differences according to tobacco use status are quite pronounced and we don't have evidence specifically linking smoking with lung cancer -- smokeless tobacco, I'm sorry, with lung cancer and COPD.

However, for oral cancer and heart disease, the magnitude of the differences in risk according to tobacco use status are somewhat different, particularly with respect to heart disease. And we also know, too, that while risk after quitting smoking does occur with both of those endpoints, we do see evidence in the U.S. literature that each of these endpoints, both oral cancer and heart disease, can be caused independently by smokeless tobacco use, even among nonsmokers.

It's just, you know, potentially a piece of evidence that the Committee may want to consider as they're thinking about these four statements. Does that clarify your question?

DR. THRASHER: Yeah, I believe so. And I assume that also, at least with regard to the oral cancer outcomes, encompass the concerns about not having data on switchers.

MS. COREY: Right. So the Henley study produced estimates

looking at the differences between switchers and former cigarette smokers, we presented that evidence yesterday. I think the relative risk for switchers versus quitters for oral cancer was around 2.56. But what they said they didn't produce was a comparison to never tobacco users and that referent category was the comparison for all of the other endpoints.

DR. MERMELSTEIN: Thank you.

Jim, was there --

DR. THRASHER: I guess I'm confused, then, because -- and what it is, I thought that what both the Applicant and FDA presented yesterday and what I understood from the background document that there is no information on switchers to smokeless tobacco versus never users with regards to oral cancer.

MS. COREY: That's correct.

DR. THRASHER: Okay, thank you.

MS. COREY: Yeah, so the evidence that's available from Henley uses a comparison of oral cancer for switchers compared to former smokers, but there's no comparison of oral cancer among switchers compared to never tobacco users. There's two different referents that are used in the Henley study and one of those explores the outcome of oral cancer and the other one doesn't.

DR. MERMELSTEIN: Thank you.

Dr. Weitzman.

DR. WEITZMAN: I just wanted to briefly go back to Dr. Ossip's concern about the word "their." As a clinician, I just want to point out that we're dependent on taking population-based data and applying it to individuals. When you counsel a parent to have their child vaccinated, you know, it's -- you're going to decrease the risk of that particular illness. When you counsel somebody about weight loss, we're dealing with their hypertension. It's all based upon population-based data that we present to individuals.

DR. MERMELSTEIN: Thank you.

Dr. Giovino on the phone.

DR. GIOVINO: Yes, hello. Two thoughts. One just in response to Jim Thrasher's question, and I believe the FDA scientist was referring to the 2005 Henley study when she said we have comparisons with never smokers, not to the 2007 switching study because they don't include oral cancer in the 2007 switching study. I just wanted to sort of say something along a similar vein as Dr. Weitzman just said about population data and I think perhaps address Dr. Ossip's concern.

You know, there are people who quit smoking and don't use

any other tobacco products who get lung cancer. It's because they quit too late. But we do not say there are benefits to quitting smoking because some people do and I wouldn't -- you know, I just want to, you know, present that perspective for you to consider. Thank you.

DR. MERMELSTEIN: Dr. Ossip.

DR. OSSIP: Thank you, Dr. Weitzman and Dr. Giovino. I raise it in this particular context because the product to which they're switching is not without risk, so that's why I perhaps am taking greater care in looking at how that's being conveyed.

DR. MERMELSTEIN: Thank you.

Dr. Wackowski, did you have a question?

DR. WACKOWSKI: Yeah, just a few general comments. Regarding the generalizability issue, I think it was said that perhaps the earlier epi studies were based on white men, but I think we've also seen that the current users of smokeless tobacco and the people most likely to use these products are also -- remain to be white men.

Regarding the statement itself, the claim itself, it does explicitly say switch completely and I think we've been, you know, shown that the evidence regarding dual use might not

indicate a reduced risk but that the reduced risks are associated with switching.

Regarding the "significantly reduce their risk" part, the "significantly," if my understanding is correct, that was only in one of the proposed executions and it was changed to "greatly" later on.

And regarding the specific diseases, I think the decision about the oral cancer claim is important because I think that's the -- the disease risk that consumers are most unclear about. For lung cancer, if this says that it reduces the risk of lung cancer, we saw some of the data where for risk perceptions that is one of the diseases that people have more accurate risk perceptions for already. So I just think that the decision about the oral cancer claim is important in terms of the potential impact on changing consumer perceptions. Thank you.

DR. MERMELSTEIN: Dr. McKinney.

DR. McKINNEY: I also want us to be mindful that the mandated warnings will also be on the product, such as "this product can cause mouth cancer," so those warnings will also be on the product. When it comes to absolute risk.

DR. MERMELSTEIN: Yes. Okay, other comments that would help clarify or questions for discussion relative, again, that

this is -- we will be asked to vote on whether the evidence does substantiate that smokers who switch completely to cigarettes -- to Camel Snus can significantly reduce their risk. So it sounds to me like the comparison here is relative to cigarette smokers and the comparator is not necessarily relative to nonsmokers but again, it's reducing their risk from continuing to smoke and if they switch completely.

This isn't asking about dual users but rather validity of the statement that if you switch -- if you're a smoker and you switch completely from cigarettes to Camel Snus, can you reduce your risk of each of those. So any other comments before we're going to vote on each of these?

DR. GIOVINO: I'm sorry.

DR. MERMELSTEIN: Yes, Gary. Go ahead.

DR. GIOVINO: This is Gary. I just have a -- and I'm sorry to have to do this. Could Olivia please repeat the comment she made about oral cancer?

DR. MERMELSTEIN: Yes. Olivia.

DR. GIOVINO: Sorry.

DR. WACKOWSKI: My comment was just that I think the decision about that claim is particularly important because that is the health risk that consumers most associate with

smokeless tobacco and if it is agreed that this is less of a risk, that switching is less of a risk, then I think that would be important in changing the perceptions about the harms of these products.

DR. GIOVINO: Yeah, okay. Thank you. I agree.

DR. MERMELSTEIN: So first Dr. Kozlowski and then we'll get back to -- okay. Dr. Kozlowski, you had a comment?

DR. KOZLOWSKI: Yes, I'd like to endorse what Olivia mentioned here about oral cancer. I know a number of former smokeless tobacco users who switched to cigarette smoking entirely on the grounds that they were afraid of oral cancer and so I think one does have a sense of the impact of the packaging of all of this information and -- enough.

DR. MERMELSTEIN: Dr. Blaha.

DR. BLAHA: Yeah, I was going to give my interpretation of this question, just kind of value judgments and anecdote side, I was going to interpret it just on the available scientific evidence regardless of, kind of -- I'll just give, I guess, my viewpoint about the importance probably in a later statement.

DR. MERMELSTEIN: Did you have a comment about the scientific evidence, though, that you want to --

DR. BLAHA: Just to say that might be -- everyone can

interpret this the way I was going to interpret it just in terms of this question of scientific evidence and not on its relative importance compared to the other outcomes in my view. Just my interpretation of the way this is written.

DR. MERMELSTEIN: Right, we want to evaluate the evidence here, correct.

Dr. Ossip.

DR. OSSIP: In terms of the oral cancer discussions, I agree with Dr. Wackowski and others that this is an important discussion. All of these are important.

In terms of biological plausibility, I keep -- what I keep thinking about is the slide that showed the much higher rates of oral cancer, which many of us have seen before in India and in some other countries, as well, which we didn't see, where the level of tobacco-specific nitrosamines is considerably higher and there may be other difference in product formulation as well. We know that NNK and NNN are elevated and are higher in Camel Snus than in some of the other products in comparison to cigarettes.

The number of pouches used is relatively low. When we think about the impact and how it will actually be used, this is in the absence of a modified risk campaign to get people to

switch or -- and potentially could impact on the number of pouches that they use, particularly since we've seen that it gives incomplete replacement of nicotine. So if they're moving towards complete switching to accrue health benefits to get full replacement, then this may either be combined with other sources of nicotine where they may increase the number of pouches that they use per day.

So the other issue that -- and this, maybe, is a biological plausibility issue, is in terms of the flavorings. So given the products have evolved and the types of flavorings that are being used are different, are likely different from what we've seen in the evidence from the epidemiologic studies, is it -- is it plausible that the place where you might see that greatest impact would be in the oral cavity? I mean, I expect there -- you could anticipate some somatic effects from whatever happens in the oral cavity or from ingestion of those products, but might that have -- is it plausible that that would have its greatest impact in the oral cavity?

DR. MERMELSTEIN: Dr. McKinney.

DR. McKINNEY: So those are great questions. I just want to comment on -- I think there were several questions there and I'll just comment on one of them. In terms of the different

patterns of use, I thought that was -- and I actually remembered that it was incorporated into the model and the use patterns were there significantly in the model and the model still showed some significant reductions in risk and lifesaving, because your question was about use.

DR. OSSIP: That was aggregated, it wasn't specific to --

DR. McKINNEY: Okay.

DR. OSSIP: -- a disease.

DR. MERMELSTEIN: Okay. So I think we're going to move to voting on Question 1. So we will be using an electronic voting system for the meeting. If you look at your microphone, you have three voting buttons on the microphone that say yes, in the middle is an abstain, and then on the right is no. So once we begin the vote, you're going to press a button that corresponds to your vote. I'm not sure how that works with people on the phone.

MS. COHEN: They're going to email their votes.

DR. MERMELSTEIN: Okay, they will email, okay. And then after the voting members have voted, the votes get locked in and then the results get displayed on the screen and I'll read the vote from the screen into the record, then we go around the table for each voting member to state your name and vote into

the record and the reason you voted as you did.

So we're going to begin voting now for Question 1a, okay? So Question 1a is to vote on the extent to which the available scientific evidence substantiates the following modified risk information in the advertising: Smokers who switch completely from cigarettes to Camel Snus can significantly reduce risk -- reduce their risk of -- and we're voting on (a) -- lung cancer. So vote by pressing your button.

(Committee vote.)

DR. MERMELSTEIN: It takes a little longer with call-ins.

(Pause.)

DR. MERMELSTEIN: Sally, have you sent in your vote?

MS. HERNDON: Yes.

DR. MERMELSTEIN: We haven't received it. You want to try sending it again?

(Pause.)

DR. MERMELSTEIN: Okay, we've got that.

(Pause.)

DR. MERMELSTEIN: So the votes are complete and locked in. I'm going to assume that -- well, there are eight of us were entitled to vote. Green is yes. So the vote is eight yes, no abstentions, and no -- for no, we just need to go around the

table among the voting members to just state your name and why you voted what you did. We won't --

DR. BIERUT: I think I'm the first one?

UNIDENTIFIED SPEAKER: You're the first voting member.

DR. BIERUT: Oh. I voted yes. I think the epidemiologic evidence was quite clear with the reduction of lung cancer risk.

DR. MERMELSTEIN: Okay.

Dr. Weitzman.

DR. WEITZMAN: It's the exact same answer.

DR. MERMELSTEIN: Okay.

Dr. Duffy.

DR. DUFFY: I was satisfied with the evidence.

DR. MERMELSTEIN: Okay.

Dr. Ossip.

DR. OSSIP: I agree. I think the evidence is compelling.

DR. MERMELSTEIN: Dr. Giovino.

DR. GIOVINO: Agree, very strong evidence both epidemiologically and no combusted tobacco smoke.

DR. MERMELSTEIN: Sally.

MS. HERNDON: Yes, I agree that the evidence is strong; however, as a practitioner, I am concerned about the lack of

morbidity data and the lack of consideration for other lung cancer risk factors.

DR. MERMELSTEIN: Okay.

And Dr. Thrasher.

DR. THRASHER: Yeah, I agree for the same reasons already voiced.

DR. MERMELSTEIN: Okay. And as well, the same reason, strong epi evidence. Okay, we're going to move now to the second question, which is to vote to which extent the available scientific evidence substantiates the following modified risk information that smokers who switch completely from cigarettes to Camel Snus can significantly reduce their risk of -- and now we're up to oral cancer. So vote about oral cancer.

(Committee vote.)

DR. MERMELSTEIN: Sally, we're just waiting for your vote. You just need to vote without that, don't need to put in the comment at this point.

(Pause.)

DR. MERMELSTEIN: Okay, we have three yeses, two abstentions, and three nos. So we will go around the room and we'll start over here with Dr. Ossip.

DR. OSSIP: I voted no because I believe we're still

lacking evidence to be able to make this decision. I'm particularly concerned about the impact of the evolution that's occurred in the products and the impact that that may have on oral cancer and also particularly here the lack of evidence on vulnerable populations like youth.

DR. MERMELSTEIN: Dr. Duffy.

DR. DUFFY: I voted no because I felt like the epidemiological evidence was based on products that were different from the ones proposed here.

DR. MERMELSTEIN: Dr. Weitzman.

DR. WEITZMAN: And I voted abstain, which I think is probably closer to no in terms of my interpretation. I just think that the data are insufficient for me to make a conclusion.

DR. MERMELSTEIN: Okay.

Dr. Bierut.

DR. BIERUT: I voted yes based on the epidemiologic data on Slide 50 that the FDA presented to us yesterday, that the point estimate was lower and I think that this is an important point of information for people who are going to use the product and that there is this greatly increased risk in combustible cigarette smokers.

DR. MERMELSTEIN: Thank you.

Dr. Thrasher on the phone.

DR. THRASHER: Yeah, I was challenged by this, but I think in the end I was relying on some of the -- well, the variety of studies that were shown yesterday around smokeless tobacco use having a lower association with oral cancer relative to smoking although they weren't directly compared and that's part of the hesitation that I have here.

I'm also consoled by the fact that the labeling would include a message or does include a message around how oral -- how around smokeless tobacco still can cause mouth cancer.

DR. MERMELSTEIN: Thank you.

Sally.

MS. HERNDON: I voted no because I am really still unsure that the evidence is completely there to state this specifically.

DR. MERMELSTEIN: Thank you.

Gary.

DR. GIOVINO: I abstained and my abstention was more leaning on the yes side. Obviously, I think it's really important that people who have a choice to make between cigarette smoking and smokeless tobacco select smokeless

tobacco if that's the only choice. I just was responding to the question of did I think the scientific evidence was sufficient.

DR. MERMELSTEIN: And I voted yes. In part, I also -- the relative risk data, there was some data there and so on balance, I felt that that was enough to vote yes.

Okay, we're going to move to part (c), so this time we're going to vote on whether the available scientific evidence substantiates the following statement: Smokers who switch completely from cigarettes to Camel Snus can significantly reduce their risk of -- we're up to (c) -- respiratory disease. So please vote.

(Committee vote.)

DR. MERMELSTEIN: People on the phone, make sure you're voting, send in your vote.

(Pause.)

DR. MERMELSTEIN: Sally, if you could send your vote in, we're just waiting for yours still.

MS. HERNDON: Sorry, I sent it. It might be weather-related delays. I don't why it takes so long for mine to go in.

DR. MERMELSTEIN: Oh, we also need -- Gary and Jim, we all

need yours apparently this time too.

DR. GIOVINO: I sent it.

DR. THRASHER: Weather related for me as well. I sent it a couple of minutes ago when we needed to cast our votes.

DR. GIOVINO: As did I.

DR. MERMELSTEIN: Try sending it to Caryn's email.

(Off microphone discussion.)

DR. MERMELSTEIN: Yeah, maybe Caryn can confidentially, without anyone hearing, ask each of them what their votes are.

(Pause.)

DR. MERMELSTEIN: The votes are being swept up in the hurricane.

(Off microphone comment.)

DR. MERMELSTEIN: Okay, for the people on the phone, we're going to actually try texting to you and you're going to get a text message, if you could text back your vote. Check your email, though, because your text number will be on your email for where to text to.

DR. GIOVINO: I don't know what you mean. My landline at the office won't accept a text. I'll have to give Caryn my cell phone number, and if I do --

DR. MERMELSTEIN: You can call the number. If you could

call the number, Gary, that's fine. That way we just want it to be confidential, your vote, until it's all released, so we don't want you to speak into the microphone what your vote is.

DR. GIOVINO: Call which number? I'm sorry.

DR. MERMELSTEIN: Look in your email, look in your email. Hopefully you'll get a phone number to call.

DR. GIOVINO: Right, I see. Okay.

(Pause.)

DR. THRASHER: This is Jim here. I just want to say I haven't received any email around this number to use or call or text.

DR. MERMELSTEIN: So is there a phone number that they could just call on line to talk their -- to state their vote or is there a way to turn off their voice on the microphone? Is there any way to isolate them like we do at other meetings?

(Off microphone comment.)

DR. MERMELSTEIN: Did any of you receive an email with a number? Maybe it's at the end here.

(Pause.)

DR. MERMELSTEIN: It seems likes there's an email issue probably here, so maybe we can try calling each person separately on a different line.

(Electronic audio recording.)

DR. GIOVINO: Hello.

DR. MERMELSTEIN: All right. We're checking to see what we have here. Besides hearing Buffalo's propaganda.

(Laughter.)

MS. COHEN: Sally, are you on the line? This is Caryn.

(No response.)

MS. COHEN: Sally, are you on the line? Are you muted?

(No response.)

(Off microphone comments.)

MS. HERNDON: Can you hear me? This is Sally.

MS. COHEN: Sally, you're the only one left, so you can go ahead and just say your vote. Yes, no, or abstain.

(No response.)

DR. MERMELSTEIN: Sally, you need to speak your vote.

MS. HERNDON: Can you hear me now?

DR. MERMELSTEIN: Yes, go ahead and let us know your vote. Sally, are you still there?

MS. HERNDON: Can you not hear me?

DR. MERMELSTEIN: Can you now just tell us your vote, please?

MS. HERNDON: I have done that, yes.

DR. MERMELSTEIN: No, we need you to speak it.

MS. HERNDON: The vote for 1c is yes.

DR. MERMELSTEIN: Okay, thank you.

Okay, for 1c we have eight yeses. Let's just go around the table quickly to state your name and yes and why.

Dr. Duffy.

DR. DUFFY: I voted yes because I thought the evidence was sufficient and also because of my clinical experience, I've seen that as well.

DR. MERMELSTEIN: Dr. Weitzman.

DR. WEITZMAN: I voted yes with a proviso that the data is particular to chronic obstructive pulmonary disease rather than respiratory disease.

DR. MERMELSTEIN: Dr. Bierut.

DR. BIERUT: I voted yes because I thought the data were compelling.

DR. MERMELSTEIN: Dr. Ossip.

DR. OSSIP: I voted yes because I thought the data were compelling for COPD and I thought the effect sizes were sufficiently robust, even with product changes that it was still a reasonable vote.

DR. MERMELSTEIN: Dr. Thrasher.

DR. THRASHER: I voted yes for the same reasons mentioned.

DR. MERMELSTEIN: Okay.

Dr. Giovino.

DR. GIOVINO: I voted yes for the reasons, and of course, no smoke.

DR. MERMELSTEIN: Sally.

MS. HERNDON: Yes, same reasons.

DR. MERMELSTEIN: Thank you.

And I also voted yes for all the reasons stated. Okay, we're going to vote on the last one on Question 1 and then we can take a break.

So for the last one for Question 1 is that we're voting on the extent to which the available scientific evidence substantiates the following risk information: Smokers who switch completely from cigarettes to Camel Snus can significantly reduce their risk of (d) heart disease. Yes, no, abstain.

(Committee vote.)

DR. MERMELSTEIN: Sally, we're going to need you again to state your vote, please, on this one.

MS. HERNDON: Are you ready for it now?

DR. MERMELSTEIN: Yes, go ahead.

MS. HERNDON: Abstain.

DR. MERMELSTEIN: Thank you. All right, this one we have three yeses, two abstains, and three nos. We need to go around the table. Okay, we'll start with Dr. Bierut.

DR. BIERUT: I voted yes because the epidemiologic data supported this. Though the change in risk was not as great as for the other diseases, the prevalence of heart disease is so common in the United States and in the population level, I think that this is an important strong message to give.

DR. MERMELSTEIN: Dr. Weitzman.

DR. WEITZMAN: I voted yes for exactly the same reasons as Dr. Bierut.

DR. MERMELSTEIN: Dr. Duffy.

DR. DUFFY: I abstained because I thought the evidence was unclear.

DR. MERMELSTEIN: Dr. Ossip.

DR. OSSIP: I voted no. I wavered between abstain and no, but I voted no because the risks were more similar for heart disease. There are independent effects on heart disease of smokeless tobacco and I thought there wasn't enough room for the evolving product to perhaps produce some different effects were those specifically to be studied.

DR. MERMELSTEIN: Dr. Giovino.

DR. GIOVINO: I voted yes because of the lack of oxidative gases and the epidemiologic evidence.

DR. MERMELSTEIN: Sally.

MS. HERNDON: I voted abstain because I still have questions about this one.

DR. MERMELSTEIN: Dr. Thrasher.

DR. THRASHER: Yeah, I wavered between abstain and no and landed on no primarily because of the much lesser reduction in risk and we're being asked to evaluate the claim about significantly reducing risk and it didn't seem to rise up to that level.

DR. MERMELSTEIN: And I also voted no for the similar reason as Dr. Thrasher felt that there were many other complications with heart disease risk.

Okay, we're going to now take a break before we move to Question 2, so let's just take a 10-minute break and we are going to come back here at 10:30 promptly for Question 2.

(Off the record at 10:18 a.m.)

(On the record at 10:30 a.m.)

DR. MERMELSTEIN: So we can begin our discussion. Okay, we're going to move to discuss the second question and the

second question consists of a variety of modified statements that describe less -- that are not as specific as those that we've just discussed, so they don't reference reduction of a specific disease or they don't discuss the need for complete switching and they are all to be evaluated. So we're going to take each of these one by one and discuss each since I think they are different and then we will vote after discussion of each one.

So let's start with the first statement in which we want to discuss the available evidence that the first statement is Camel SNUS contains less of the harmful -- sorry, Camel SNUS contains less of the harmful chemicals than cigarettes. So it's open for Committee discussion about the statement that it contains less of the harmful chemicals than cigarettes.

Dr. Weitzman, you look like you're poised to --

(Off microphone comment.)

DR. MERMELSTEIN: Oh, this is just if you have any comments before we vote. I'm just opening to see, before we vote --

(Laughter.)

DR. MERMELSTEIN: People are ready to vote, any comments from the --

DR. GIOVINO: I'm sorry.

DR. MERMELSTEIN: Gary, go ahead.

DR. THRASHER: Go ahead, Gary. I'll ask afterwards, we may have some questions or some issues with trying to tell you all that we have questions by email.

DR. GIOVINO: Right, so we might have to speak up. Jim, why don't you go ahead?

DR. THRASHER: Yeah, I mean, I guess for me, one of the main ambiguities of this statement is around snus containing less of the harmful chemicals in cigarettes versus exposure being less when using Camel Snus versus using cigarettes, and that's partly because of what we've seen in some of the discrepancies between the analysis of the chemical composition in the product itself versus where snus often has much higher levels of cadmium, arsenic, and TSNAs compared to the cigarette smoke, but when we look at actual exposure, we see a different picture.

So I'm still struggling with the language here and like I said, I just wanted to put that out there. I don't know if anybody else had any similar concerns.

DR. GIOVINO: This is Gary and I -- that's exactly what I was going to say. I think it's not as precise as it could be

and less of many of the harmful chemicals or most of the harmful chemicals or -- I mean, I would advise FDA, I would ask that FDA either comment on this or, regardless of the vote, work on tweaking this to make it more accurate. I mean, if FDA were to approve such a statement and the very obvious data on arsenic, cadmium, and two TSNAs were presented, it would lose a lot of credibility, I think, so that's my concern.

DR. MERMELSTEIN: So that's the value of our discussion, is that, I think, that votes may go one way or another here because of the specific statement and I think that it would be good to have this discussion, which is that the language here is particularly challenging when you see the actual product chemistry which looks different than exposure and yet this statement can lead people to view things one way or another. So it's the statement itself can be challenging, exposure may be less, but the actual product chemistry leads you to make a different, perhaps, decision here.

Anyone else on the phone?

MS. HERNDON: Yes, this is Sally. I agree with the concerns that have been raised and want to add to that, that I did see some variability in these products from year to year and want to take that into consideration as it relates to

thinking about how to present those to the public, especially if this is -- if this gets approved and is locked in for 5 years, what if the product actually changes over that time.

DR. MERMELSTEIN: Um-hum.

Other comments from the Committee?

DR. KOZLOWSKI: This is Lynn Kozlowski.

DR. MERMELSTEIN: Yes, go ahead, Lynn.

DR. KOZLOWSKI: Just one comment, that I think if this statement had been worded "Camel Snus contains fewer of the harmful chemicals in cigarettes" it would be easier to support.

DR. MERMELSTEIN: Yeah, I think this is perhaps a challenging statement that, I think, our sentiment that I'm hearing expresses that there are -- this might just be a work in progress and that some of the sentiments here of indeed there may be fewer or certain chemicals or exposure, but it's not well represented, perhaps, in this statement.

Other comments?

Dr. Wackowski.

DR. WACKOWSKI: I guess there's also potentially a question about the intention of the statement and how it might be understood in terms of is it fewer or less different types of chemicals or a lower concentration of the total number of

chemicals, which both might be true or they might be different but, you know, I think those are two different things. And so I'm not exactly sure what the intention was with the claim or necessarily which way it would be interpreted and if any research was done on how that was being interpreted.

DR. MERMELSTEIN: Yeah. Any thoughts, Dr. McKinney?

DR. McKINNEY: Yeah, I had a very similar question in looking at what's written in (a) but also what was written on the slide in terms of the actual advertising, just has less of the harmful chemicals found in cigarette smoke and I'm unsure of the relationship between what's written here and what was written in the book in terms of what's being asked for.

DR. MERMELSTEIN: So I'm going to ask FDA, then, to comment on that one. We are voting on what's on the slide versus not what's in the execution, right?

DR. KITTNER: I didn't realize that it was different, what's written on the slide versus the execution. So we want to vote what's in the execution, so let me just double check what's in the execution.

DR. McKINNEY: And I'm looking at CC-20 provided by the Sponsor.

(Pause.)

DR. KITTNER: So there are a variety of statements across the different executions, so we just picked one of them, so we would like to vote on this one.

DR. MERMELSTEIN: Okay.

DR. McKINNEY: Thank you.

MS. HERNDON: This is Sally. I also had a comment about the interpretation of the -- depending on how the product is actually used by the snus user and seeing that the executions also are doing things like promoting customizing your enjoyment with up to 30 minutes of flavor per pouch. With that kind of length of use there may be variations among users.

DR. MERMELSTEIN: Okay. So I think we're going to vote on this specific statement, which is that Camel Snus contains less of the harmful chemicals than cigarettes. So is the Committee ready to vote on that? Okay, the voting now on this specific statement, Camel Snus contains less of the harmful chemicals than cigarettes.

DR. KITTNER: Dr. Mermelstein, I have a correction.

DR. MERMELSTEIN: Okay, let's -- can we retract whatever we've just done?

(Laughter.)

DR. MERMELSTEIN: Go ahead.

DR. KITTNER: Okay, so the specific statement that we would like the Committee to vote on is Camel Snus contains less of the harmful chemicals than cigarette smoke, it should be cigarette smoke, not cigarettes. That's the exact language that's in one of the executions.

DR. MERMELSTEIN: Okay, thank you, Dr. McKinney, for pointing that out. Okay.

DR. KITTNER: So we're going to change it on the slide. Do you want to go to --

DR. MERMELSTEIN: You know what, let's come back to this one --

DR. KITTNER: Yeah, okay.

DR. MERMELSTEIN: -- while you change that and let's go instead to (b). So we're going to come back to that and let's move to (b), which is that smokers who use Camel Snus instead of cigarettes can significantly reduce their health risks from smoking. So this statement, as is written -- excuse me, Dr. Shiffman.

(Off microphone comment.)

MS. COHEN: He needs to use the microphone.

DR. MERMELSTEIN: Okay, so Dr. Shiffman made the point that that's Execution 1 but that Executions 2 and 3 have the

words "switching completely," so is this another one that we want you to decide about what we're voting on here?

DR. KITTNER: We're not interested in voting on all of the language across all of the executions, we just picked some that we felt were important to get the Committee's input on, so yes, the way it's worded here is how we would like the Committee to vote.

DR. MERMELSTEIN: Okay.

DR. THRASHER: This is Jim here. I guess, for me, one of the primary concerns is whether this message communicates the completely switching notion because also using the "instead of cigarettes" suggests that a substitute -- substituting some cigarettes for Camel Snus, in my interpretation. So I just say that because that's going to be one of my concerns and so my vote is going to depend on which language we use.

(Off microphone comment.)

DR. MERMELSTEIN: So the point that Dr. Shiffman is making, which I agree, is -- I mean, there is a difference when it does not say completely switch. So I think we're going to deal with this specific comment unless Dr. Kittner -- and then we can have our discussion which explains exactly why we might vote a certain way.

DR. KITTNER: So this is exactly the kind of discussion that we wanted to hear in terms of what language is clear and what language might not be clear.

DR. MERMELSTEIN: Okay.

DR. KITTNER: So this specific statement is on the execution, so that's what we would like the Committee to discuss and vote on.

DR. MERMELSTEIN: Okay. So we're going to vote on this statement as it is, which is smokers who use Camel Snus instead of cigarettes can significantly reduce their health risks from smoking.

My understanding, Jim, is from you and your comment on the phone that you would have felt differently when you -- I'm not asking at all what you're going to vote, but rather that because this does not say completely switch, that's an important distinction in how you think about this; is that correct?

DR. THRASHER: That's correct.

DR. MERMELSTEIN: Okay. So right now, just again, we are discussing Item 2b, Question 2b, which is smokers who use Camel Snus instead of cigarettes can significantly reduce their health risks from smoking.

Other comments from the Committee about your thoughts of this language?

Dr. Ossip.

DR. OSSIP: Another concern that I have about this language is that it is broad and so, for example, in the case of a pregnant smoker this could pretty readily be perceived as that I will have a better birth outcome, it does say their health risk, but I think that's a distinction that is a technical distinction but would not be one that would necessarily be perceived. So I'm concerned with the lack of specificity of health risks, not in a context of what particular ones are reduced or what ones may not be reduced.

DR. MERMELSTEIN: Okay. So it's a broad statement and this statement doesn't imply anything about for whom.

Sally, did you have any -- did you have a comment or question on the phone?

MS. HERNDON: Yes, I think we should be voting on it as it's written here because of the concern over the practice in the real world and --

DR. MERMELSTEIN: Okay.

MS. HERNDON: -- dual use.

DR. MERMELSTEIN: So here, again, it's just smokers who

use -- 2(b), who use Camel Snus instead of cigarettes can significantly reduce their health risks from smoking.

Dr. King.

DR. KING: Yeah, so as someone who is primarily tasked with messaging scientific information, I can appreciate the need to put it in very simplistic terms. That means that I think there's a very important balance and particularly for this purpose, you've got to get it right and you need a certain level of specificity with the nomenclature and terminology so that people don't misconstrue it.

That being said, I have two concerns, primarily, with this language. The first gets to this exclusive use and I think that it's critical that it be messaged to the public, you know, if you're going to, that you have to switch completely, that's where the net benefit is going to be in terms of health and that's what the science has shown for certain health indicators. And so, you know, I think that the, you know, the broader -- the notion of it could be scientifically defensible in some context, but you need key caveats.

My other concern is the overbroad -- and generalization to health risks more broadly and I think that after the discussion we just had on the other health outcomes there is clearly some

variation in, you know, the different risk factors. And so I think that you need more specificity on the specific health outcomes for which there would be that reduced risk and ideally you'd want that in alignment with whatever was determined based on the first round of voting we did.

But I think the broad nomenclature over just reducing health risks is so general that it has a potential to be misconstrued, particularly for vulnerable populations such as pregnant women but also, I think, kids as well and that's something important to consider in the health risk communication to the general public.

DR. MERMELSTEIN: Okay. It's broad, it doesn't say anything about complete switching and it could be in any pattern, so -- Dr. Bierut.

DR. BIERUT: I just want to make a comment in my role as a physician and as a leader of -- in a large healthcare system. So we're always talking about the public here but there's also physicians, and one of the issues that I'm seeing again and again with physicians is that they are unwilling to talk at all about modified risk products and reducing risk because of language issues that we have. And I think we're also missing an opportunity by getting healthcare providers across a system,

nurses, physicians, not giving these messages because we are not giving clear messages, ourselves.

So when I look at this, I do think it's important to say completely switch, I think that that's really key. I see it in the executions that were presented here. I see a different thing in the -- what the FDA is asking us to vote and I'm going to vote on the spirit of what we're trying to do here, which is really we're trying to communicate that completely switching can significantly reduce the health -- and especially given that we just voted on Number 1 about the decreased health risks, not necessarily all of them, but some of them.

DR. MERMELSTEIN: Okay.

Dr. King.

DR. KING: Can we just clarify what exactly would you like the Committee to vote on, then? Is it in the spirit or is it the exact terminology used here? Just so we make sure that everyone on the Committee is clear on what exactly they're voting on.

DR. MERMELSTEIN: Okay.

DR. KING: And I'm not voting, so it doesn't really matter --

DR. MERMELSTEIN: I know.

DR. KING: -- but for you that are voting --

DR. MERMELSTEIN: It's a very good question.

DR. KING: -- I think this is a critical distinction at this point in time.

DR. MERMELSTEIN: All right. So I'm going to turn that back to the FDA in terms of the vote and the spirit of what's being communicated versus the actual language and do you want us to vote on the actual language and then communicate our comments? And while they're debating that -- no, go ahead.

MR. ZELLER: We definitely want you to vote on this, what we're discussing in real time, is do we add another one for you to vote on, but we definitely want a vote on this.

DR. MERMELSTEIN: On 2b you want us to vote on the language as it is and which is how it says, okay.

Dr. Thrasher, you had a comment on the phone.

DR. THRASHER: Yeah, I mean, I guess the data points that I'm looking at around this question about overall health risks are around, kind of, all-cause mortality and there are some data that FDA presented yesterday that compared switchers to people who quit showing there was an elevated all-cause mortality risk for switchers versus the quitters and Dr. Kozlowski, earlier in the day, said something about how

much higher that the relative risk for all-cause mortality is amongst smokers versus quitters.

I didn't see the data points on that, that for me it will help in evaluating this broad category of health risk if we can look at the all-cause mortality compared to switching, which is quitting versus all-cause mortality comparing smokers, smoking versus quitting. Does FDA have any data that they can share with us on that?

DR. MERMELSTEIN: Well, I'm not sure that's what this question though, Jim, is asking, it's just if you're using snus instead of cigarettes.

DR. THRASHER: I mean, I don't know. I'm interpreting reducing health risk as kind of a global statement around all health risks.

DR. MERMELSTEIN: Um-hum.

MS. HERNDON: This is Sally. I have a comment on that.

DR. MERMELSTEIN: Go ahead.

MS. HERNDON: I think some smokers could interpret this sentence as "if I just substitute two of my cigarettes per day for snus I'm significantly reducing my health risk," and I agree with what Brian said earlier that we need to be communicating that completely switching is critical and the

words "health risks" are overbroad because it doesn't relate to other health risks like for pregnant women and the risk of addiction for young people.

DR. MERMELSTEIN: Okay. So let me ask a clarifying question of the FDA because I think this also gets at the question about are we voting about the spirit or the wording. So I'm going to ask Dr. Kittner, because I do think if you're debating whether you're going to add something for us to vote on that might reflect more precise language, that will influence how we might vote on this one. So if you could let us -- let us know if you're going to be adding one for us to vote, I think that will -- that might have an influence on this vote.

DR. KITTNER: Thank you for your patience. So we were able to get a lot of what we needed from the discussion from Question 1 around the completely switching. So now what we would like to do is ask you to devote your attention to Q2b, which is around smokers who -- is that right? Smokers who use Camel Snus instead of cigarettes can significantly reduce their health risks from smoking. And, again, you've touched on some of the questions that we had in terms of health risks and how is that understood by potential consumers.

DR. MERMELSTEIN: Okay. And so in just this language about smokers who use instead as opposed to switching but just however any -- however we each individually interpret this question, which is going to be in a variety of ways, and what the question says and so we each may have a different interpretation of what this means is what you are --

DR. KITTNER: Yes.

DR. MERMELSTEIN: -- saying that we should do. So we should -- yes.

MR. ZELLER: Let me add. The discussion that has taken place is what animates the vote.

DR. MERMELSTEIN: Right.

MR. ZELLER: We're not going to add anything for you to vote on here.

DR. MERMELSTEIN: Right. And I think --

MR. ZELLER: And when we take the transcript back, we look at all the comments that were made to best understand where individual members of the Committee were coming from and what they were thinking about if they choose to speak into the microphone to inform the vote that they made. So we will get what we need from the discussion that's taken place on this so far, the vote that's about to happen, and any other comments

that individual Committee members, voting or nonvoting, want to make on 2b.

DR. MERMELSTEIN: Okay. So I think that the debate has been about what does "use" mean here and which is different from complete switching or just level of use and continued level of cigarettes and uncertainty about that as well as uncertainty about the broadness of health risks. So I think we each have a different level of comfort with the broad statement, that's not specific, but I do think that what's been expressed is the Committee's been more comfortable when there's levels of complete switching and more specific health risks involved.

So are we ready to vote on 2b? Again, everyone may have a different interpretation, but we're voting on this specific language as it is written and we will each have an opportunity to make a comment explaining our vote after we vote, so those will be important. So we're going to vote on 2b, smokers who use Camel Snus instead of cigarettes can significantly reduce their health risks from smoking. Yes, no, or abstain. So let's each vote now.

(Committee vote.)

DR. MERMELSTEIN: Sally, you know, I think we just need

you to clarify your vote for 2b over the phone, if you could just state your vote.

MS. HERNDON: No on --

DR. MERMELSTEIN: No? Okay, thank you.

MS. HERNDON: -- 2b.

DR. MERMELSTEIN: Okay, I think we've got everybody's votes now. Okay, the vote is one yes, two abstentions, and five noes, so we're going to go around. Okay, we'll start with Dr. Duffy. State your vote and a brief explanation.

DR. DUFFY: I voted to abstain primarily because I'm -- I agree with the spirit of it but I think it needs to say "completely switch" and I think the specific health risks need to be explicitly stated, like lung cancer or -- I think there's some evidence in the literature that shows consumers respond better to more specific health risks.

DR. MERMELSTEIN: Great.

Dr. Weitzman.

DR. WEITZMAN: I found this one pretty easy and voted no because of a lack of specificity of population and health outcome being described and not mentioning complete switching.

DR. MERMELSTEIN: Dr. Bierut.

DR. BIERUT: I voted yes because I viewed the "instead of"

as the switching component and thinking that the spirit here was in the switching and knowing that communicating with patients is messy and I didn't want to get caught up in the exact words here and thinking that there will be other words surrounding messages that I hope will clarify things and I have faith will clarify things.

DR. MERMELSTEIN: Thank you.

Dr. Ossip.

DR. OSSIP: I voted no, pretty much a duplicate, I'd say, of what Dr. Weitzman had said.

DR. MERMELSTEIN: Okay.

Dr. Thrasher.

DR. THRASHER: Yeah, I voted abstain because of the lack of specificity around switching and concerns about the current language and implying dual use is okay or -- results on reduced risk.

DR. MERMELSTEIN: Sally.

MS. HERNDON: Yes, I voted no because of the lack of specificity, the overly broad generalized risk reduction statement and working with smokers who are struggling to quit, they often will grab at straws. I'd like us to do more to communicate what we really know works in terms of tobacco

treatment and really giving people sound information about standard of care tobacco treatment which we know a good deal about.

DR. MERMELSTEIN: Thank you.

And Dr. Giovino.

DR. GIOVINO: Hi. I voted no. I would've voted yes if it said "completely switching" instead of "instead."

DR. MERMELSTEIN: And I also voted no. As with Dr. Giovino, had it said "completely switching," I would've voted yes. I was less concerned about the health risk part but just would've preferred the "completely switch."

We're going to move back to 2a. The clarification on 2a is that Camel Snus contains less of the harmful chemicals than cigarette smoke. Okay, so are we ready to go back and vote on 2a? This is now talking about cigarette smoke and Camel Snus. Okay, people can vote.

(Committee vote.)

DR. MERMELSTEIN: Sally, we need your vote on the phone. If you could just speak your vote.

MS. HERNDON: On 2a I'm voting no.

DR. MERMELSTEIN: Okay, thank you. So I think we now have all votes in.

(Pause.)

DR. MERMELSTEIN: Okay, we have two yes, three abstain, and three no.

Okay, Debbie. Dr. Ossip.

DR. OSSIP: I don't think the addition of the word "smoke" changed the concerns that I had about this wording.

DR. MERMELSTEIN: Okay.

Dr. Duffy.

DR. DUFFY: I abstained. I felt in general it was an okay -- in spirit, as we're calling it, but felt that I also wanted a quitting completely statement in there and I wanted it to say reduce exposure rather than contain.

DR. MERMELSTEIN: Okay.

Dr. Weitzman.

DR. WEITZMAN: I voted no but had difficulty between no and yes. I voted no because there are some constituents that are harmful that this does not apply to. But in totality, if you look at 7,000 chemicals versus a substantially lower number of chemicals, the answer is yes, but I did vote no

DR. MERMELSTEIN: Dr. Bierut.

DR. BIERUT: Cigarette smoke, I think, is really the great enemy that we have here. Combustible, inhaling any type of

combusted -- combustion products are terrible. And so I think that, again, with this spirit of going from the different type of mechanism of use of the tobacco product is conveyed in here and important.

DR. MERMELSTEIN: Thank you.

Dr. Thrasher.

DR. THRASHER: Yeah, I voted to abstain because in the end, the wording really matters here and although I'm in agreement with the sentiment, it does need to be expressed more clearly for me to get on board with saying that the evidence supports it.

DR. MERMELSTEIN: Sally.

MS. HERNDON: Yes, I voted no because even though I agree that combustible cigarette smoke is the most hazardous, I'm concerned about the interpretation of the statement in practical settings, especially in most young people.

DR. MERMELSTEIN: Dr. Giovino.

DR. GIOVINO: Since the table that was presented had data on cigarette smoke and not the tobacco in cigarettes, after inserting the word "smoke" I did not change my vote. That said, I think that just a minor tweaking of the statement would be good to convey the importance that there are a lot of -- a

lot fewer cancer-causing and deleterious chemicals in unsmoked tobacco compared to smoked tobacco.

DR. MERMELSTEIN: Okay. And I voted yes because I do think the addition of "smoke" made a difference and it puts the emphasis that it is the smoking and the combustion that matters.

Okay, we're going to move now to 2c, which is the statement that switching to snus means less risk for you. And I can anticipate that the Committee discussion may focus on the word "switching" as opposed to "complete switching" for you and how personal that is anticipating the discussion we've already had. But, Committee members, comments you'd like to make about this one?

Dr. Ossip.

DR. OSSIP: So yes to those two points. I think also, you know, with these -- so I agree with the spirit of it, you know, kind of looking at a combustible versus a noncombustible smokeless tobacco, but I do think the details matter in terms of how it's perceived and it's hard to disentangle that from voting on these kinds of statements.

So I also would like to see kind of less risk in some sort of a context, you know, because it's not less risk for

everything, it's less risk for particular things. And so, again, if we get back to vulnerable populations and it's saying less risk to you, they may be perceiving it as less risk for things for which they are especially vulnerable and it would not be so. And so in that case it would be misleading.

DR. MERMELSTEIN: Dr. Wanke.

DR. WANKE: And the one additional lack of specificity is switching without specifying that it's cigarettes or cigarette smoke. So given the popularity, say, of e-cigarettes, this statement, taken in isolation, say -- or in the ad with just this statement, switching to snus, does that mean switching away from e-cigarettes or if it's the class of smokeless, would this be switching from -- would somebody interpret this as switching from dip or chew to snus? And, again, it would depend on whether this is taken in isolation on an ad or if were in the context of any of the other statements that were clarified.

DR. MERMELSTEIN: Thank you.

Dr. Bierut.

DR. BIERUT: So I think that this is really a critical point with electronic cigarettes in here and throwing that into the kind of landscape that we have of smoking. So just to

clarify this discussion, I have been considering all of this comparing combustible cigarette smoking to the change of snus, and all the data that we have been presented had to do with combustible cigarette smoking and the epidemiologic data versus this other type of tobacco product.

If we bring electronic cigarettes into this discussion, it changes the whole spirit here. So just for me to be consistent, I'm just saying, for the FDA, when you're reading the transcript, I'm clearly thinking about combustible cigarette smoking.

DR. MERMELSTEIN: Dr. Holman, do you want to --

DR. HOLMAN: Yeah, just to provide a little context. I mean, I think it's a very good point. In all three versions of the label they gave us, this statement appears below a header that says "I am a smoker. Why should I switch?" And then it says "Switching to snus means..." and this is one of those statements. And so just to provide more context of where we pulled that statement from, in case that helps with your deliberations.

DR. MERMELSTEIN: It does, thank you.

First we'll go to Dr. Kozlowski, McKinney, then Dr. -- Dr. Kozlowski.

DR. KOZLOWSKI: No, I just want to make a comment about Point (d), so not right now.

DR. MERMELSTEIN: Okay.

Dr. McKinney, did you have a comment?

DR. McKINNEY: Yeah, and it's kind of a question for you. There could be a lot of questions about the consumer's perception of these statements and I think Dr. Holman did a great job of putting it in context in terms of the -- it's like this was a statement that was pulled out and there's more context that's perhaps missing.

In addition to that, and you knew I was going to say this, that I think if there is a -- if there's more than one question about consumer perception, perhaps the Sponsor has that data and could share it, and what the consumer said verbatim about seeing these advertisements. I know they covered it, but I don't think they answered specifically the questions that you have.

DR. MERMELSTEIN: Dr. King.

DR. KING: So I just would like to reiterate some of the other issues that have already, you know, come across. I think, you know, switching completely is a key distinguishing factor in this and again, I understand the importance of

communicating health risks to the public and it's something that I take very seriously, but you need enough specificity to get it right.

And I also think that it's being presented with a lot of information and this notion that the public is going to sit down and read this entire document with all of this information, I think, is a bit misleading.

You know, most people look for the big things that are -- you know, that are going to be striking and come across and that being said, it has to be worded very specifically to get it right. And I also think the lack of a comparator is very concerning to me and I think, you know, is it less risk compared to what? I mean, that could be anything. And if you just isolate that even with the other information, counting on the person in the general public -- remember that these documents are going to be plastered all over the place if they were to be approved and, you know, you can't rely on the consumer to read every single component in these documents.

And so I think, you know, it's just really important that the language that is there is as precise as possible to avoid things being misconstrued and not assuming that the consumer would do, you know, either. Or the language there has to be

factually accurate as written.

DR. MERMELSTEIN: Dr. Wanke.

DR. WANKE: Yeah. So in following up on that and Dr. Holman's comment, given that this was presented -- you clarified that this was presented in a context for the purposes of the vote. When you're voting yes or no, is it voting on that statement, then, it could be used in isolation or voting on that statement knowing it has a context? It's just I don't know. Since we don't have an example from a previous MRTPA that's been approved, we don't know how these kinds of things would be allowed to be used. Would the Applicant, if that phrase were approved, would they be allowed, almost as a modular kind of a thing, if they could take any of these statements and use them in different combinations or in isolation in an ad?

DR. HOLMAN: For purposes today, we'd like you to consider some of the contexts that I just provided, not as an isolated statement in any other context.

DR. MERMELSTEIN: Dr. McKinney.

DR. McKINNEY: Yeah, very briefly. In response to Dr. King's comment, the industry is asked to conduct studies on comprehension and they do those studies and so I just feel like

we didn't necessarily -- we aren't incorporating that into some of the discussions and things that we're saying. That's some very important data.

DR. MERMELSTEIN: Dr. Duffy.

DR. DUFFY: Yeah, I understand that there is a step, you know, preceding these bullet points, but a lot of times people look at the bullet point in isolation and it just doesn't seem like it would be that difficult to say something like switching from smoking completely to snus means less risk of lung cancer for you. I mean, that's the message I hear coming up repeatedly from everybody, is the specificity about switching completely and then specifying the risk.

DR. MERMELSTEIN: Okay, I think we've probably come to a point where we're ready to vote on this because I do think that the key points, again, that are being -- coming up with each item are the level of comfort people have with, or lack of comfort with, the lack of specificity and the sentiments are there.

So I think these are the same things we're hearing echoed, but I think we're ready to vote on (c). So we're going to vote on switching to snus means less risk for you, again considering the context that this appears, it's not a statement in

isolation but in that context that we were being presented with. So go ahead and vote, switching to snus means less risk for you.

(Committee vote.)

DR. MERMELSTEIN: Sally, we need you to state your voice -- your vote, please.

DR. HERNDON: My vote on 2(c) is no.

DR. MERMELSTEIN: No. Thank you.

Okay, we have all the votes in. We have four yes, one abstention, three noes, so we'll go around. This time we'll start with Dr. Bierut.

DR. BIERUT: Placing this in context, I think that this statement is capturing the switching from combustible to snus and I think it's a clean statement that hopefully will push people.

DR. MERMELSTEIN: Dr. Weitzman.

DR. WEITZMAN: That was very interesting because it was your previous comment that pushed me to say no, my concern about e-cigarettes and it not being clarified in that particular statement.

DR. MERMELSTEIN: Dr. Duffy.

DR. DUFFY: I abstained once again because I felt like the

bullet point needed to stand alone and needed to say completely switching from cigarettes to snus and it needed to specify the health risk.

DR. MERMELSTEIN: Dr. Ossip.

DR. OSSIP: I voted no for the reasons of lack of clarification of switching from what, complete switching and from what, the lack of specificity around risk and the personalization of "for you" because it would not apply necessarily to everyone. I do want to comment that I have heard what Dr. Bierut has said in terms of a clear message not only to the public but also for healthcare providers who need to have some clear messaging and I think that this could be a statement that in a context that a healthcare provider could make in working with a patient, knowing the specifics of that patient's situation, it would be in a broader context. But I'm voting on this as something that would be used in marketing that would go out to the general public where that context would not be present.

DR. MERMELSTEIN: Thank you.

Dr. Giovino.

DR. GIOVINO: I voted yes because of the context of the statements. If upon further review FDA sees the need for

"completely," then I would totally understand, but I think, in the context, the statement stands.

DR. MERMELSTEIN: Sally.

DR. HERNDON: I voted no because, as I understood it yesterday, these ads -- this product can be promoted in lots of different ways and these ads don't necessarily stand completely and I think there's lack of specificity and lack of clarity about completely switching from combustible cigarettes. It could interpreted as switching from other tobacco products or it could be easily misinterpreted.

I would like to say though, however, that outside of the context of this discussion, I am encouraged about some of the work that we're starting to do with the FDA and with CDC about trends in work to educate providers and tobacco users about whether it's evidence based in terms of tobacco treatment and that includes both fairly sophisticated coaching methodologies to help people really understand these nuances that we're talking about and clarity about what we really know works, it's less of a risk than using an alternative tobacco product.

We do have strong FDA-approved tobacco treatment methodologies that aren't being used in the United States. For example, many physicians don't know the evidence about

combination therapy or varenicline fully at this point. So I'd like to see it be more to really help tobacco users quit, but it's the failed science and the evidence.

DR. MERMELSTEIN: Good point.

Dr. Thrasher.

DR. THRASHER: Yeah, I voted yes primarily because I was considering this in the context of the other information about completely switching from smoking to snus. And then, although I was a little bit concerned about this issue of addressing "you," as a smoker, and individual benefits versus, you know, population-level benefit, I ended up landing on -- well, having less concern about that, just because of what Dr. Giovino mentioned earlier about how so much of our sufficient messaging is also based on the population-level benefits and those benefits may or may not accrue to individuals. So, anyhow, that helped to alleviate the concerns.

DR. MERMELSTEIN: Thank you.

And then I also voted yes and that I do think the context matters here and there, I think, the context was -- would be interpreted as switching is safer, so that's good.

Okay, we're going to move to the last item for the vote and this is a simple statement that no smoke equals less risk.

Dr. Bierut.

DR. BIERUT: So this statement actually was the one that I thought about most as I was going to sleep last night, because of electronic cigarettes, and I'll just say that I came down on the side of -- I don't hear people who use electronic cigarettes talking about smoking. They describe themselves as vaping. And so because of that, I think that this is more specific to combustible cigarette smoking and so -- but this one gave me concern.

DR. BLAHA: I'll just say I find this one interesting because, you know, of course we'll consider it in context, but it's sort of true, separate from snus. It doesn't have anything to do with the snus per se, at least as written, but of course it has context. But no smoke equals less risk is kind of a nice public health message, I think.

DR. MERMELSTEIN: Laura, back to you. This one gave you concern and I wasn't quite sure what you were saying.

DR. BIERUT: Because I was concerned do people who use electronic cigarettes think that they're smoking.

DR. MERMELSTEIN: Oh, I don't think -- yeah.

DR. BIERUT: And that was my concern, is how do they think about it? But I think that they will interpret it as no,

they're vaping, they're not smoking.

DR. MERMELSTEIN: Dr. Ossip.

DR. OSSIP: I like the simplicity of this message and I think, you know, it's compelling to say no smoke, less risk, but I do get concerned about vulnerable populations who would -- you know, like pregnant women or -- well, let me take the case of pregnant women who would think that this may apply to them and, in fact, the risks of smokeless tobacco are not different in terms of pregnancy outcomes from what we've seen.

And so I am concerned about -- I think, in a context, this would be good, you know, you're speaking to your patients, you're -- or with some caveats around it. But I think, as is, it leaves open a very clear message to vulnerable populations for whom it may be inaccurate.

DR. MERMELSTEIN: Dr. McKinney.

DR. McKINNEY: Again, I'd just like to remind us that there are mandated warnings that will go with this and they would also warn about a risk with pregnancy and etc.

DR. MERMELSTEIN: Yeah.

DR. OSSIP: Thank you. And I thought about that. There's no mandate that they be paired with this particular message. So if they are separated in time, then there may be no

connection made. If they were paired, that could also create confusion on the part of consumers, that one thing is saying less risk but at the bottom it's saying the risk in pregnancy and it could still be interpretation of either I don't know what this means or okay, it's still a risk, but it may be less risk.

DR. MERMELSTEIN: Yeah.

MR. ZELLER: Just again on the issue of context, taking Brian's point that individual consumers may see things in isolation even if context is provided, but in the spirit of explaining the context as we're looking at the second execution, it appears on a -- this statement appears on a panel along with what Matt had described earlier about I'm a smoker, why should I switch, but also with information on the same panel that says no tobacco product is safe. That includes the statement, minors and pregnant women should never use tobacco products.

DR. MERMELSTEIN: Dr. McKinney.

DR. McKINNEY: And so in that regard, actually, Dr. Ossip, I was going to agree with you because the mandated warnings are rotated -- so one-fourth of the time, I guess. But relative to what Mr. Zeller said, that statement is constant and with the

advertisement.

DR. MERMELSTEIN: Dr. Wanke.

DR. WANKE: I will note that in the executions there were three pages and this statement, the no smoke, less risk, is the most prominent, biggest thought size next to the product. And so I don't know how these could be presented if it's on a billboard and you're on the Metro and it's up there, that may be the one thing you see, not being able to read the smaller text. So this, of all of the messages, seems like the one that could most likely be seen in isolation.

DR. MERMELSTEIN: Dr. King.

DR. KING: Yeah. So out of all of them, this actually gave me the most agita, and I think it's oversimplified, and it's like me Tarzan, you Jane, and you know, it's so simple that you are potentially, you know, causing some issue, particularly for vulnerable populations. I would agree with the statement that was just made, particularly for young people.

You know, obviously, there was some data presented from the Applicant, but there was not one iota of data among kids and I would be very concerned about where these are available and the extent to which youth would interpret that,

particularly the big shiny prominent text that would say something like that, which again could have a lot of implications for a lot of populations. So, you know, I've reinforced this through all of these that have been voted on. I think specificity is key and this one, out of all of them, is the one that would probably make me the most apoplectic.

DR. MERMELSTEIN: Dr. Duffy.

DR. DUFFY: Gosh, I don't know how to respond because I'm kind of on the opposite point of view, but there is some beauty in the simplicity of it. It's just kind of no smoke, no risk, and it speaks the truth, I guess, in some ways. It's the smoke and the combustion.

DR. MERMELSTEIN: Dr. Shiffman, you had raised your hand, I don't know if -- or has that moment passed?

(Off microphone response.)

DR. MERMELSTEIN: Okay, thank you.

Dr. Wackowski.

DR. WACKOWSKI: Yeah, I agree with some of the concerns that Drs. King and Wanke brought up. This particular claim doesn't really allude to the theme of switching or switching completely really at all, whereas the other ones have and there's the possibility of this one, in particular, being kind

of viewed and considered in isolation because of the way in which it is presented in these materials. And I think it's also relevant to think about the different channels. So for example, for this advertisement, you know, imagine somebody just flipping through a magazine and this really stands out. Are they going to necessarily read the next two pages in detail? You know, I don't think that the data that was presented really explored that.

If you think about the website, it looked like the website homepage, you know, this was sort of the tagline that is highlighted and you kind of have to click on different things to kind of read more of the details. So I think that's sort of important context. That might be more related to how it's interpreted, which is our next question, versus whether, you know, this is an accurate statement, but those are just some comments I had.

DR. MERMELSTEIN: Dr. Weitzman.

DR. WEITZMAN: Despite being a pediatrician and caring desperately about kids and pregnant women, the reason why we're convened has to do with the deleterious effects of smoking cigarettes. I found this a very compelling statement and would like to remind people that there's going to be a surveillance

period, and we will know if this has an influence on pregnant women or youth uptake in a short period of time. So I really like that statement.

DR. MERMELSTEIN: Thank you.

Ms. Becenti.

MS. BECENTI: This statement is the one that I'm most concerned about because I think that those who are -- with low health literacy will see this and just take it. And then other vulnerable populations who will actually uptake tobacco, there is those with lower socioeconomic and then those who are a minority population, I think they will actually interpret this and just see it as is and then -- and because I think there is really no specificity and I think it's important to go communicate that to the public in the ad.

DR. MERMELSTEIN: Great. So not surprising, we have a variety of opinions about this particular statement and how it will be interpreted within the context.

So, Dr. Shiffman, this is your one moment.

DR. SHIFFMAN: Now you're making me nervous. I want to comment not on this particular vote but on the context of context, which is what I'm hearing the Committee say is each statement has to be incredibly detailed and now the Committee

is saying that you have too many statements, no one's ever going to read them, it's too complicated.

What was done was composing an overall message that does create a context. Each of these statements, as FDA has pointed out, is they're under a heading that creates a context, so there's something -- I think it's difficult and problematic to evaluate them one by one and what you saw, I hope you -- presented, was that more people viewed them in context than they could read individual bullet points, they could just look at the front.

What we saw was very modest expectations of reduced risk, actually less than the epidemiology would indicate, and again what we saw was virtually no interest from non-tobacco users, including -- tobacco users in the product and the interest was concentrated pretty much exclusively in smokers who were not expecting to quit. So I think we have to look at the fact that the ad would be presented as a whole, it's been evaluated as a whole, and we've seen data that it is not misinterpreted.

Thank you.

DR. MERMELSTEIN: All right, thank you. And I think we'll be able to discuss that with the next item.

And, Dr. McKinney, you had -- no, we're done. I think, as

I said, there are a variety of --

DR. GIOVINO: Robin --

DR. MERMELSTEIN: Oh, yeah.

DR. GIOVINO: May I make a comment?

DR. MERMELSTEIN: Please go ahead.

DR. GIOVINO: I think that the no smoke equals less risk message is one that, in fact, would be overall constructive even if it wandered away from the precise context. I think it's a powerful message. It needs to be understood in the context of the public, generally, misunderstanding the differential risks of these products very seriously.

Now, there have been comments about vulnerable groups. I would note that in the FDA backgrounder they did allude to issues related to gateway effect, but they only cited the peer-reviewed literature that supported gateway effect and, in fact, there's a sizeable peer-reviewed literature which they don't mention at all, that doesn't find gateway effects.

It finds it's more in the person rather than the product, that they're more high-risk individuals who are getting into tobacco products and, in fact, the product itself is changing things. To that end, even for vulnerable groups like youth, I think it's constructive for the message to be out there that no

smoke is less risk, that we don't want any kids to start, but the reality is that's when tobacco use starts and that I think it would be constructive for this to be well known in contrast to the belief that smokeless tobacco products are as dangerous or more dangerous than cigarettes.

Thank you.

DR. MERMELSTEIN: Thank you.

Anyone else on the phone have any comments before we vote?

DR. HERNDON: Yes, this is Sally. I have a comment about this particular item and how it could be misinterpreted. I work with a lot of young people who are senior high, high school age, educating them about tobacco, and no smoke equals less risk could be interpreted by young people that it's less risk of getting caught using by parents or teachers. So I do agree that we would need to look at how the message is being interpreted in real-world settings, particularly with young people, because we're trying to reduce addiction and having people move on to combustible tobacco products as well.

DR. MERMELSTEIN: Thank you.

Okay, I think we're now ready to vote on (d) and we're voting now on the statement "no smoke equals less risk." So please indicate your vote.

(Committee vote.)

DR. MERMELSTEIN: Sally, we need you to state your vote.

DR. HERNDON: On 2(d) I abstained.

DR. MERMELSTEIN: You abstained, thank you.

Okay, we should now have all votes. Okay, we have six yeses, one abstention, one no. I'll start on the phone. Dr. Giovino, state your vote and your reason.

DR. GIOVINO: Sure, thank you. I voted yes for I do think it's a simple message and I was looking at the execution and there is, you know, an image of a crushed-out cigarette. I was taken aback a bit by Ms. Herndon's concerns, Sally's concern about how youth might interpret it. But overall, given decades of misperception and Commissioner Gottlieb's concerns about the -- and many people's concerns about the deleterious effects of combusted tobacco products, I think this is a powerful message.

DR. MERMELSTEIN: Thank you.

Sally.

DR. HERNDON: Yes, thanks for calling on me next. I am saying, because I really do think that this could be a powerful message, if it were clear that it were directed to current smokers and I didn't feel that I got a really strong response

when I asked the question yesterday about how these -- will be marketed and whether they will be marketed broadly, generally, like in a magazine, as somebody said earlier, or to current smokers.

I have similar kinds of apoplexy that, I think, probably that Dr. King spoke and it depends on who's getting the message, it could be a really strong message for current smokers. It may not be the message for vulnerable populations.

DR. MERMELSTEIN: Thank you.

Dr. Thrasher.

DR. THRASHER: Yes, I voted yes because I do like the simplicity of the message and do believe that smoke is the main problem and I agree with Dr. Kozlowski that we need to be thinking about this within the broader context of misperceptions about relative risk.

I'm somewhat concerned about the lack of the switching component being included in this, but I just assumed that the switching message would be part of the overall package. And I'm also concerned about its use with regard to consumer