FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

(TPSAC)

Friday, January 20, 2012

8:00 a.m. to 2:30 p.m.

9200 Corporate Boulevard

Rockville, Maryland

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C O N T E N T S

P R O C E E D I N G S

(8:05 a.m.)

Call to Order

DR. SAMET: Good morning. I think we'll go ahead and get started with today's TPSAC meeting. I'm Jon Samet, chair of the Tobacco Products Scientific Advisory Committee. Good morning and thank you for joining us. I wanted to make a few statements and then we will introduce the committee.

For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues and that individuals can express their views without interruption. Thus, as a gentle reminder, individuals will be allowed to speak into the record only if recognized by the Chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine

Act, we ask that the advisory committee members take care that their conversations about the topics at hand take place in the open forum of the meeting.

We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topics during breaks. Thank you.

Caryn?

Conflict of Interest Statement

MS. COHEN: 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. With the exception of the industry representatives, all members and nonvoting members are special government 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 the federal ethics and conflict of interest laws, covered by but not limited to those found at 18 U.S.C., Section 208 and Section 712 of the Food, Drug, and Cosmetic Act, is being provided to participants in today's meeting and to the public. FDA has determined that members of this committee are in compliance with federal ethics and conflict of interest laws.

Under 18 U.S.C., Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts of interest when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Under Section 712 of the FD&C Act, Congress has authorized FDA to grant waivers to special government employees and regular federal employees with potential financial conflicts of interest, when necessary, to afford the committee essential expertise.

Related to the discussions of today's meeting, members of this committee have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their spouses or minor children, and, for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, CRADAs, grants, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children. Discussions will include such topics as the composition and characteristics of dissolvable tobacco products, product use, potential health effects, and marketing. This is a particular matters meeting, during which general issues will be discussed.

Based on the agenda for today's meeting and all financial interests reported by the committee

members, no conflict of interest waivers have been issued in connection with this meeting. To ensure transparency, we encourage all committee members to disclose any public statements that they may have made concerning the issues before the committee.

With respect to FDA's invited industry representatives, we would like to disclose that Drs. Daniel Heck and John Lauterbach and Mr. Arnold Hamm are participating in this meeting as nonvoting industry representatives, acting on behalf of the interests of the tobacco manufacturing industry, the small business tobacco manufacturing industry, and tobacco growers, respectively.

Their role at this meeting is to represent these industries in general and not any particular company. Dr. Heck is employed by Lorillard Tobacco Company; Dr. Lauterbach is employed by Lauterbach and Associates, LLC; and Mr. Hamm is retired.

FDA encourages all other participants to advise the committee of any financial relationships that they may have with any firms at issue.

I would like to remind everyone present to

please turn off your cell phones completely. The microphones in this room are very sensitive, so even if you have it on mute, the microphones still pick up any signals. So if you could, just turn off your cell phones, we would appreciate that. And I would also like to identify the FDA press contact, Michelle Bullock.

Ms. Bullock, if you are here, please stand up. Thank you very much.

Introduction of Committee Members

DR. SAMET: Thank you. So let's proceed with committee introductions. And let me ask, first, Mark and Arnold, are you on the phone?

MR. HAMM: Yes. I'm here. This is Arnold Hamm. I'm representing the interest of U.S. tobacco growers.

DR. SAMET: Thank you. Mark, are you there?

DR. CLANTON: Mark Clanton. I'm representing pediatrics, public health, and oncology.

DR. SAMET: Thank you. And you're up early again, unless that was a recording.

John?

DR. LAUTERBACH: John Lauterbach, Lauterbach and Associates, representing small business tobacco manufacturers.

DR. HECK: Dan Heck with the Lorillard Tobacco Company, representing the tobacco manufacturers.

DR. DJORDJEVIC: Mirjana Djordjevic with the National Cancer Institutes, representing NIH.

MR. MCAFEE: Tim McAfee, representing the Centers for Disease Control.

DR. PIRARD: Sandrine Pirard, representing the Substance Abuse and Mental Health Services Administration.

DR. EVANS: Sarah Evans, Center for Tobacco Products.

DR. ASHLEY: David Ashley. I'm the director of the Office of Science at the Center for Tobacco Products.

DR. PETERS: Ellen Peters. I'm a faculty member at Ohio State University.

DR. SIMONS-MORTON: Bruce Simons-Morton,

National Institute of Child Health and Human Development.

DR. BENOWITZ: Neal Benowitz, University of California San Francisco.

DR. EISSENBERG: Tom Eissenberg, Virginia Commonwealth University.

DR. HENDERSON: Good morning. Patricia Nez Henderson, Black Hills Center for American Indian Health.

DR. BALSTER: I'm Bob Balster. I'm on loan from Virginia Commonwealth University.

DR. HATSUKAMI: Dorothy Hatsukami from the University of Minnesota.

DR. PAMPEL: Fred Pampel from the University of Colorado, Boulder.

DR. SAMET: Let's see. Sherry, I am reminded that you're on the phone. Are you with us?

[No response.]

DR. SAMET: Perhaps not yet.

Okay. So we'll proceed then with opening remarks from Sarah Evans.

Opening Remarks – Sarah Evans

DR. EVANS: Good morning, everybody, and welcome to the third and final day of the second round of TPSAC meetings on the topic of dissolvable tobacco products. I remain the lead scientist, Sarah Evans. And I promise you, this remains our disclaimer, which you've seen before, basically telling you this is not a formal dissemination of information by FDA.

Let's see. Today's meeting consists of presentations on youth perceptions of dissolvable tobacco products and what we hope will be a robust committee discussion. And now I'm going to talk to you a little bit about the report on the nature and impact of the use of dissolvable tobacco products on the public health, what to expect.

In terms of future TPSAC meetings, the tentatively scheduled next meeting is for March 1st and 2nd, but the official notice with the actual date will come up in the Federal Register. As a reminder, the nature and the impact of the use of dissolvable tobacco products on the public health,

this tells you from the statute more about the report, which I shall read for you now.

"The Secretary shall refer the Tobacco Products Scientific Advisory Committee for the report and recommendation under Section 917(c)(4), the issue of the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children.

In its review, the Tobacco Products Scientific Advisory Committee shall address the considerations listed in subsection (a)(3)(b)(i), report and recommendation, not later than two years after its establishment. The Tobacco Products Scientific Advisory Committee shall submit to the Secretary the report and recommendations required pursuant to paragraph 1.

We anticipate holding one meeting on this topic before March 23rd, 2012. Detailed minutes and verbatim transcripts will be prepared for each meeting. The compiled minutes, transcripts, and other materials from this series of meetings will be included in the committee report.

The final report from TPSAC will be made available to the public on the FDA's website once it has been reviewed for redaction of any commercial, confidential, or trade secret information.

Once the report from TPSAC is received, FDA will consider the report and recommendations of the committee, as well as other scientific evidence concerning dissolvable tobacco products and make a determination about what actions, if any, are warranted. There is no required deadline or timeline for FDA to make such a determination.

Any sale, distribution restrictions, or product standards will be implemented through notice and comment rule-making."

Any questions?

DR. SAMET: Neal?

DR. BENOWITZ: You said that the report -- or the committee shall submit the report and recommendations. But the charge of the committee just says we're supposed to address the issue of the nature and impact of the use.

What's meant by recommendations?

DR. SAMET: So I think we're going to come back to this point.

[Laughter.]

DR. SAMET: I actually think this is a matter for committee discussion, and we'll come back to this when we begin committee discussion.

DR. BENOWITZ: Okay.

DR. EVANS: Any other questions?

[No response.]

DR. SAMET: Thank you.

So we'll go ahead, then, with a set of presentations. And I want to thank the presenters for coming, both related to young people and dissolvable tobacco products, the first by Mark Wolfson from Wake Forest School of Medicine. Thank you for coming.

Presentation – Mark Wolfson

DR. WOLFSON: Thank you, Dr. Samet.

Good morning. I'm very pleased to be here, to have the opportunity to share some of the data that we've been collecting and looking at in

relation to smokeless tobacco use by college students, including dissolvable use.

So these are the topics that I'd like to cover today in the time that I have. I'll give you a little bit of background about the overall study that we have been conducting and talk about analyses to date on dissolvables. So what I'll talk about is data we've been looking at on awareness, appeal, likelihood to try a free sample, and risk perception. And then I'll talk a little bit about our next steps. I forgot to mention at the outset, this study is funded by the National Cancer Institute.

So a little background on parent study. We know from national data that young adults in the 18 to 25 age group have the highest prevalence of smokeless tobacco use of any adult age group. We also know that smokeless tobacco products are marketed to college students, bar promotions in bars, surrounding campus ads, and student newspapers and such. And we also know that new products, such as snus and dissolvables, are

marketed as ways for smokers to get nicotine in situations and places where smoking is not permitted. And this is increasingly the case on college campuses with smoke-free policies, various policies related to smoking.

So in terms of the overall study, these are specific aims to look at trajectories of smokeless tobacco use; a variety of products, all smokeless products, including dissolvables, among undergraduate college students over the course of their college careers. And the kinds of things we're looking at that we're interested in are initiation, progression, cessation, substitution.

I should also say we're very interested in this issue of supplementation as well. We're quite interested in co-use smokeless products and cigarettes. That was one of the interests that really animated this study. We're also looking at, environmental and an individual level, correlates of these trajectories of smokeless use and patterns of use.

So in terms of the study design, it's an

observational cohort study. We recruited 11 colleges and universities in North Carolina, seven in North Carolina and four in Virginia to participate. Tanner Public, one, is private, a variety of demographic settings. You can see the range of undergraduate enrollment from medium-sized schools to large universities.

Subsequently, we assessed the density of tobacco retail outlets within a two-mile radius of school, and you can see there's a pretty wide range in outlet density.

We did a screener survey of freshman in fall 2010. I'll give you some more details on that, but that was to help draw out our sample, recruit our sample for the cohort. And then we're conducting a survey of the cohort for seven semesters, so the entire college career from first semester of the freshman year through the first semester of senior year.

So these are some of the things that we're interested in and that were included in the survey. I will mention that, in addition to the cohort

survey, we conducted an environmental assessment, which includes an assessment of school policies and also point-of-purchase surveys in retail outlets in the area surrounding campus.

So these are the constructs and behaviors that we're interested in, smokeless use, awareness, and risk perceptions, exposure to marketing, as well as sensitivity to marketing, nicotine dependence, and quit behavior, use of other tobacco products. We're asking about the whole range of products, smokeless cigarettes as well as who can use the e-cigs, et cetera; family and peer smokeless and cigarette use, binge drinking, and illicit drug use, and of course demographic characteristics and background characteristics.

So we've branded the survey. It's ACE. We found in focus groups that that appealed to college students. That stands for the Assessment of the College Experience. So the screener survey, again, was to try to recruit individuals into the cohort. So we obtained lists from the registrars of each of the schools that were participating. We had

completions from about 10,500 students, which is a 36 percent response rate, which is pretty typical for college surveys. We've been doing college student surveys for about 10 years now on alcohol, and tobacco, and other behaviors.

So then as far as the cohort, we provide incentives. These are graduated incentives, $15 at baseline, and they increase by $5 each semester. Based on responses to this short screener survey, we oversampled smokeless tobacco users and cigarette smokers in males. And the reason for that is because we thought those were the people who were most likely to become smokeless users or experiment with smokeless products in the future.

So about 3100 students joined the cohort and completed the baseline survey. That was 64 percent of those invited. And although I'll just be focusing in this presentation on our baseline data from fall 2010, I will mention that we have been fairly pleased with our retention rate of around 80 percent in subsequent surveys.

These are the characteristics of the sample,

about half male, exactly half male. These are freshman, so the vast majority are age 18, 84 percent white, 7 percent Hispanic. A majority have over a hundred dollars per month in spending money, and it's a fairly well-educated higher SCS sample, at least in terms of parents' education. And this is fairly reflective of the college populations in North Carolina and Virginia.

So this is just a slide to explain that we waited to account for the oversampling that I described, as well as the nesting of data within schools. So the data that I'll be presenting throughout the remainder of this talk will reflect these weights and their attempts to estimate the prevalence of the behaviors and the perceptions that I'll be reporting on.

So this is what we found in terms of tobacco use. About 14 percent reported current tobacco use past 30-day tobacco use. This is generally on par with the national surveys that we've looked at. The majority of those are cigarette users only, but then, about 3.4 percent were smokeless users. And

interestingly, the biggest group is the co-users and that's a relatively small group of smokeless tobacco users. So co-use is the norm in terms of smokeless tobacco use in this population.

So this is the framework that we used for asking the questions about awareness, appeal, and likelihood to try a free sample. This was a Web-based survey. So we first introduced the product. We say, in this case for chewing tobacco, one type of smokeless tobacco product which is not burned or smoked is chewing tobacco, and then we show some examples. And then we ask, are you aware of this type of smokeless tobacco? How appealing is it to you? And how likely would you be to try a free sample if offered one? So I'll be presenting data on each of these, broken down by product and by user group of the individual respondent.

This is the way we asked -- so the same framework for asking about snuff, moist snuff. This is the way we asked about snus, same framework, with pictures of products that were on the market at the time. And this is the way we

asked about dissolvables. I'll show you another slide because, as we know, there was a change in packaging between the first survey, the baseline survey, and subsequent surveys.

Let me acknowledge at the outset one complication, which is we struggled with some of the same issues that I heard you all struggling with or talking about yesterday, which is the lumping and splitting issue. So we lumped together Stonewall and Ariva, along with orbs, strips, and sticks in this question. One of the things we're interested in doing in future surveys is disentangling that so we can have a more nuanced and sensitive understanding of what the students are responding to. But anyway, this is the way the data look now.

So in terms of the test markets, we know that there were three test markets for the RJR products, beginning in 2009. None of them included, at the time, North Carolina. These reflect the older packaging, the packaging that I just showed you, and this is what I'll be

presenting on from our fall 2010 data.

Then there was a change. In March 2011, there was a change in packaging and a change in the test markets as well as the Marlboro products coming on the market. So in the surveys we've conducted since baseline, we reflect those changes in terms of packaging.

One of the things we'll be able to do in subsequent analyses is look at the kids from Charlotte. We don't have a school in Charlotte that we recruited. UNC Charlotte is not one of the participating schools, but we do have their permanent home address, so we'll be able to look at whether exposure has increased, now that Charlotte is a test market for these products. And so this is the newer slide that we use, reflecting the change in packaging.

So awareness. So these are the percentages of students who reported that they were aware of the product. I'll point your attention in particular to those who reported that they were aware of dissolvables. This question does have

some demand characteristics. Some proportion of students will probably say they're aware of it without actually having been aware of it prior to the survey, but this is what we found.

So what I would highlight, I think, is that the cigarette and the smokeless co-users have the highest rate of awareness of dissolvables, 36 percent. And we thought that was actually fairly high, given that there wasn't a test market anywhere in sight. This was before Charlotte became a test market.

In terms of appeal, this is the percentage of students reporting that they rated the product somewhat or very appealing. And again, I should have explained this in the beginning, but I think it's fairly obvious. The tobacco user groups are at the bottom, so among non-tobacco users, zero appeal. Interestingly, among cigarette users only, we found low levels of appeal as well. But then once you get into the current smokeless user population, much higher levels of appeal, and you can see that for the co-users in particular, of

cigarettes and smokeless, 36 percent found -- thought that dissolvables held some appeal.

So then we looked at likelihood to try a free sample, and we see a very similar pattern, interestingly even higher levels. We see the same differential between the smokeless users and the non-smokeless users in terms of interest in trying. And in particular, again, the co-users of cigarettes and smokeless tobacco had the highest rate of interest in trying the product. And almost 50 percent said that they would try dissolvables. So we thought this was quite interesting.

This is a breakdown of the last slide, so in this slide, in terms of the tobacco user group, we lump together all the different forms of smokeless. This is an effort to break out the different kinds of smokeless users, so chew, moist snuff, and snus. And what we see here is that in terms of likelihood or interest in trying a free sample, the dissolvable, the snus users, over half the snus users, 56.2 percent, said that they would be likely

to try a free sample if offered.

This is just a multivariate model, looking at this likelihood-to-try outcome; and so you can see shaded in darker brown the statistically significant variables, predictors. So the people who are most likely to report that they would try a free sample are current cigarette users, current users of dip and snus, males, people over 18. In other words, it's an odds ratio of less than 1 for those who are 18.

Sensation seeking. This is the standard eight-item sensation-seeking scale, so high sensation seekers were 50 percent more likely to say that they would try, and also we found an association with lifetime illicit drug use.

The final topic, risk perception. So this is the way we asked about risk perception. I believe we borrowed this from Dorothy's work. "Think about each of the smokeless tobacco product types using the risk ladder below. Please indicate what you believe the risk is for people who use each smokeless tobacco product for developing the

following health problems." And we ask then about a range of problems.

So these are what the data look like. And just to make it a little less busy or to point you to what we think might be important, I circled the -- actually I highlighted -- I circled and then highlighted. So I circled dissolvables and then we highlighted in red the lowest score, which is the belief that the product is the least harmful.

So I think the first thing that jumps out at us is that the snus users and dissolvable -- that people thought that snus use and dissolvable use was the least harmful of any products; cigarettes, but also the other forms of smokeless tobacco products. If you tally these up, there's a slight lead for dissolvables. I think there were 10 or 11 that rated them the lowest, compared to about 8 or 9 for snus.

One thing that we thought was quite interesting is that in particular for oral cancers and dental problems, our students thought that dissolvables were the least harmful for those

particular health problems.

So just a few take-aways that we've taken away from this analysis; we thought awareness of dissolvables is higher than might be expected, especially given the limited test marketing at the time of the survey. I recall some data that was covered yesterday from Indiana, which, of course, does have a test market where I think there was about 40 percent awareness of dissolvables. So we thought the rates that we found were surprisingly high.

Dissolvables are most appealing to co-users of other smokeless tobacco products and cigarettes. In terms of willingness to try a free sample, almost half of co-users of cigarettes and smokeless tobacco said they would try a free sample, and over half of snus users would try a free sample. Then finally, dissolvables are viewed as the least risky category of tobacco product.

In terms of next steps, we're going to be finalizing these analyses and publishing them. We'll look at dissolvable use and perceptions in

the subsequent surveys among all students, and in a subset to have students from the Charlotte area so we can get a sense of the importance of proximity to the test market.

As I mentioned at the outset, we plan to revise the fall 2012 survey to disentangle responses regarding Stonewall, and Ariva, and stick strips, and orbs, and then of course look at shifts in perceptions and behaviors within individuals over time.

I want to acknowledge my study team, especially my co-principal investigator, John Spangler, and co-investigators Erin Sutfin, Beth Reboussin, and Kim Wagoner.

Committee Discussion

DR. SAMET: Thank you very much for your interesting presentation.

I'm going to suggest we have time for committee discussion following the second presentation. But I think if there are very specific questions on this presentation, why don't we spend a few minutes addressing those and then

come back for a more complete discussion?

Sandrine?

DR. PIRARD: Thank you for the presentation. A quick question. Do you think that you will be ready to present the next steps by the next TPSAC meeting in March?

DR. WOLFSON: In March?

DR. PIRARD: Yes, before I give the report?

DR. WOLFSON: Well, I think my statistician is watching, so maybe.

DR. SAMET: Ellen?

DR. PETERS: Do you have an idea from your surveys what characteristics these college students are finding as important to their choice? So you suggest -- you show in your data that the dissolvables are actually not perceived as particularly high in risk. In fact, they're probably the lowest of risk of all the various things; and certainly, it looks like overall lower in risk than cigarettes.

But is that an important characteristic in terms of their choice?

DR. WOLFSON: So we have a number of questions that we pose to users about why they use and what they perceive the benefits to be. Unfortunately, we have a very small number of dissolvable users in our sample. I think we have two. Now, that may change with the opening of the Charlotte market, so those questions didn't get presented to people who would just consider using. We only asked those questions of actual users.

DR. SAMET: Bruce?

DR. SIMONS-MORTON: I realize you don't have very many smokeless tobacco users in the group. I think the multiple users maybe you had 50 or 60 of smoking and multiple use.

DR. WOLFSON: It's higher than that, I believe.

DR. SIMONS-MORTON: Yes, 2 and a half percent times 3,000 would be -- or 2 percent times 3,000 would be about 60. So maybe you had 60 or 80 people who use. But can you tell us a little bit about them? I mean, it strikes me as strange that anyone in college would be using these products,

but who are they?

DR. WOLFSON: So we've done some analyses of these data and also data from an earlier study, focused on alcohol, but we did an analysis looking at smokeless tobacco users. And so first off, we found lots of variation across schools, across universities. Secondly, obviously, males have much higher rates than females.

We found an association with sensation seeking and smoking and illicit drug use. We found whites typically, white students, are more likely. So in many ways, it reflects what's already known about the demographics of smokeless tobacco use.

DR. SAMET: Dan?

DR. HECK: Yes. Thank you very much for what I think is an interesting study. I'm just kind of wondering, the risk awareness scores for the cigarette smokers here, are these scores fairly typical for what is seen in these studies? They're, indeed, somewhat higher, but at some level, I'm kind of surprised they're not even higher than they are.

Are these fairly typical findings?

DR. WOLFSON: We have not yet compared those results to what may be in the literature. I don't know if anybody on the committee can address that, but I can't at this point.

DR. SAMET: Tim?

MR. MCAFEE: A quick follow-up to the line of inquiry that Ellen was sort of suggesting. I guess one of the things that we've been talking about is we've looked at the question of the role of dissolvables in the market, which you might be in a position to answer in this future round of questioning. It sounds like you probably wouldn't have information, but it's essentially for those who might intend to use dissolvables or intend to accept a free sample, the question of what their intent would be around this.

Are they thinking of this -- again, for those who are currently using cigarettes, are they thinking of this as, this would be nice because I could use it when I'm in a situation where I can't smoke? Or are some of them thinking, I'd really

like to quit smoking and maybe this would be a mechanism by which I could completely substitute?

So I'm assuming you don't currently have data that would help you, but is that something you could inquire in the last round?

DR. WOLFSON: Yes. So that's a really interesting idea. So of course, we're constrained by the fact that this is a longitudinal survey, and so we want to retain some continuity from wave to wave. That said, we have some room for experimentation and change from wave to wave. We're also constrained by space because we try to minimize the burden on the students.

That said, I think it's a really interesting idea. Again, we only ask those sorts of detailed questions about the sorts of benefits you would see and the nature of the appeal of the users. But I think we could look at the possibility in our fall survey of this year. Spring is too late because we're gearing up to go into the field now, but we could look at doing that in the fall of this year, adding some of those questions that we ask of users

about context and appeal of people who, as we say in North Carolina, are fixing to use.

DR. SAMET: Neal?

DR. BENOWITZ: Are you collecting any data on patterns of use, for example, cigarette smokers, how many cigarettes they smoke per day, or how frequently? Certainly, for dissolvables, how much do they use, how regularly? I would think that those data would be really informative.

DR. WOLFSON: Yes, yes. We do. And so that's something we'll look at for dissolvable users if we get a critical mass of them. But we can certainly look at that in terms of other products. Yes.

DR. SAMET: Ellen?

DR. PETERS: Even with the dataset you have right now, there are some interesting regression type analyses you could do. So if you took, as your dependent variable, the likelihood of trying a free sample, have you taken a look at whether risk perceptions predict that, for example? So you might expect -- so from a rational standpoint, you

would expect that the higher risk that's perceived, the lower likelihood of trying the product.

With this group, you might find the opposite. Or for example, if you crossed it with sensation seeking, you might find maybe in general, for most people, as risks increase, they're less likely to try the dissolvables, but maybe for the sensation seekers, you'd find the opposite.

DR. WOLFSON: Yes. That's a great idea. Like I said, these are fairly early analyses, so it's great to get this input. And I think that is something we could look at. The other thing that I've been thinking would be useful to look at would be we have information among the smokers about quit attempts and interest in quitting. And so we could look at whether that's an indicator of interest in trying dissolvables as well. So thank you.

DR. SAMET: Let me check on the phone. Any questions?

DR. CLANTON: No questions here.

MR. HAMM: No questions, either.

DR. SAMET: Thanks. Let's see.

Sherry, are you on?

[No response.]

DR. SAMET: I guess not. Thank you very much. And we may certainly get back to you as we continue our discussion.

Next, we're going to move onto a presentation by the Virginia Foundation for Healthy Youth. And I guess there will be three presenters. And excuse me if I don't quite pronounce your names right, but Danny Saggese, Jeff Jordan, and Judy Hou. Thank you.

Presentation – Danny Saggese

MR. SAGGESE: Good morning. I am Danny Saggese, the director of marketing for the Virginia Foundation for Healthy Youth, and it is an honor and privilege to be invited to present to you today.

Joining me here will be Judy Hou, who is a youth activist for Y Street, which is our youth-led advocacy movement in Virginia, and Jeff Jordan, representing the Rescue Social Change group, who's been a partner of the Virginia Foundation for

Healthy Youth for eight years now.

A little background on the Virginia Foundation for Healthy Youth, we were created as a result of the Master Settlement Agreement and initially called the Virginia Tobacco Settlement Foundation. We're provided 10 percent of Virginia's allocation of the MSA payment.

In about eight years, that resulted in us lowering tobacco rates in Virginia by about half for youth prevalence. So we're pretty proud of that. And we did such a decent job that the Secretary of Health decided that we should take on childhood obesity as well, which resulted in our name change to the Virginia Foundation for Healthy Youth and also resulted in a 25 percent reduction in our budget, but we still proudly fight the two leading causes of preventable death in Virginia and in the nation.

A great deal of our success we feel like is owed to the comprehensive approach that the foundation has taken to fighting tobacco use amongst youth, which is our primary mission. Part

of that comprehensive approach has been a multimedia marketing campaign, which I'm responsible for. And a big portion of that has been the youth advocacy movement, and that is what we call Y Street.

That began in 2004, but it didn't initially begin as it is now, in that it's taken a lot of time and effort, a study of best practices, trial and error, to really learn how to create a true youth-led advocacy movement. And we feel like we have one of the nation's premier youth-led advocacy movements. Of course, I'm a bit biased in that opinion, but the accolades and some of the things that our youth have achieved I think speak for themselves.

Over the time since it's been created, we've trained over 6,000 high-school-aged youth. We typically have anywhere from 800 to 1,000 active at any one time, which is typically over the school year. Some of our past campaigns -- and really, the way a campaign is launched is simply presenting some of the issues that are relevant or timely to

our youth, to our leadership team, primarily, and letting them provide us feedback on something that they might be passionate about, something that intrigues them or interests them.

Some of the things in the past they worked on is completing a survey throughout Virginia about the interest in clean indoor air legislation, which did not exist in Virginia until recently, a campaign educating the public about the proliferation of smoking in movies; an online campaign helping convince Kelly Clarkson to not take tobacco advertising sponsorship for one of her Indonesian tours; and even a campaign to assess the relevance and the effectiveness of the tobacco pack warnings. On Y Street's behalf, we actually submitted to the FDA docket for that recently.

That is how the campaign for what we call Meltdown came to be. And not quite three years ago, we presented to the youth these new products that were on the market. And immediately, there was significant interest on their part in that these products could potentially be confused,

particularly by youth, because of their packaging and because of their flavoring. And their hypothesis was borne quite quickly, in that they simply wanted to find out whether or not, because of the flavoring and because of the packaging, could they be confusing.

So what we do is take their passion for a particular issue and then try and give them all the resources they need to answer the question they're after or to complete projects in support of the campaign.

So this campaign, again called Meltdown, had two primary purposes, assessing, again, the public perception or public opinion about what they thought these products were, and then education, which is usually a big part of any campaign we conduct, and training the youth to hand out the surveys. And these were surveys that were collected exclusively by high-school-aged youth, except for the online survey.

We would train them to hopefully eliminate some of the answering bias by having them not

mention what these products were, simply saying they were new products they were trying to find opinions on, not mention tobacco, not mention that they worked in tobacco, or anything like that, to hopefully get as unbiased answers from the public as we could. Then they would explain the campaign and the mission afterwards. However, despite its scope and its diversity, this is a gigantic sample of convenience.

Here is the survey itself. I think it was a six-inch by four-inch card that the youth would literally hand out to the public. On the left-hand side there is the front, which focuses on the packaging. And the question -- it's difficult to see. And I have to apologize because the slides here are slightly out of order of what you have printed. I want to thank Caryn and the group here for being so gracious as to take our last-minute change in what you have, so my apologies there.

But what you have there is -- the question is what product do you think is in this package? And that's an open-ended question there. And then,

would you try it or would your friends try it? And as you can see, we had three of the newer tobacco products on the market at the time, and then three either candy or gum products.

On the back side is where we dealt with the flavoring issue, using the flavors of frost, wintergreen, java, and again, asking them what product do you think this is. Would you try it? And would your friends try it?

So what were they able to achieve? Over the time period of data collection, we were pretty astounded. Over 8,000 valid surveys were collected in over 200 communities across Virginia. And so we were, despite it being a sample of convenience, pretty impressed and pretty amazed by the findings as well.

So to get into that, I should turn it over to Judy, since her and her colleagues did all of the collection, and let her explain some of that to you.

Presentation – Judy Hou

MS. HOU: Hi. My name is Judy Hou, and I

have been a Y Street youth advocate since my freshman year, so since 2008, and I will be going to Princeton University this fall.

So I would like to say that Meltdown, first of all, has been a really huge part of my Y Street experience. I've personally collected around 260 surveys. And I would just like to talk about the major findings that we got from these results.

So first of all, Meltdown sought to look at how the packaging itself would affect the perceptions of the public. And we examined three different products. Over here, you can see Snus Mellow, Snus Orbs, and Stonewall Natural.

So what we did was we went into our community and we talked to not only youth, but also to adults. So we asked them, based on the packaging alone, what did they think was inside of this product? As Danny mentioned before, we tried to make this as unbiased as possible, so we didn't give them any of our own opinions beforehand.

What we found was really surprising. We had 23 percent of our respondents say that based on the

packaging alone, they thought snus contained, inside, a product associated with candy, mints, or gum, so nothing with tobacco. And additionally, 37 percent of our respondents thought that Camel Orbs was associated with candy, mints, or gum based on the packaging alone. And around one-third of our respondents said that, looking at the packaging of Stonewall Natural, that they thought it was associated with candy, mints, or gum.

So in addition to looking at the packaging itself, we also wanted to see how the specific flavorings affected the perceptions of the public. So the three flavors that we examined were frost, wintergreen, and java. And what we found was definitely very alarming. I would say, looking at the stats, they were very surprising.

Around one-half of all of the respondents, when looking at the flavor frost, did not associate it with tobacco, but rather, they associated it with something that's completely harmless, such as candy, mints, or gum. Eighty-three percent of our respondents when looking at wintergreen, thought

that it was associated with candy, mints, or gum. And only 14 percent, when seeing the flavor java, thought it was candy, mints, or gum. But it's important to take into account that 64 percent of our respondents associated it with a beverage such as coffee, which, as we're well aware of, is not tobacco.

Now, because Meltdown is looking specifically also at how the tobacco marketing is targeting teenagers, we did a separate and individual analysis of people under the age of 18. And the results we found were very similar to the full sample, with 23 percent of minors who responded saying, looking at the snus packaging alone, they thought it was associated with candy, mints, or gum, not tobacco.

Thirty-five percent of those who saw the orbs packaging thought it was associated with candy, mints, or gum. And once again, around one-third of our respondents, looking at Stonewall who were under the age of 18, believed it was a candy, mint, or gum.

So similarly, like I mentioned before, looking at people under the age of 18, we also analyzed how they perceive certain flavors, frost, wintergreen, and java once again. And one-half of people who perceived frost thought that it had to do with candy, mints, or gum, not tobacco. Eighty-three percent, once again, the astounding number, had thought that wintergreen had to do with candy, mints, or gum, and then 13 percent for java, with the 64 percent on the side.

Personally, I think that this is something that should cause a lot of concern because these tobacco products are not being immediately recognized as such. They're being seen as something that's completely harmless, and that might lead people to be more inclined to try these products, which is what we looked at next.

So in addition to how the public perceived these products, we also examined whether or not the public would act upon the perceptions. So looking at people under the age of 18, we asked them, based on the packaging alone, would they be inclined to

try these products.

So looking at Camel Orbs, we found that 23 percent of all of our minor respondents said that yes, based on the packaging alone, they would be inclined to try the product. And even more alarming, 21 percent of non-tobacco users said that, based on the packaging, they would be willing to try this product for the first time.

In addition to seeing whether people would try it themselves, we also asked how they thought their peers would perceive these products, whether or not it would make them inclined to try it. And we found that around one-third of our respondents said that yes, based on the packaging, they think their peers would be inclined to try this.

I personally, in my youth advocacy work, when talking to a lot of my peers, I know that they've been extremely surprised with the way that these tobacco products are marketed, especially Camel Orbs, because I think that they look a whole lot like the Tic Tacs. If you look at the colors, they're very similar in terms of the green. And

also, if you look at the leaf, it's actually the same logo as a Tic Tac, just flipped horizontally. And in addition, if you examine the actual pellets inside, they're very round. They're small. They're similar to Tic Tacs.

So we did the same thing for Snus Mellow, and we found that 17 percent of our respondents said that, based on the packaging alone, they would try this tobacco product, with 14 percent of those being non-tobacco users.

Then the same thing with Stonewall, 18 percent said that based on the packaging alone, they would be willing to try it, and 16 percent of those were non-tobacco users. And around one-third of our respondents said that they felt that their friends would also be inclined to try this product, based on packaging.

So with the Meltdown campaign, when it was first launched, even we as youth advocates -- and I'm speaking on behalf of the Y Street leadership team -- we're are extremely surprised that these type of products existed. And we were also

surprised that they were being marketed towards teens in this fashion. And I've heard the same sentiments echoed by people from around my community. I've talked to school teachers, my peers; even just like, people in the community as well as parents, they've all been surprised that these tobacco products are being marketed in this fashion.

So what we tried to do with the Meltdown campaign is, in addition to providing just raw data through the surveys, we also wanted to generate public awareness. So we did this through a variety of ways. If you look at the picture on the top left, that's me talking to media outlets, so local TV stations. We've also given newspaper interviews, as well as radio interviews, just trying to generate as much awareness as possible.

Another really fun thing that we as Y Street members do is we have our team, the youth, actually plan as well as execute project days. So if you look around, we have a lot of different Y Street members planning these project days, getting out

into their community, and having these community events.

So some of these events are really fun. They're such events such as sports events. We've hosted dances. We've even hosted a fashion show. So it's just a really great way for us to get our community involved while getting these surveys filled out and also generating public awareness at the same time and educating them.

With that, I will let Jeff take it away.

Presentation – Jeff Jordan

MR. JORDAN: Thank you, Judy.

It's impressive. Right? No wonder she's going to Princeton next year.

So Rescue Social Change group is a social marketing organization that develops and manages Y Street. And Judy gave you a lot of facts, so four key points from the data that we found was that 35 percent of teens thought that Camel Orbs were a candy, mint, or gum. Eighty-three percent thought that wintergreen was associated with candy, mints, or gum. Fifty-three percent thought that frost was

associated with candy, mints, or gum. You see another big portion was associated there with beverages. Remember that, on the survey, these were all open-ended questions, so it's whatever they answered, and most of them answered candy, mints, or gum, throwing in beverages for an even larger majority. And then finally that 23 percent of teens would try Camel Orbs based on its packaging. This is of all teens. If we looked at just teens who were not current tobacco users, it was 21 percent who said that they would try it based on its packaging.

Now, it's important to recognize the limitations of this study. This was not designed to be a scientific study. It was designed to be a project that youth can execute and manage on their own, so it is a convenience sample, albeit a huge convenience sample of over 8,000 adults and youth in Virginia from over 210 communities.

So definitely, we have to treat it as such, and hopefully the diversity and size of the sample gives us a little bit more confidence; but

nonetheless, it is still a convenience sample.

Like Danny bragged at the beginning, Y Street is a great organization, and some of the evidence of that is that the Y Street model has been replicated in other states, so the same model is also being implemented in New Mexico, Nevada, and St. Louis. And New Mexico actually borrowed the Meltdown campaign from Virginia, and its youth in New Mexico implemented the same campaign with the same process, the same survey, to understand New Mexicans' opinions of these new tobacco products.

So here we have almost 6,000 surveys in addition to the 8,000 that we're talking about that were completed by New Mexico youth, and we found similar results. So about 39 percent of New Mexicans believed that Camel Orbs were a candy, mint, or gum. About 80 percent of them thought that wintergreen was actually associated with candy, mints, or gum.

Another 48 percent of them thought that frost was associated with candy, mints, or gum.

And here, we had a slightly larger group, 26 percent of teens said that they would try Camel Orbs based on their packaging alone. And if we looked at just non-tobacco-using teens, that went down to about 23 percent that said they would try these products based on their packaging alone.

So again, it's another convenient sample, but now we're talking about close to 14,000 surveys from youth and adults that are giving similar results on their impression of the new tobacco products.

Now, we know that the packaging for Camel has changed, but when this study was implemented, it had not changed yet. So right now, the youth are working on other projects, so that's why we have not yet done a survey with the new packaging.

So in closing, the public, especially youth, associate the flavors and packaging of dissolvable tobacco products with that of candy, mints, or gum, and it's something that we think should be looked into and addressed. And we're happy to take any questions now.

Committee Discussion

DR. SAMET: Thank you all for your presentations and for coming.

So why don't we address any questions specifically about this, and then we'll go on to our broader discussion about perceptions. So we'll start with Bob.

DR. BALSTER: So first off, as a Virginian interested in public health and tobacco control, I wanted to tell everybody how proud we are of the Virginia Foundation for Healthy Youth. I mean, not only have they been doing a program like you saw today, but they support a lot of school-based prevention programs, and really a wide diversity of things across a lot of age groups. And even in their infinite wisdom, they support research in the form of the Virginia Youth Tobacco Project. So we're very proud of their work.

I have a question that confuses me a little bit about the data. I'm not sure which of you would answer, maybe Judy. You have a large percentage of respondents saying that they think

that these products are candy, mint, or gum, but really only 20 percent would try them. And I guess I would be wondering why, if they really were convinced that they were candy, mint, or gum, if they were offered a Life Saver or something or something like that -- I mean, why would only 20 percent want to try one if in fact they thought they were candy, mint, or gum?

Do you have any explanation for why people would then turn down a candy product?

MS. HOU: In addition to them wanting to try it, it's not necessarily that they'd be willing to try it, but maybe like they would be willing to buy it. Because you've seen lots of candy, mints, or gums. If I have a new candy on the market, I'm not necessarily going to try it, even though it might be attractive.

But just knowing that it's not as harmful as -- or thinking that it's not as harmful as a traditional tobacco product is something that's extremely dangerous.

DR. BALSTER: So just to clarify, the

question wasn't worded in such a way that if you were offered a free sample. You didn't word it that way. I mean, it was worded in such a way that it could imply purchasing or --

MS. HOU: Yes. It was just worded, would you be willing to try this product based on the packaging alone or based on the flavors alone?

MR. JORDAN: Yes. And I think the saturation of the candy, gum, and mints market makes them a little less inclined to try everything that's new out there. So you're looking at, if 39 percent of them thought the packaging was candy, mints, or gum, over half of them would have tried it. So it is a large percentage of them who thought it was candy.

DR. SAMET: Continue around. Ellen?

DR. PETERS: Have you guys looked to see whether -- this is going to be similar to my question from the last presentation. Have you looked to see whether those free responses of yes, this is candy, mint, gum, and maybe even coffee, does that predict their likelihood to try it?

MR. JORDAN: No. We have not looked at that yet.

DR. PETERS: It might be a good idea to take a look because from what you guys are talking about, you're sort of inferring that, that you can actually look at that within your data.

The other thing I just wanted to comment on is -- first, great job with the presentation. It was really interesting. The data are fascinating. It is still a scientific study. It happens to be a convenient sample, so it has limits, but this study is incredibly timely. And so from that perspective, it may also be publishable if that's something you guys are interested in. I would at least consider doing that.

But I would dig in the data a little bit more, too, to see whether your inference about this candy, gum, or mints really does make a difference to whether they would try it.

MR. JORDAN: I appreciate that, and I'm sure now we will look into publishing it.

[Laughter.]

DR. SAMET: Dan?

DR. HECK: Yes. I had two quick questions, and I thank the presenters for their contribution here. Maybe I missed it. Are there data here that would allow us to -- on the willingness-to-try question, I'm wondering was there a difference in the willingness to try between smoking youth and the non-smoking youth, which is data we saw. And I guess my second question is, I think at least one of these products wasn't available on the market, I don't believe, in your region, so I guess the youth would have only seen the image.

I wonder if there are any differences in the willingness to try and other numbers for the products that were actually on the market and potentially seen by these individuals versus just seeing the image.

MR. JORDAN: Yes. The percentage of youth smokers versus non-smokers, I only gave that number verbally. So the 26 percent here, which is the New Mexico number, is of all youth willingness to try. And then the number that is of only non-tobacco-

using youth is actually 23 percent. Similarly, the Virginia one is 23 percent overall versus 21 percent for only non-tobacco-using youth.

Then for your second question, did we see a difference between Stonewall and the Camel products?

I'm looking at one of our team members in the audience. I think, just from a personal impression, the Camel Orbs was a little bit more -- because it's brand new, I think it's designed to be a little bit more appealing. So even if familiarity with Stonewall may have been more than familiarity with the new Camel products, the new Camel products are still designed a little bit more attractive. So that may have offset that potential difference.

DR. HECK: If I could do a quick follow-up, the percentage of non-smokers we see, and then the total youth. Is the difference between those numbers, the numbers of smokers -- there was only a few percent or smokers, like 3 percent, in general.

Is that correct?

MR. JORDAN: Yes. Do you know what percentage?

DR. SAMET: Perhaps, if you want to come to the microphone, please.

MR. JORDAN: This is Mayo, also from Rescue, who's helping us.

DR. SAMET: Please identify yourself. Thanks.

MS. DJAKARIA: Hi. My name is Mayo Djakaria from Rescue Social Change group. I help with the Meltdown campaign.

So to address your question, the number of teens who said they would try Camel overall and the number of teens who currently do not use tobacco products is from a different sample size. So for the teens who currently do not use tobacco products, it was a smaller sample size than the overall under-18 sample.

MR. JORDAN: Do we have the percentage of current tobacco users who would try?

MS. DJAKARIA: No. We didn't look at that.

MR. JORDAN? Okay.

MS. DJAKARIA: But we can.

[Laughter.]

MR. JORDAN: But we will. I'll shoot you an e-mail.

DR. SAMET: Neal?

DR. BENOWITZ: A couple things I just didn't fully understand. Forty percent thought it was candy, mints, or gum. Did the other 60 percent think it was tobacco?

MS. DJAKARIA: We have the full -- so the way that it was analyzed is that it was open-ended, so we had to code them. But we coded it based on candy, mints, or gum, medicine, tobacco, and other, meaning that it was food, or a beverage for the packages. For the flavors, how we coded it was based on if they believed it was an alcoholic beverage, a non-alcoholic beverage, candy, mints, or gum, food, medicine, other, and tobacco.

DR. BENOWITZ: So what percentage thought it was tobacco?

MS. DJAKARIA: I'm sorry. For which one?

DR. BENOWITZ: For these products, what

percentage of the respondents thought that this was tobacco?

MS. DJAKARIA: It's different for each --

MR. JORDAN: What would you say is the range that we had?

MS. DJAKARIA: I'm not sure off the top of my head. I'd have to look at the numbers. But I would say anywhere between 20 to 30.

MR. JORDAN: So we still had -- besides this 39 percent, we still had a large chunk that thought it was something else. I know Stonewall got a lot of medicine responses. A lot of people thought that might be -- some people even said birth control pills that they thought Stonewall was.

[Laughter.]

MR. JORDAN: So there was a lot of different responses. It doesn't mean the whole remaining was tobacco responses.

DR. BENOWITZ: A follow-up on that, I'd like to know, of the people who recognized this as tobacco, how many would be interested in trying it?

MR. JORDAN: That's a good cross-step for us

to do.

DR. SAMET: I notice that TPSAC is full of suggestions for everybody today. I do think it might be valuable, going back to Neal's question about how many perceived these products as tobacco products, that would probably be useful information, I think for us and for others in general.

Dorothy?

DR. HATSUKAMI: Yes. Actually, when looking at the information that was submitted to the FDA, it looks like, for Stonewall -- among those who are under 18, it looks like 54 percent consider it a tobacco product. For orbs, it was 56 percent. So those are among people that are under the age of 18.

MR. JORDAN: In the very original report?

DR. HATSUKAMI: In the very early, yes.

DR. SAMET: Other? Yes, Tom?

DR. EISSENBERG: I want to echo Dr. Peters' enthusiasm for the presentation on the data, and I do think they should be published. I'd also echo

Dr. Balster. As a Virginian, I'd echo Dr. Balster's pride, though that's tempered with the fact that we are the home of Altria.

I wish you had been here yesterday when, in the public comments, we heard that it was the public health researcher's juxtaposition of these products with candy that leads to the perception that they are candy-like. What I'm hearing from you today is that you presented an open-ended questionnaire and that there was no prior association on your part of these products with candy.

Am I hearing that accurately?

MS. HOU: Yes. That's definitely accurate. And I just want to also mention that in the survey itself with the pictures, we did not blot out any of the actual logo. We had Camel there for everybody to see. So it was not close-ended. We said anything that you could possibly think it was and a lot of people responded with candy.

DR. EISSENBERG: It's hard for me to tell in the picture of the survey how legible the products

were. So could you see the word "tobacco" and read the word tobacco?

MS. HOU: On the Stonewall products, you could actually read the word tobacco and you could read spit-free. For the other products, snus, it says Camel Mellow, spit-free tobacco. Those are all very visible. It's a bit easier to see when you have it like this big in person.

DR. EISSENBERG: In the picture where -- I think I may have interpreted this incorrectly. It looked like, in the picture, that these surveys were filled out in what could have been a group setting.

Is that correct?

MS. HOU: Yes. That was possible, but most of the people I talked to did it one on one just because it was easier. And after filling out the survey, it was really great for them to talk and actually educate them. But some were filled out in a group setting.

DR. EISSENBERG: So in that education -- and I'm not asking this in a critical way; I'm asking

it because I can see how it could be criticized -- is it possible that folks you educated spoke with folks who then filled out the survey?

MS. HOU: I guess that is certainly possible, but we did make it a point to make sure that we educated them afterwards, so I would say we did as much as we could to minimize that.

DR. EISSENBERG: So help me understand a little bit about the way the survey was filled out. You said you did some 200 or something.

MS. HOU: Yes.

DR. EISSENBERG: How did you approach people? Was it over the course of many hours? Just give me a quick view of that.

MS. HOU: Personally, I split it up into a couple of different what we like to consider projects, which are 30 surveys at a time for a minimum. But I went out into my community. I've done things in the park. I've been to Wal-Mart, to say the least. Most of it was with people in my school, just during lunch.

So I approached them one on one, and I didn't mention anything about the tobacco products. I just mentioned that this was a survey we were doing and if they could answer the questions. I didn't impose any of my own opinions; and have them fill out the survey.

If they had questions, sometimes they asked us like for clarification on the product. And it was just pretty much -- I was just there to administer the survey. I didn't really provide them with anything extra.

Then after filling out the survey, that was where the education component came in, and we told them exactly what the goal of Meltdown was and the dangers of these tobacco products.

DR. EISSENBERG: Thank you.

DR. SAMET: John?

DR. LAUTERBACH: Question for the adult leadership of the organization. Do you think these products taste like candy?

MR. SAGGESE: Sure. Some of them.

DR. SAMET: Come to the microphone, please.

MR. SAGGESE: Sorry. All of the snus I think is fantastic, quite delicious, actually. Some of the sticks are horrible. Now, this is my personal opinion. The strips, which we didn't test, I think, are probably the most dangerous because they dissolve in about 20 seconds and taste and look just like the breath strips. The orbs, the mints, are pretty good. They taste like candy. The Mellows are not so good. And the Stonewalls -- the Naturals, equally as gross, but the wintergreen and the java are pretty good. So I would say some of them, yes, do taste like candy. But again, that's my pallet, which has been burned on coffee way too many times.

DR. SAMET: Thank you for that.

Ellen?

MR. JORDAN: We do not all try the tobacco products. We have a guinea pig.

DR. PETERS: I had a couple other sort of devil's advocate questions for your study, if you don't mind. You mentioned, for example, that when you were collecting data, that you sometimes

collect in your own school.

Do the kids in your school know that you work with an anti-tobacco group?

MS. HOU: Initially, they didn't, but as I progressed in my youth advocacy work, I believe they had heard. But hopefully that didn't skew the data too much. Only a portion of it was collected at school, so we did do some other more random sampling.

DR. PETERS: But it suggests that you may want to do analyses with and without your school, simply because people may be aware of your positioning. And even though you didn't mention tobacco, that may come to mind right away for them.

MS. HOU: Yes. We could definitely look into that.

DR. PETERS: The other question I had is -- and again, this is just a devil's advocate question. I think the study's terrific, but it's things that you would deal with if you end up wanting to publish. And I'm curious about this.

So adolescents are great. I've had one

before. They're wonderful people.

[Laughter.]

DR. PETERS: They occasionally give responses that are, I don't know -- how shall I phrase this -- contrary to perhaps what they even believe.

What did they say for Tic Tacs, about what it was? Did any of them say tobacco? Did anyone say anything other than candy, mints -- I guess they're not a gum, but --

MS. HOU: Well, I mean, I can't speak for the entire 8,000, 14,000 samples, but personally, with my friends, pretty much everybody knew that it was a Tic Tac and they were straightforward with that. So I didn't really have anybody trying to pull my leg or anything.

DR. PETERS: It would be good to look in the data. Your friends might all be going to Princeton.

[Laughter.]

MR. JORDAN: I think Mayo might know.

MS. DJAKARIA: There was a very small

percentage that actually thought Tic Tac was tobacco; I think about 1 or 3 percent. I can't remember. And thank you for somebody who brought the report, but we actually have an updated report that we'll make available soon.

MR. JORDAN: Yes. And one more comment on the impression of the youth. The way all of these programs work, they actually work through existing clubs. So we don't establish anti-tobacco clubs. Judy's a rock star who has TV interviews and all of that. So her friends may have known, but most of these youth are known as a cheerleader or a DECA club member, a key club member, FBLA, because that's where they get their little mini-grant to do this work. So most likely, they're known as a club member before they're known as any kind of anti-tobacco advocate, for the most part, except for when they get news articles and things.

DR. SAMET: Let me check on the phone and see if there are any questions.

MR. HAMM: No questions.

DR. CLANTON: This is Mark and I have no

questions.

DR. SAMET: John?

DR. LAUTERBACH: Yes. Dr. Heck reminded me that I had brought this along. This is something that I picked up at my local Wal-Mart. And anyone want to say whether this tastes like candy or not?

DR. SAMET: What is it?

DR. LAUTERBACH: It's a Nicorette gum package with the labels "fruit chill" and "coated for bold flavor."

DR. EISSENBERG: I don't know what it tastes like, but it sure doesn't look like candy from here.

DR. LAUTERBACH: It looks like to me like a Chiclet. And I assure you, this product tastes better than any of the products you listed up there as tobacco products. And I've tasted all of the ones you have up there, both old and new versions. This tastes far, far better.

DR. SAMET: Thank you, John.

[Laughter.]

DR. SAMET: Is that a comment from the

phone? Is that a voice?

DR. CLANTON: This is a voice. This is Mark Clanton.

DR. SAMET: Go ahead, Mark.

DR. CLANTON: Again, first the compliments to the study and the data on the candy, mints, or gum. But I'm particularly drawn to the respondents who look at this as medication or medicine. I'm curious, were there any additional question that helped you understand, for those who thought it was medicine, if they thought or could respond that it was a stimulant medication versus some other kind of medication?

MR. JORDAN: No. There wasn't any kind of follow-up. Unfortunately, because of the way the survey's administered by youth, it's a short survey and we just take what adults wrote down on there.

DR. SAMET: Let me ask a question.

DR. CLANTON: I just had to take a chance, then, and we also will sort of ask unfair questions. But the reason why I ask that is, when dextromethorphan, which is a cough suppressant in

various cough medications, was put on the market, neither public health, nor medicine, or anybody else associated it with a stimulant medication, which now has to be protected in sales because some youth use it as a stimulant.

So I would be very curious to know. And maybe in future surveys, you could drill that down a bit and understand whether for those who identify it as medicine, if in fact they perceive that there's any stimulant effects from it. It could end up being used that way, certainly in the larger market.

MR. JORDAN: Yes. We agree, and we can look into some sort of follow-up questionnaire that we can do with people based on their answers.

DR. SAMET: Actually, my question was what follow-up are you planning? In other words, is this going to be an ongoing project and survey, looking at what happens over time? Is this a one-time shot? Where are you going next?

MR. JORDAN: The way that Y Street works, they look at campaigns on an annual basis,

sometimes pick one or two campaigns that they work on. So it has to do with what the youth leaders are interested in working on and what the demand is.

For example, when the FDA put out the call for public comment on the warning labels, the youth jumped on that and created a campaign immediately to do something. So if the FDA, similarly, said we need data on this, we would present it to the youth leaders and they would respond. But as of now, there isn't another dissolvable study going on in any of the states.

DR. SAMET: Any other questions for our presenters?

[No response.]

DR. SAMET: At a historical note, I actually grew up in Virginia, in Newport News, and somewhere deep in the last century, my elementary school class made a trip to the Philip Morris factory in Richmond. So it sounds like perhaps things have changed for Virginia youth. I actually still do remember the factory because it was very impressive

to see this production line of machines with thousands of packages rolling off. I'm not going to reveal what year that was, but you can all take your guesses as to when that was.

[Laughter.]

DR. SAMET: But thank you very much for your presentations. Good luck at Princeton.

MS. HOU: Thanks.

Committee Discussion

DR. SAMET: So I think what we need to do is, now, come back and see. We've heard two very interesting presentations I think that peaked everybody's interest. I think we had some window of insight into perceptions of these products by high school and college-age students.

I think we can all understand that at this point, these perceptions are based on, obviously, where the market is, what contact these students may have had with these products and awareness, so I think this is sort of a first snapshot at a particular moment.

But I think probably in terms of our

discussions, I think the question ought to be to try to crystallize what lessons learned might be embedded here. So why don't I open up for discussion?

[No response.]

DR. SAMET: That means you say things.

So let me ask, actually, Ellen, for your thoughts, perhaps first, in terms of both perceptions of products and any perceptions of risks that we can feel we've gleaned from this.

DR. PETERS: I was just sort of trying to organize my thoughts. This to me is a really strange consumer good, in the sense that, from the perspective of what we heard yesterday, they are accessory products that are not intended to stand on their own. They are products that appear to be designed as a stopgap so that people can continue smoking, but they don't want to in this particular environment for whatever reason. But they appear to be designed that way. There's very little evidence on perceived risks and perceived benefits, although we have now heard some of that today.

The things that occur to me is that we know very little at this point about what attributes people are seeing as important to choosing or not choosing the product. And because we don't know that, we also don't know whether there are attributes of the products that should be important to that choice, but perhaps are not being marketed to people in ways that would help. And I say would help with respect to the public hearing session yesterday, where we heard a variety of people saying that there was a lack of understanding of the risks of this product class versus cigarettes, for example.

The main thing that I thought about as we were doing this is that, when we're making choices in life, there's so much information and so many options, it's really difficult to make choices. And we're all boundedly rational, so we take mental shortcuts in order to decide how we're going to make these choices.

But the way that we tend to take these mental shortcuts is that we use comparisons. The

mind tends to encode information in terms of changes or differences. And so the overall choice context ends up being very important.

This, again, goes back to the public hearing session yesterday. It wasn't entirely clear to me -- yesterday it appeared as if people didn't understand the relative risk versus cigarettes. And maybe we don't have a scientific consensus yet on what the relative risk is versus cigarettes. That's not my field. That's something you guys will know better. But if it's the case that the relative risks of these products, relative to cigarettes, that they really are far less risky, then that is an important attribute that perhaps is missing within this choice context. But again, what those scientific relative risks are, I'll leave for you guys to do.

The array of choices that consumers perceive is really important, and I don't feel like we know what that array of choices is, as perceived by the consumer. We are lumping categories of products together, and I'm not clear at this point whether

consumers are lumping those products together in the same categories and by what attributes they're lumping those categories together. But those attributes and the comparisons are going to be critical to these kinds of choices that people make.

We talked about it. I talked about it a second ago in terms of just that relative risk versus cigarettes. There are other things that can happen in terms of the array of choices, as perceived by the consumer. You can, for example, make dissolvables an extreme option and encourage choices of a middle option. There's potential to do that there in the marketplace.

That may or may not be something that you'd want to do. But my main point here is that we want to know more, I think, about what is the context of the choice situation that consumers are perceiving, not what we think are the product categories and what we think are the important attributes, but what is it that consumers are perceiving? And it doesn't seem like we really have as much

information as we should have there yet. That context, then, is going to have a large influence on choice.

As a quick example, there was a bread maker, Williams-Sonoma. Williams-Sonoma introduced the first bread maker into the marketplace somewhere in the $200 range, I think. And it wasn't clear whether that was a good price for that product or not.

They went ahead and introduced, maybe a year later, a very high-end bread maker onto the market that cost maybe $400. And I'm making up the numbers a little bit. But $400 in that context is now very expensive. And what happened was is they hugely increased their sales of the $200 product because it was within the decision context. Those kind of comparisons are critical.

Now, that's a hard number. People are very good at comparing those kind of dollar values. And there are those kind of hard monetary values here as well, but it's not just monetary values that people compare on. They compare on other

attributes, but we need to know what those attributes are.

DR. SAMET: I think that was helpful. Let me just ask you a follow-up. We are completing our work on dissolvables by March 23rd, so we only have this initial context of test marketing.

So one question I guess is how far -- since we don't actually know what the future context might be if these products are moved out into markets nationally -- I mean, we have some experience with, I guess, Ariva and Stonewall. But these other generations of new products, are we left to -- at this point can we -- how much can we say with certainty -- since we don't have that context yet in hand. We only have, again, these test markets and what we've seen. It's a relatively limited database without information. I think a lot of what you said about aspects of the context will be so critical.

DR. PETERS: From the presentations today, we have some data on the notion that the dissolvable products are perceived as lower in risk

than many of the other products that are out on the market. But if you look at that scale, I would argue that they still perceive the risks of those products as pretty high. I mean, that was a scale from 1 to 10. And I think I don't remember the numbers exactly, but I think they were coming in around a five, 6 or 7; 5, 6, 7? Yes, right around in that range.

So I think based on that data, the college students are still perceiving the risks as, I would say, quite high. If that does not accurately reflect the scientific consensus on what the risks are actually posed by those products, then I think the risk perceptions are discordant. But again, I don't know what the scientific consensus is on the actual risks of these products. That's up for you guys to decide. I'm a risk perception person.

From the very last presentation that we just heard on the packaging, I thought that was -- that's a very important topic here. There is a reason why so much money is spent on packaging. It's because packaging frames the

decision situation. It is the initial information in some cases that people initially get that then frames the whole context of their experience. It can not only have an impact at the moment of, do I want to pick that package up and maybe try once, it can actually potentially have an influence on how they experience the product when they're trying it. There's data on those kind of framing effects that suggest that that initial framing will influence the actual taste experience.

I'm using some data on -- the data that I'm drawing from there is based on using verbal labels, positive verbal labels versus negative verbal labels that they get before they try something. And those positive versus negative verbal labels actually influence how people perceived the taste of something in an actual experience situation. And I think that packaging does something similar to that. It provides a very positive frame going into an experience.

That data suggests, from this very last experience, from this very last presentation, that

these kinds of products, while they may be lower in risk compared to cigarettes, particularly for smokers who are trying to quit, that there may be some potential danger here for teenagers up-taking and suddenly getting more of whatever the risks are of these products. It's suggestive of that. But I would still argue that I think these guys need to do a little more data analysis of their own data. But the data is very interesting.

DR. SAMET: John?

DR. LAUTERBACH: Question for Dr. Peters. If I heard you correctly, you said that these products were only used when people could not smoke.

Is that correct, your perception of them?

DR. PETERS: My perception of them is that, based on the presentation that was given yesterday, of the marketing documents in the tobacco industry, that it looks as if that's the way that they're designed, that it appears as if they're designed in terms of the benefits to avoid social experiences where smoking just isn't acceptable.

I'm trying to remember some of the other benefits that were mentioned in that product design presentation. But my impression from that presentation was that that was how they were designed.

Now, my impression from the public presentation is that that's not how they're only used, that in fact some of the people yesterday very strongly said, "I use this for smoking cessation." It was not used as a stopgap measure by the people who spoke in the public session yesterday.

DR. LAUTERBACH: You are aware that at least one group of these products has been around on the market since 2001, 2002, and are not new products that have been pretty much available from a pharmacy, CVS, whatever, for the last decade?

DR. PETERS: Yes. We heard that in some presentations yesterday.

DR. SAMET: Bob?

DR. BALSTER: So I can use some clarification. I mean, it strikes me that the

results of a study such as this, asking perception based on packaging, is going to be influenced a great deal by the warning label on the packages. I mean, if the picture shown in the Virginia Foundation for Healthy Youth survey were pictures that did not have a warning on that part of the package that was shown, it's my understanding, right, that the individual package units for dissolvable products will contain the warning?

I would ask Dr. Peters. I suppose it will just be pure conjecture what the likelihood of having that warning on the package will be and changing the likelihood that people would label them as a non-tobacco product. But it suggests to me the importance of the labeling, of the warning.

DR. SAMET: Ellen?

DR. PETERS: Probably not just the importance of having the warning, but where it's placed, and how large it is, and basically, do people actually read it or look at it. I don't think these products are up for graphic warning labels, probably just text-based, according to the

Tobacco Act. But it would depend on whether people look at it and process it.

DR. BALSTER: So since we have this ready research team of Virginia youth who want to do just quick studies, it would be very interesting for them to do a comparative study, somehow comparing the labeled and unlabeled products, and see how the results would differ.

DR. SAMET: I think they're listening.

Let's see. Neal? I'll keep going around.

DR. BENOWITZ: Someone mentioned yesterday -- and I just wanted to get a clarification -- the extent to which these products are behind the counter versus openly available because I think that's an important question for a kid interpreting this as candy, because behind the counter, they're not going to see it as candy. But I don't know what the regulations are.

Are these widely available for kids to see, or are they mostly behind the counter? Does anyone know that?

DR. HECK: Yes, behind the counter, like

other tobacco products.

DR. SAMET: Yes. And we heard that yesterday from the gentleman from the Alliance of -- that store owner group.

DR. EISSENBERG: There is an important point to make there. The product is behind the counter. I thought we also saw a waist-level advertisement of the product, depicting the pictures that we looked at on the door of the store. So adolescents are quite clearly going to see the product in the picture.

DR. SAMET: We did see such a picture. Yes.

Let's see. Bruce?

DR. SIMONS-MORTON: Yes. That's pretty much the point I was going to make, too. I mean, purchasing is very contextual and perceptions of products are very contextual. So if it's behind the counter with other tobacco products, you're going to assume that it's that kind of product. So it's true with surveys.

So I think, while the data from Virginia and other states that was just presented is impressive,

mainly because we don't have any other data, you really worry about a survey that presents these products with candy and then asks you about your perceptions of them. So I think we need to interpret these data very cautiously.

DR. SAMET: Sandrine?

DR. PIRARD: Yes. We could argue that, supposedly, people under 18 won't buy them in a retail store and won't see them behind a counter. Where they will see them is popping out of the pocket of a friend who might be 18 and above. And they might see them as very attractive. I don't think they will ask, did you buy that behind the counter or as a candy. So I think we have to think about that, too.

DR. SAMET: Tom, did you have more?

DR. EISSENBERG: I guess one thing I was looking for was some clarification from FDA, the extent to which the report can make a recommendation with regard to labeling and packaging.

DR. ASHLEY: I think TPSAC is able to make

recommendations on just about anything you want to.

DR. EISSENBERG: Then I was struck by Dr. Peters' discussion of context and then Dr. Lauterbach's repeated questions about individual experience. And so I thought, with your permission, I would share individual experience as well.

There are cough medicines, and I vividly remember Triaminic Red being quite a tasty cough medicine. And Nyquil Green, I can't even describe the adverse effects that that has on me.

[Laughter.]

DR. EISSENBERG: And yet I do know that they're both medicines, and I think that's critical, that context. Whenever I want a tasty treat, I don't reach for Triaminic Red.

[Laughter.]

DR. EISSENBERG: And so I think that's important to keep in mind.

DR. SAMET: Fred?

DR. PAMPEL: This gets very complex because on one hand, smokers who would benefit from

substituting dissolvable tobacco for cigarettes are scared away because they think it's too dangerous. But then on the other hand, the information we're getting is that kids who shouldn't be touching this thing think it's harmless, that it's like candy.

So on one hand, you have to convince people that it's not as bad as they think it is; on the other hand, you have to convince people that it's worse than they think it is. So there's two sorts of groups here to satisfy. And I'm not sure what kind of message you'd need to develop, but there would have to be some very careful thought to try and satisfy both those issues.

DR. SAMET: Dan?

DR. HECK: Well, I guess going back to some of the prior discussion, we all recall when the NRT products first became available. They were cautiously offered under prescription and they were designed to be relatively difficult to chew and not particularly tasting very good. And as time and experience gathered, now they've been more flavorful options, such as the one John brought

that are now available over the counter.

We did hear from the FDA officer previously about the experience with those NRT products, nicotine-delivering products, where the more flavorful, or attractive, or pleasant, as we might say, versions of those products really have not been shown to be markedly more subject to abuse or youth appeal; again, not an identical circumstance, but some existing data on a somewhat analogous product where I think we can draw some useful information.

DR. SAMET: Bob?

DR. BALSTER: I sort have been viewing this issue about retail underage sales as really a bit of a red herring. I mean, I don't doubt the good intentions of regulators that made those types of regulations, or the industry, or the retailers. I think there's a legitimate attempt to prevent retail sales to children of these products, as well as cigarettes. But we know that that isn't fundamentally working. I mean, underage smoking is a major public health problem in the United States.

So if, in fact, these products offer abuse potential, the fact that they are sales restricted is certainly good, but it isn't going to prevent kids from gaining access to them.

So I believe that this is probably -- the age restriction for these is no more, no less effective than age restriction for cigarettes.

DR. SAMET: I want to make a comment on the comparison to candy or other. For example, basically, if you're going to make something that people are going to put in their mouths, there's probably certain constraints on size and form, no matter what, that bring this certain resemblance. You're not going to put this in your mouth. Maybe some people do.

I mean, I think a pill is a pill. There's certain size ranges as to what people actually want to pick up and put in their mouth. So I think we're left with that, perhaps, as a given.

Let me ask, on the phone, comments?

MR. HAMM: No questions.

DR. CLANTON: This is Mark. I don't have

any summary comments.

DR. SAMET: Let me just try again and see if Sherry's joined and has any comments.

[No response.]

DR. SAMET: Okay, maybe not. Dan?

DR. HECK: Just a very quick follow-up for something earlier I neglected. In terms of the warning labels, I think we're probably mostly aware, and we have discussed maybe a desirability for some enhanced or different warnings, but those warnings are mandated by law now and are in place on smokeless products. So we might broadly discuss, as I relay it, different warnings, but that would be a large topic for maybe a different forum.

DR. SAMET: Ellen?

DR. PETERS: I wanted to just respond a little bit to a couple of the comments over here. First, it is a complex topic. I would guess it wouldn't come to this esteemed committee if it wasn't.

You said something, though, that you thought

that adults thought it was too risky and kids don't think it's risky. I think from the data we saw, the kids do think it's risky, maybe not quite as much as cigarettes, but that they do think it's risky, perhaps.

DR. PAMPEL: They think it's candy.

DR. PETERS: But they may think that risky -- but they may think it's candy, and they may also think that risky is a positive attribute. They may also see the packaging as a positive attribute. And so I think the question from that perspective -- I think more data is needed here, but I'm not convinced that kids don't think it's risky. I just don't know how they're using that data.

Also, the other point that was made after that I thought was also very important. Kids do need help, too, to smoke less or not to smoke at all. And I think that is something that the committee should consider as an important potential question here. I don't think we know at this point whether having these on the market is attractive

only to the kids who might have ended up being smokers otherwise and they only use this product, then, or whether it's attractive to kids who would never have started smoking; and so now they're suddenly going to be exposed to risks that they would never have been exposed to anyhow.

I'm not sure we know enough about what kids are going to be exposed to this just yet.

DR. SAMET: Anything else? Dorothy, do you have any comments?

[No audible response.]

DR. SAMET: Okay.

Anyone else? I think this has been a useful set of presentations and I think a very helpful discussion. And thanks to the presenters and Ellen, for your thoughts.

So I think what we will do is we will take a 15-minute break. Committee members, remember, there should be no discussion of the meeting topics during the breaks, amongst yourselves, or with any member of the audience. And we'll start again at 10:00, by that clock.

(Whereupon, a recess was taken.)

DR. SAMET: We're ready to reconvene; if everyone could take their seats, please. And just as a reminder of what goes on the rest of the day, it's us having a discussion about the evidence that we've heard and thinking about our task of responding to the charge that is in the Act.

So just a couple of reminders. Again, remember that for those of us who were here on Wednesday, we did hear some commercial confidential information that sits in a different part of your brain where you don't discuss it out in the open. Second, that we really need to do sort of the hard work of digesting the information that we've heard and thinking about what are the points that we've learned that will go into our report to FDA by the March 23rd submission.

Actually, I'm working on a paper with a colleague who just recently sent me a revised draft with a quote from Ernest Rutherford. He's a nuclear physicist. And the quote is, "Gentlemen, the money has run out. Now, it's time to start

thinking."

I actually think that fits pretty well with where we are now. We've sort of run out of having people bring information to us, and now we have to think about what we've heard. And for those of you who are new to developing a report with TPSAC, we really are going to sit here today as a group and discuss what we've learned and what goes on.

I recognize this is not the usual way one might think about doing a report. You're usually sitting in a room somewhere under less formal circumstances, but we actually do this in the open, so that's what we'll be doing. And I think we need, nonetheless, to have free, unconstrained discussion.

I think actually as a first point, before we start thinking, we have one little respite. I think we're going to take a look at the packages.

David?

DR. ASHLEY: Yes. FDA has arranged to get most, if not all, of the products, and we thought it would just be worthwhile to pass them around and

let people see exactly what those are. And so we don't have one for each of you, but we do have, I think, one of pretty much everything.

So, Tom, can you start it moving around? We'll just start on that side of the table and pass them around.

DR. SAMET: We are not functioning as a tasting panel.

[Laughter.]

DR. ASHLEY: We are not functioning as a tasting panel.

DR. EVANS: I would like to remind you that the facilities here are tobacco-free, so there will be no sampling of these products today.

[Committee views products.]

DR. SAMET: Let's just pass these around for a few moments. Then we can just get back to our business.

[Pause.]

DR. SAMET: We might have a contest on getting these open, though.

[Pause.]

DR. SAMET: The sticks might work for the opening contest.

[Pause.]

DR. SAMET: Mark and Arnold, sorry you can't see this, but what's going on now is that people are looking at the various packages. And we will circle and start. I will ask for any comments or reactions that you may have. And in fact, Tom, if you want to --

DR. EISSENBERG: I just want to ask Dr. Heck a question.

You mentioned that the warning labels are mandated, and I saw that. Maybe you could clarify for me because I haven't studied the law. It looked like there were four mandated labels, and you could choose which one you put on there.

That's not the case? Can you explain it? And they must rotate?

DR. LAUTERBACH: Yes.

DR. MCAFEE: So several of the products, like one of these products here that I'm looking at, Silver Eagle Labs NicoSpan, does not have a

warning on it. What's the explanation for how you either do or don't report?

DR. SAMET: Yes, David?

DR. ASHLEY: I don't know if you were here. NicoSpan does not contain powdered -- what is it? Ground tobacco. It doesn't contain tobacco, ground, powdered, tobacco.

DR. MCAFEE: So it's neither a drug or a tobacco product, sort of, something like that.

DR. ASHLEY: It's a tobacco product, but it's not under the jurisdiction of the Center for Tobacco Products as far as we know, at this time. I don't know that a jurisdictional determination has been made.

DR. SAMET: Let me ask -- let's take just a few minutes, since we've taken the time to pass these around -- if anyone has thoughts or comments after seeing the packaging, Dorothy?

DR. HATSUKAMI: I thought the Marlboro sticks were really quite easy to access, and I would be a little bit concerned about kids getting a hold of them because they look like

chocolate-covered sticks in some respects. But circling back to what Dr. Boja had said yesterday, I think he had mentioned that what you want to do with the packaging is to make sure that's not easily accessible to kids, but easily accessible to adults. And so one of my concerns I have about some of the packaging, especially the Camel products, is that it's very difficult to have access to it. And one of the concerns about having it more difficult for adults to have access to the product is that they will transfer some of those products into vehicles that are a lot easier to have access to.

I think one of the poisoning that had happened with a child was a result of an adult transferring the product to one that's more easily accessible. So that's kind of my reaction to the packaging or the way it's packaged.

DR. SAMET: Bob?

DR. BALSTER: Just for clarification also, with the new graphic warnings that are mandated, they will also be appearing?

Is that correct? No?

DR. DEYTON: That's only for cigarettes, and cigarette advertising, and cigarette cartons.

DR. SAMET: Other? Tim?

DR. MCAFEE: The other observation that I would have, looking at these, is I think another issue that we haven't talked about very much -- again, this is another thing that distinguishes the marketing of these as a variant or a subunit within smokeless, is co-branding of this sort of plethora of different types of products; that I look at this and say, oh, this reminds me of a toothpick; oh, this reminds me of a blister-pack medication; oh, this reminds me of candy. But they all may be -- or some of them are co-branded with, oh, a Camel; that reminds me of cigarettes.

So I think this is another interesting issue, again, with what's going to be very difficult for us to struggle with, without data, is how these are going to impact adolescence around their uptick, but also adult smokers in that,

essentially, what I would think we are probably going to do around this is that we're going to be normalizing tobacco products because we're taking something where, currently, we have mostly things that are just associated with the larger brand of being a tobacco product, i.e. a cigarette or very distinctive smokeless products, for which I think people have very specific ideas about, that have taken decades of very hard work on the part of society to establish, around risk.

I'm not saying that this is through ill intent or whatever, but I think it's a fairly predictable side effect of doing this, at a minimum, which is that we would have to think about how to not normalize -- having this have a larger impact of normalizing tobacco products in society, and that this would transfer, particularly in adolescents' psyche, but probably in adults as well, to other types of products that we don't associate with risk, regardless of whether they're sold that way or whether they're behind the counter. I see a blister pack of something that

looks like medication. I think of positive things. I think of safety. I think of cleanliness. There's a lot of subconscious associations associated with this type of packaging that will, I think, create effects.

DR. SAMET: John?

DR. LAUTERBACH: But Dr. McAfee, this product has been in the market and its co-product, Ariva, has been on the market for a decade. And to my knowledge, we haven't seen a great deal of adolescent or young adult use of it.

DR. MCAFEE: Yes. In that stage, it was kind of the micro-niche. I think the question is, what will happen if these become a much larger portion of the market? And I don't know if they will because of product characteristics. Clearly, again, we're talking about packaging at this point.

DR. SAMET: Other comments on what we've seen? Sandrine?

DR. PIRARD: Yes. I'm referring back to the comments we heard yesterday about many users saying please don't take this off because it really helps

me. I think that if there is indeed some use there, I mean, it would be great. But then obviously, what's the need, then, to kind of put them into very nice packages, to kind of imply that, in a sense, you could also have them in your pocket along with your cigarettes, and along with your matchbooks, and things like that.

So I think if there is a use to use them as smoking cessation, a lot of the marketing around it, a lot of some very nice phrase about, you know, take it whenever you want, or this is a very nice alternative, smoking wherever -- I mean, not smoking but using tobacco wherever you want.

Clearly, nothing is talking about smoking cessation, not about the warnings, not about labeling, not about the packaging. So I wonder about that.

DR. SAMET: Mirjana?

DR. DJORDJEVIC: I just noticed that all their products, like Stonewall, they were making labeling on the side. It took me really twisting the pack many different ways until I found it. So

that is something that would need to be standardized. And then there was no wonder in that last study which we heard about, youth study, which only showed the front of the picture, there was no label to indicate that that was tobacco products. So labeling should be standardized.

DR. SAMET: Dan?

DR. HECK: I guess the FDA can clarify. I think that labeling in terms of warning labels is standardized now, so maybe these are older market samples. And just to the point of, your relatively simple message is communicated in the ads, again, the manufacturers are constrained in their ability to give, "May aid cessation," or "May reduce risk," those messages. So I think the convenience of use or the brand name familiarity are really about the limits of the kind of advertising speech that the companies are presently able to do for these products.

DR. SAMET: Ellen?

DR. PETERS: To be fair to the tobacco companies, they're not allowed to market it as

cessation, as far as I know. And that's an important consideration.

Hang on just one second.

The one question I had, though, as the market develops -- I mean, you guys have to make money. That's your job. That's just what for-profit companies do. But as the market develops, it may be important -- as the market develops and also as regulation develops, it may be important for you guys to do research on things like what packages wouldn't be attractive to kids, what advertising wouldn't be attractive to kids, at the same time as you promulgate this income-producing product. And I'm curious whether you guys have any thoughts around that.

DR. HECK: I guess I'm not aware to the extent such work may be underway or may have been done, but certainly in academic world, which might arguably be the more appropriate venue for such research, those kinds of topics have been explored, I don't know, previously. But I guess I'm not aware, personally as I sit here, to what extent

that sort of research may have been done.

DR. PETERS: Why do you think that's more appropriate for an academic marketplace as opposed to the companies that are producing the products?

DR. HECK: Well, I know that -- I've just seen in the -- all the companies have youth smoking prevention programs active. And I've seen criticism of these in the literature in that some critics will argue that they're not effective or not effective enough, even though I think in the main -- well, in the main, I believe these are contracted to external agencies, and the companies don't tightly control the content.

DR. SAMET: We may be wandering too far from the dissolvable point, I think, but thanks.

Let's see. Mirjana? No? Okay. Tim?

DR. MCAFEE: Well, I just wanted to point out -- we talked about this a little bit yesterday and I've not heard -- I don't believe there's anything that would make it impossible for a tobacco company that was marketing a dissolvable product to pitch it as a substitute to smoking.

They can't pitch it as a smoking cessation device, but they are pitching it as a bridging device to allow people -- clearly, explicitly, this has been done both with dissolvables as well as other smokeless products.

So there's no reason that they -- there's no regulatory thing that would keep a tobacco company from encouraging people to switch. And I think the bottom line is this is a very important thing. I think if there is evidence to the contrary, it should be surface. But it does not look like most of the dissolvable products have been developed or marketed for that purpose, to serve as a substitute of product that would compete with people for being the primary mechanism by which they get nicotine.

I actually wanted to do a correction, or at least I had a different perception, listening to the public comments yesterday. I did not hear anybody say that they had used dissolvables as their primary means of quitting smoking. I heard people who, because this is a dissolvable meeting, talked about, yes, I use dissolvables. But it was

predominantly e-cigarettes, which have a dramatically -- appear to have -- their product characteristics are different from dissolvables. And as with smoking, they also use dissolvables. But it was almost, again, they were using it in an ancillary capacity, not as a primary tool.

DR. SAMET: I think our last two comments on this topic, and then I think we're going to move on.

Bob and then Dorothy.

DR. BALSTER: One thing -- obviously, in looking at this array of products, it would be my hope that the committee would be thinking about generating a report that would address future products and product types that may be coming along. This is a relatively broad diversity. The tobacco sticks have a pretty different characteristic product than some of the other ones. So I think we can't exactly predict what is going to come out. There are other versions of dissolvable and smokeless tobacco products that are going to emerge. And I would encourage us to make

sure that we're considering recommendations that could apply to newer products that would have different characteristics, for example, different nicotine deliveries and things of that type.

DR. SAMET: Dorothy?

DR. HATSUKAMI: I just wanted to make a comment related to the whole issue of cessation and what Tim had brought up. The ads for Camel snus do talk about completely switching to the product. Those are some recent ads that have come out. And so certainly, tobacco companies aren't prevented from making a complete switch type of advertisement.

But the issue with the dissolvables is that it's unlikely to occur because of the low levels of nicotine, although I cannot speak for the strips because I'm not really sure how that would perform, but for some of the other dissolvables, the levels of nicotine are quite low.

DR. SAMET: Let me check. Mark and Arnold, you're disadvantaged by not having seen this, but you want to respond at all to the discussions that

we've just had?

DR. CLANTON: No. Not having seen the packages, no, but I will have some comments about the report and maybe how it's structured.

DR. SAMET: Good. Thank you.

Arnold?

MR. HAMM: And I have seen most of the packaging; however, I really don't have any comments about it.

DR. SAMET: Thank you.

So let me suggest that -- we actually had a reminder this morning of our charge -- that we perhaps go back. I think it was the slides we saw on Wednesday that I thought were perhaps most useful. And go back to, yes, this just as a starting point and I think to have a discussion about the charge.

We've certainly touched on it already, but I think just to make certain that we have a clear vision of what we are up to. So this is straight out of the Act.

You might notice, "impact" is an open word,

and that could be positive, negative, mixed, whatever, but it's open. And of course, our charge, as for menthol, extends to children.

So why don't we go on?

So we have our population charge, risks and benefits to the population as a whole; increased or decreased likelihood that existing users of tobacco products will stop using such products. And I will interpret that as saying, would the availability of dissolvables in the marketplace affect the likelihood of established users changing their use of tobacco products. I think that's tobacco products construed generally; and then a similar comment around initiation, for getting some similarity to the menthol, of course; and March 23rd, not too many shopping days left.

Bruce?

DR. SIMONS-MORTON: I guess one of the issues that would be helpful to discuss is the extent to which we should be thinking in terms of the available data and to what extent we should be thinking about the potential future.

This is kind of hard to reconcile because it's hard to know, in this early market, where this is going. But any decisions that are ultimately made by FDA may be in place for the next 20 or 30 years, or some period of time, before there's another chance at this.

DR. SAMET: Right. And I think when we get to sort of the proposed way that I've thought about how we might put things together -- I've said we should crystallize what we've heard and what we have identified as the points where we learned something from the materials available, and then I think those for the future-looking recommendations for what additional information should be collected as this story unfolds. I think you're exactly right. And I think you'll find that in the outline.

Why don't we look at the next -- so a definition of tobacco product, and then onward, just a reminder. And does everybody want a reminder about what the second bullet refers to?

Do you want to comment? Yes, Bob.

DR. BALSTER: Going back to that previous slide, again, I am admittedly confused about the definition with respect to the nicotine-only products that have not gone through FDA consideration as drugs, over-the-counter or prescription drugs. So that other thing, which I gather is not considered a tobacco product, but is also not considered a drug because it hasn't been through an FDA approval process as a medication.

So what is that, or why is that not? Because it is a component of a tobacco product. I don't understand the placement of that particular type of product, a nicotine-only product that's not been positioned as a medication.

DR. SAMET: And if I understand our charge, which is dissolvable tobacco products, that particular product would be -- but would not meet the definition for tobacco.

David, help.

DR. ASHLEY: You have to remember that the definition of tobacco product is greater than the definition of the products that are currently under

FDA's jurisdiction. And so what we're looking for is tobacco products broadly because we have -- and it said it on the slide -- maybe it's the next slide -- "We have expressed the intention to deem all tobacco products within FDA's jurisdiction."

So we don't want you to limit right now your discussions. We want you to -- as we said before, there's currently no statutory definition of dissolvable. Many dissolvable tobacco products may meet the current statutory definition of smokeless tobacco. But there may be some dissolvable tobacco products that may not meet the definition of cigarette, cigarette tobacco, roll-your-own tobacco, or smokeless tobacco, and so may not be currently subject to the FDA regulation. But for the purposes of this discussion, we want you to keep the discussion broad.

DR. SAMET: Okay, as we broadly discuss -- and I think this is what we just heard from David, in fact. And I think this question of no statutory definition of dissolvable tobacco products, we're probably going to need to make some

statement about what we're referring to one way or another, I think, as we talk about that. So I think we should keep that as an important point.

I think here, maybe I want to distinguish between what we're not asked to do and what we are asked to do. So we were asked in our charge to look at increased or decreased likelihood of users of tobacco products not using them or changing use, I guess, and the same issue on non-smokers or non-users of tobacco products and likelihood of increasing or decreasing use.

So I think the distinction lies in the kind of evidence that one would use actually to determine if it's a cessation aid, which we know specifically the kinds of randomized control trial data that one would look for. So I think that distinction should be clear to everyone.

The substantial equivalent, I think we understand, that's not our issue. And then hiding down there is to evaluate individual applications -- that's product applications -- and to address use of dissolvable tobacco products as

potential modified-risk tobacco products.

So we I think do not have a charge to specifically address that last point, which I think is important.

Bob?

DR. BALSTER: Just to be really clear, that first bullet there about dissolvable products as a cessation aid, I take that to specifically mean that we are not to be considering, in effect, what would support a claim of a use as a cessation aid, that that's simply not being asked of us, whether the data exists or does not exist for a claim, as a cessation aid.

DR. SAMET: Right, right. Tim?

DR. MCAFEE: Just two clarifying questions around this. What I would say is the first bullet does not, however, mean that we are not to consider the impact of the further expansion of dissolvables or continuation of dissolvables in the market in terms of the population behavior of smokers, smokeless users, and non-smokers, which is -- because we had this earlier conversation

about cessation, that cessation is different than what happens at the population level, in terms of whether people quit smoking, switch over, et cetera. Those things are part of the charge.

DR. SAMET: Say that again, Tim. Let me just try and get it.

DR. MCAFEE: Well, one of the things that we're specifically being asked to do is to look at the population effects of dissolvables on people's behaviors in terms of initiation, quitting, et cetera. That's separate than it being a cessation aid. Right?

Then the last one, I guess, although we're not being asked to weigh in on the question of whether, essentially, FDA should allow dissolvable manufacturers to make a modified-risk claim, which is a very specific thing, still we are going to be considering issues associated with whether their use does actually decrease risk.

DR. SAMET: To users?

DR. MCAFEE: To users.

DR. SAMET: Yes.

DR. MCAFEE: So in other words, that's a very technical -- these are each very technical, specific things, but the concept of whether or not dissolvable use might modify risk would still be something that would weigh into deliberations.

DR. SAMET: I thought I heard something else in your comment originally. And let me see if I can phrase it, that you talked about the expansion, or pool or suite of smokeless products. And I thought you were in part saying, or going to say, that as we consider dissolvables, we have to consider them in the context of the enlargement of the array of smokeless products, that that's part of our context here.

I don't know whether you meant to say that, but I think that should be part of what we think about.

DR. MCAFEE: It's an interesting and important point that I would like to be able to claim credit for, but I think you get to claim credit for it.

DR. SAMET: No need. David?

DR. ASHLEY: Let me try to clarify and probably confuse it more, but I will try. We clearly want the committee to consider the impact of dissolvable tobacco products on the use of tobacco products. But we don't want the committee to consider tobacco products in the same context that CDER would be looking at these products, as cessation aids.

The second thing is to be clear that when we have to consider whether something should be a modified-risk tobacco product, there are many considerations that are very specific to that particular product, its advertising, its labeling. There's a whole list of things that we've got to consider very specifically related to that particular product.

So we do not want the committee to go in and make generalities that we can't interpret because we have to look at specific products and understand those details of the specific products.

Again, I hope that didn't confuse you more.

DR. SAMET: I think the first point was

clear. I think the second point, a little less clear, but I think I understood what you're asking for. You want something useful.

[Laughter.]

DR. SAMET: Okay, just continuing down.

Let me ask, actually, David, you want to amplify a little bit on this? I think that might be helpful.

DR. ASHLEY: Again, the first one is what I was saying just a few minutes ago. We don't want you just to limit to the things that are currently under our jurisdiction. So we don't want you to say, are they cigarettes, are they smokeless tobacco, are they roll-your-own. We want you right now to be inclusive even if they don't fall within our jurisdiction, but as long as they do fall within the definition of a tobacco product.

The second one is, there is no definition in the statute of what a dissolvable tobacco product is. We're not asking the committee to come up with a dissolvable tobacco product definition as advice to FDA. But we are interested in the committee, as

appropriate, to say, for our own deliberations and what we are doing today, this is what we're going to call a dissolvable tobacco product; so as is appropriate.

DR. SAMET: Neal?

DR. BENOWITZ: Could you just clarify, David, what is the definition of smokeless tobacco?

DR. SAMET: We've seen it.

DR. ASHLEY: That's the definition of smokeless tobacco right there.

DR. BENOWITZ: It would seem from that, that there is no way that dissolvable tobacco would not meet that definition. Right?

DR. ASHLEY: I'll read these to you again. "Many dissolvable tobacco products meet the current statutory definition of smokeless tobacco." Many of them do. "Some dissolvable tobacco products may not meet that definition."

DR. BENOWITZ: Yes. I'm just trying to figure out how they may not, how that would work.

DR. ASHLEY: Well, if it doesn't consist of cut, ground, powder, or leaf tobacco, or if it's

not intended to be placed in the oral or nasal cavity, then it wouldn't be smokeless tobacco.

DR. SAMET: I'm tempted to ask what cavity it might be placed into.

[Laughter.]

DR. SAMET: Was that all cleared up for you, Neal?

I think we just need to say what we're referring to explicitly, and I think that will get us off the hook.

So I think now this is just the things that we've -- and then, of course, what we've done. So I'm not sure. So I think we should probably move on from the charge. Let me just see if there are any last matters.

Sandrine?

DR. PIRARD: Quick question. This morning, the word "recommendation" was brought in. And basically, the comment was that we would discuss that later. So is it that in addition, to kind of provide some -- like some I guess kind of summary of the evidence, of kind of sold on whatever has

been presented, the committee has to give some recommendation or is encouraged to give some recommendation to FDA?

DR. SAMET: Yes. I think we're going to come to this.

So why don't we -- I put together just some things just to help guide our discussion. I just want to remind you of a couple things. One is that we do have the list of, I think, 13 questions. Probably, I don't want us, for the moment, to bog down in those 13 questions. There are some details, and for many of them, we have seen no or very limited evidence.

So what I think I'd like to do is start at the top about what we're going to do in terms of meeting our task. So I put together a few very informal slides; and so the things I think we need to talk about. So one is just a framework for the report, and that would be something akin to what we did in menthol, just a general way of thinking, particularly at the population level, about impact.

There was, in the note that came from

me -- I think we sent it twice now -- a figure that we'll come back. So something like that, to think about these questions particularly around likelihood of increased or decreased use of tobacco products or initiation of tobacco products.

We've heard a lot of evidence between what was presented at this meeting and at our July meeting. And one thing I think we need to do today is to really hone in on what we think we've learned, and try and identify what we've learned from the many gaps that we know are there in our understanding of these products in relationship to our charge; that we would address the charge in a brief summary -- and we'll talk about how to get there -- but what would the summary be?

Well, the summary would be related to our findings, and all the evidence that we have heard in relationship to our charge and any recommendations that we might be offering around information, future information gathering, research, and surveillance.

The summary would be a summary of a lot of

material, some of which would be recorded in the form of the record of our discussions, the presentation materials to TPSAC, the peer-reviewed literature that has been identified and summarized, and so on. And I think we subsequently have a description, but that would also be with that a summary, if you will, of all of this material.

So just a reminder about the broad classes of material we've heard, the peer-reviewed literature, a relatively small number of articles that we've discussed on a number of occasions, the industry presentations going back to July, the industry documents, both those that we've discussed openly and the commercial confidential documents, the open public hearing input, the review of the Swedish experience, and then the Indiana experience, and the presentations that we heard today about these products and youth, both high school and college.

So one of the things I'd like us to do before we go home, one of the things we have to do before we go home, is to go through each of these I

think as a group, sort of say what it is we've learned, because that's going to be an important part of our record of findings -- I think we can go on -- and that there would be a summary of this.

So I want everybody to relax. We're not talking about menthol, too. Okay? So what we're talking about is a brief summary, and we will talk about how we get there. But we'll probably need that summary relatively soon and in front of us for discussion at our March 1st, 2nd meeting. And the items in it might be what our charge was, how we approached our charge, what materials we looked at in very broad classes, but not doing what was done in the menthol report, where there were a whole set of systematic reviews of the evidence.

But that would include our key findings, so we really will have to get at that today. And our answer to the charge, our statements about impact, and recommendations for further information gathering, research, and surveillance.

So what I'd like us to do today is to really approach and discuss these elements of this summary

so that they can be summarized. And I think that might be it. So that's something for us to fill in.

So that's thoughts about the general approach. So that leaves us with our task for today, to discuss framework, to discuss findings in the evidence, to come to some initial thoughts about our impact, our overall charge, and think about research and so on.

So let me ask, first, FDA, do you have feelings about this general approach, and responsiveness to our charge and what's needed?

DR. ASHLEY: Yes. I think that's fine. I would have just changed a couple of words that you said when you said it needs to be done relatively quickly. I would say it has to be done very quickly. And when you said what we would plan to do was, at the next meeting, we would review the report; I think we will, at the next meeting, review the report. And so just changing a few words that you used, Jon.

DR. SAMET: Relatively quick, it's all

relative.

[Laughter.]

DR. SAMET: Okay. Thank you, David.

Anything else on this? So I think everybody's got a sense of what we need to get done and I think hopefully in rough agreement with the approach.

John?

DR. LAUTERBACH: Dr. Samet, you seem to be asking us to build the house from the roof down instead of from the foundation up. So do you have any idea? Can you enlighten us what you think the roof should look like? In other words, what would you like to see in the report?

DR. SAMET: So I've given you the broad -- the house analogy did not help me. But just to say what needs to go in the report, go back to this. The report is a broad set of things. So let's structure that out first.

So the report in fact includes the evidence that we've looked at. That includes presentations. That includes peer-reviewed literature. The report

includes a summary. And I think there was an outline proposed for the summary. And what we really need to do today is fill in what goes into that summary, and based on our discussions about the substantial amount of evidence that we've seen, which while substantial, we all know has many, many gaps in it.

Yes, please.

DR. LAUTERBACH: Dr. Samet, we are supposed to come up with some recommendations, and for starting the discussion, expediting things. What do you think those recommendations should be?

DR. SAMET: I actually think -- now, I'm going to go back to the house. I think you want to put the roof on when we haven't built it yet. So I think actually we need to have the discussion that leads up to that first. And again, if we go back to the description of the summary, I think the next -- so summary, I think actually what we should probably do is start with some of the elements here, discuss them, and end up at the recommendation point as a last one because I think

some of that will be around what kinds of information are going to be needed to address the many gaps we're going to find.

David?

DR. ASHLEY: Yes. And I think I know where John's coming from and Jon's coming from. I think one of the things that would be very useful is to start talking about key findings and get views of the committee what the key findings were that you have heard or you've gathered over the last meeting and this meeting, and identify what those key findings are, because, to me, that's the crux of what the report will be.

DR. SAMET: Yes. I certainly agree. If you go back to the -- that one. So if we were to start with this and maybe even, in real time, put under each of these what we think are, if you will, the key findings, I think that would be a way for us to be organized.

For example, under the Swedish experience, I think there are several points that we might put that we've discussed and I think pretty well

crystallized in our discussion on Wednesday and the bit of follow-up discussion we had on Thursday.

So I think one of the things I had intended to do is exactly what David said. So actually, I'm going to suggest, with the limited time, that we just get going and not spend too much more time worrying about the process, or we'll be rescheduling airplanes.

DR. PIRARD: I just have a quick question. And I know I missed a part yesterday, so it might be when you discussed that. But are you planning to use those questions under each of those, I don't know how many questions.

DR. SAMET: You're talking about the 13 questions?

DR. PIRARD: Yes, the 13, or use something that's --

DR. SAMET: I think the 13 questions may be something we can circle back to. I think to start delving into those in detail, knowing that many of them were just simply I'm going to be unable answer is probably not going to be too productive. I

think it would probably be most valuable first to sort of pull out our really key, big thoughts, if you will.

Yes, Bob?

DR. BALSTER: Just to be clear, your suggestion that we proceed with this step before we do the discussion of the framework that you presented to us at the forum --

DR. SAMET: Yes. I actually think we probably ought to start at this step and then see how we fit everything into the framework, because I think we've heard the presentations. It's all fresh in our minds, and I think we can pull this.

So let's actually start with the peer-reviewed literature. And we have the, what, 25 total studies, I think. And 21 of them or whatever were summarized in the RTI presentation. We have authors of a number of those studies here.

So let's think for a moment about the sub-bullets.

Actually, Caryn, what we could do is maybe start a slide for each of these, so if we had one

that said peer-reviewed literature -- just make a new slide. And let's start with the first one, would be peer-reviewed literature, and let's talk about the key points.

I'm actually going to ask Dorothy maybe to lead off the discussion on this.

DR. HATSUKAMI: So I think some of the key points for the peer-reviewed literature would be constituent yields, abuse liability, potential health effects, consumer perception, and consumer response. Those are the categories I can think of.

DR. SAMET: Your last two were consumer perception and consumer response.

DR. HATSUKAMI: Yes. I guess I'm not really sure to what extent we had information on health effects, other than the Swedish experience.

DR. BALSTER: But that doesn't come from the peer-reviewed literature. I'm just also wondering that. I'm trying to see what in the peer-reviewed literature was on health effects.

DR. SAMET: So we did have some discussion about the -- actually, we had the presentations

from RTI with the follow-up of the various cessation trials with NRT as one body of evidence that is from the peer-reviewed literature and the Swedish experience.

So let's start with -- I think, Dorothy, the first category you mentioned was constituent yields. And as an overall single-sentence finding around constituent yields --

DR. HATSUKAMI: My perception is, in looking at the literature, that there is variability across the dissolvable products, but they tend to be lower than conventional products here sold in the United States, as well as comparable or lower than what you see in snus products in Sweden. And that's related to TSNAs, and nicotine. Yes.

DR. SAMET: Neal?

DR. BENOWITZ: I think we also have the product composition, which is related to this, too. We also have data on product composition, which is related to the yields.

DR. SAMET: Bruce?

DR. SIMONS-MORTON: So for me, there are two

questions. One is about the variability in the products. It seems that the manufacturing process, as well as the tobacco that's used, can result in different levels of nitrosamines. It would make sense to have products that are as low as possible, and it seems like there's some potential to do some good there.

The issue of nicotine level is a whole nother issue because I would be interested in the committee's view about whether the relative advantages of having these gradients or of having higher levels -- which would be less encouraging for initiation, or lower levels, which would be more encouraging from a health point of view, if any substitution were to take place.

DR. SAMET: So it seems to me I'm going to suggest that we not quite go there because I think we should stick to the findings based on the literature we have. I mean, that may be something for the future, that there's a research need. But I think, for the moment, on the peer-reviewed literature, let's just sort of stay with what we

have in front of us.

Tom?

DR. EISSENBERG: I'm sorry. I just need a clarification. Yield, are we talking about what's in the product or what's in the user?

DR. HATSUKAMI: I was referring to what's in the product. Yes.

DR. EISSENBERG: So then I guess I hope we add to that delivery.

DR. SAMET: So if we were to crystallize this finding, it would be variability in product yield and delivery of nicotine, and the other market we saw a lot of was the TSNAs. And then the comment, Dorothy -- I'm not sure how you would phrase this, but at least in comparison to --

DR. HATSUKAMI: Conventional products sold in the U.S., as well as -- these dissolvables are lower than the yields, the TSNAs, the nicotine yields, compared to most of the conventional products sold here in the United States and are equal or lower to those products that are sold in Sweden, snus products sold in Sweden.

DR. SAMET: By conventional products, you're including smoked cigarettes?

DR. HATSUKAMI: Yes. It would be compared to smoked cigarettes, but also to the smokeless tobacco products.

DR. SAMET: Yes, Bob?

DR. BALSTER: I'm not trying to be rigid or anything, but I do think that statement is supported by the evidence but not specifically by the peer-reviewed literature, which is only really one paper on composition, that only looked at a few products; so is supported, yes, by the other information we got, say, for example, from the analyses that were commissioned.

So I support the conclusion. I'm just saying, if we're trying to categorize as where it is coming from, it's only limitedly coming from the peer review literature.

DR. SAMET: Okay. So good point, and we probably -- so as we go back through and talk, for example, about the analysis we heard yesterday, I think that's an important point, sort of the

corroboration between what's in the peer-reviewed literature and these additional analyses. So this will be just sort of an organizational issue. But just to keep our discussions a little bit organized, if we could stick with the peer-reviewed literature, that would be a very good reminder.

Let's see. And in fact -- let's see. Let's keep going down your list, Dorothy. Abuse liability?

DR. HATSUKAMI: You want me to give all the answers? Okay.

DR. SAMET: Well, certainly, you can offer, and then I think others will weigh in for sure.

DR. HATSUKAMI: So the abuse liability of these dissolvable products tend to be less than the abuse liability of cigarettes and conventional -- and the majority of conventional smokeless tobacco products sold in the U.S.

DR. SAMET: Tom?

DR. EISSENBERG: I don't disagree with that statement, but I wonder how abuse liability has been formally assessed in the peer-reviewed

literature.

Are you referring purely to subjective effect profile?

DR. HATSUKAMI: I think, in part, I'm referring to not only the studies that we've done in the laboratory, but some of the surveys as well. It appears that some of the surveys demonstrated that, for example, Ariva is not used. There isn't a high uptake of Ariva. The people that have used it have not continued to use it. So there is a lack of persistent use of these products.

In terms of the results in the laboratory, I don't know. What we find is that -- especially for the lower nicotine yield products such as Ariva, you do see less self-administration of those products as well as less positive subjective response or satisfaction of those products, less suppression of withdrawal symptoms.

That being said, I guess your point is, we haven't really tested all the products, so that it may be most relevant to the dissolvables that have been tested, which tend to be the Ariva and the

Stonewall products.

DR. EISSENBERG: We've conducted limited testing in terms of the products. We've also conducted limited testing in terms of the array of behavioral and other abuse liability testing methods that are available to us. And also, we've conducted limited testing in terms of the populations, which have been almost entirely limited, in fact, I think entirely limited to tobacco users. An abuse liability assessment would be extremely important in non-tobacco users, especially younger non-tobacco users.

DR. SAMET: So let me ask, in terms of the way Dorothy phrased the answer -- and, again, everything is based on what we have, of course, and not what we don't have. And so the question is, is what Dorothy said about abuse liability reasonably stated, with the caveat that exploration of this question is still ongoing and not all methods have been looked at, not all aspects of the question looked at. But what we've learned to date, is that a fair summary, Tom? And that's what I think is

the important point for our discussion.

DR. EISSENBERG: Well, what I heard Dorothy say sounded a little bit broader than I might want to put it.

DR. SAMET: Bob?

DR. BALSTER: I would just comment on that exact point, too. So I have a fair bit of experience on abuse liability assessment, and I have served on the CDER, Drug Abuse Advisory Committee on Abuse Liability Assessment and what it takes to make a judgment about abuse liability of a pharmaceutical product. I mean, the amount of information that's available at the present time about dissolvable products is far below what you would need to make any kind of a strong statement.

So I would certainly not disagree with what Dorothy is saying, but I would put a very strong reservation on -- that this is based on a relatively small set of data of abuse liabilities, not just laboratory studies. It involves a lot of things.

I also think we have to be really careful of

the fact that what we say may have to be referring to future products that may have different characteristics, that would be included in this branch. So I would want to see that conclusion of abuse liability be very, very soft.

DR. SAMET: Tim?

DR. MCAFEE: Yes. I would just echo that I think you need to be really careful about the wording about this and that, particularly, I think there are a number of characteristics of the dissolvables that, in fact, might make them more prone to abuse liability in terms of youth initiation as a product, the data that we saw in terms of the analogs to candy, et cetera

The lower nicotine levels, although they make them less prone to abuse liability in established smokers, may make them more prone to abuse liability in people who are virgin to nicotine and tobacco because it lowers the chances that they're going to have an extremely aversive, negative series of side effect experiences to nicotine. So they may be more prone to abuse

liability as a starter product for non-tobacco users than even cigarettes. It's speculative, but important.

DR. SAMET: Dorothy?

DR. HATSUKAMI: I'm sorry. I think you are really right, that we're talking here about pharmacological abuse liability, and there's more to the initiation of a tobacco product than the pharmacology. And so we're talking about the packaging, the appeal, the way it feels in the mouth, and so on, and so forth.

So I think you're right. We need to clarify that we're talking here about the pharmacological abuse liability and not necessarily some of the other factors that are going to be responsible for the uptake of a product.

DR. SAMET: Bob?

DR. BALSTER: Just to state quickly, the most compelling evidence -- and it's important evidence -- is essentially the relative apparent popularity of use of the existing long-term products, Ariva and Stonewall. That's been

mentioned before. They have been around a long time, and they haven't made much of a penetration into the youth consumption market. I think that's the most important evidence that we have. And to which that can apply to the other dissolvable products is unclear, but that's actually quite important evidence.

DR. SAMET: Mark and Arnold, should you want to weigh in at any point, just cough or something. Make some noise.

I think what I was going to do is move us along fairly quickly. I know there's a lot to discuss on each of these. But let's go -- the next category under our peer-reviewed literature, potential health effects. And here we have information on the presence of TSNAs and we have information on nicotine. We have oral tobacco experience generally, and we of course have no direct long-term effects of dissolvable tobacco -- I was about to say disposable tobacco products.

[Laughter.]

DR. SAMET: - but dissolvable products to date.

So again, we had some discussion about nicotine, per se. We've had some discussion about the cancer risk and the oral health risk, all of which say there should be some basis for concern, but with limited quantification of risk, I think would probably be fair to say. And in the long-term studies we represented with nicotine replacement therapy studies didn't provide any indication of risk, but a relatively small body of evidence there.

So thoughts here? Neal?

DR. BENOWITZ: Certainly, the profile looks like it should be less hazardous than smoking cigarettes, for sure. We know that.

DR. SAMET: Yes. And so that is the ceiling, if you will, of risk. And then going from there to a lack of risk, can we give an indication?

DR. BENOWITZ: I don't know if we can say that, but we can also say that it also looks less than commercial smokeless tobacco products that are

marketed in the U.S. in terms of likely risk. So we could probably say that as well.

DR. SAMET: Tim?

DR. MCAFEE: I'm looking at Dorothy's list in the peer-reviewed literature, and I think the topic that is missing here is potential population health effects. And if we don't directly address that, then I think, in this section, we have to be clear that you can't just say that the risk profile is low because if somebody only uses dissolvables, they will have less risk, because we have little or no evidence that that's the way they're being used.

Then the real health effect question is, what impact does it have as they are being used or could be used, which is that they're going to be used as a probably low grade substitute for a small number of cigarettes and all the other complex issues relating to it.

So that could be on a different topic, but we don't have to --

DR. SAMET: Right. So actually, I fully agree we need to come to what you discussed, and

that really goes back to the charge and how we'll put the charge -- how we'll put the evidence together that we glean from these separate pieces, presumably within the framework.

So what I was trying to do now is to just focus in a little bit in terms of our review, our findings from the evidence that's been put in front of us. I understand what you're saying, but that's a question of how we use all this to think about the impact.

Tom?

So it's an artificial distinction, but I'm doing it to make sure we get this review done.

DR. EISSENBERG: Okay. I don't want to belabor the point, but I guess it just seems that the language is pretty important. The profile looks like it should be less hazardous than cigarettes. What is it? I think the it, you mean is exclusive use of dissolvable tobacco products.

Is that correct?

DR. BENOWITZ: Yes. That's right.

DR. EISSENBERG: I think it's important that

we keep these qualifiers in mind.

DR. BENOWITZ: Yes. And I think we should also make it clear that our comments are made on the dissolvable products that are currently available that we looked at, because someone can make a dissolvable that looks much difference than this. And so if we're trying to generalize two dissolvable products, we can only say we looked at five products or whatever we looked at.

DR. SAMET: Bob?

DR. BALSTER: Could I ask a question? Do we think there's enough evidence to suggest that there could be variability among the existing dissolvable products in health effect risk? Is there enough evidence about that to say that there is or could be differences among them? I would say there could be differences among them.

DR. SAMET: I remember we saw differences in TSNA levels, but, again, that would relate back to actual topography of use, so we -- where that's limit.

Mirjana?

DR. DJORDJEVIC: I would just also include heavy metals, where TSNAs stand, because they're present in tobaccos, which are used in the products.

DR. SAMET: Let's see. So this potential health effects, any other comments here? And I'm still sticking, Dorothy, with your five points. So if we do, the next one is consumer perception.

Sorry to put you on the spot, but --

DR. HATSUKAMI: Then why did I deserve this?

So I think there aren't that many articles that have been published on consumer perception. The only one that I remember is the one that Mark Parascandola had published, and I may be wrong on that.

But I think that one of the findings was that the Ariva product in particular was not perceived as being a tobacco product or was perceived as being a non-tobacco product among a portion of smokers.

But I think that that's generally of concern, not just based upon the peer-reviewed

literature, but also based upon some of the presentations that we heard as well. But as I recall, that was that one piece of peer-reviewed literature that showed that there may be a misperception in terms of what these products might be.

DR. SAMET: Fred?

DR. PAMPEL: We did hear from the public comments that smokers misperceive dissolvable tobacco as dangerous. But I don't recall any surveys or any peer-reviewed literature to back up that fact.

Am I right? Do others remember any? Otherwise, we would want to add that in, but if this is peer-reviewed literature, there's nothing to back up that.

DR. SAMET: Yes. And I think we'll have to look across our different lines of evidence and come to some more synthetic findings as we go on. So hold your point. I think it's an important one.

Let's see. So consumer perception and last, your fifth -- yes, Bob?

DR. BALSTER: There is a study in the peer-reviewed literature on this issue of being used in combination with other tobacco products, and there is some evidence to support from the peer-reviewed literature that that could be the case; that there's a perception that they could be used that way. And I'm thinking of particularly the O'Hegarty article.

DR. HATSUKAMI: That's right, that there should be -- or there's co-use. The product is primarily for the purpose of using along with cigarette smoking. Yes.

DR. SAMET: Then the last consumer response -- one more to go, Dorothy.

DR. HATSUKAMI: I think that in terms of the peer-reviewed literature, my recollection is, both in the laboratory studies and in terms of surveys, that of the products that were tested, people did not respond positively to the dissolvable products.

There was not very much satisfaction from these products and, in fact, I think it was an O'Connor study that showed that they would prefer

using a medicinal product compared to a dissolvable product. So that's my recollection in the literature, that there wasn't a very overwhelmingly, positive response to the dissolvables.

DR. SAMET: Other comments? Let me check. Mark, Arnold?

[No response.]

DR. SAMET: I guess no comments.

So this was our look at the peer-reviewed literature. The next broad category that we looked at was the industry presentations. Is that number 2?

So here, I want you to be careful about what we heard on Wednesday morning in the commercial confidential material versus what we heard in July and outside of that; so findings in the industry presentations, again, relevant to our charge.

Ellen?

DR. PETERS: Actually, I had a point back on the last slide, if I could, just very quickly, on the health risks that are posed. I don't think

there was a comment made about the absolute risk of the product. Now, mind you, that's only important if there are people who otherwise wouldn't have used to tobacco, use dissolvables. But it's sort of -- there's something that's missing in there, if we think there are --

DR. SAMET: I think that comes in the impact. I think that's where we're going to get to that. That's really part of the likelihood of non-smokers; the availability of these products will influence use of tobacco products by persons who are otherwise non-smokers or not users of tobacco.

DR. PETERS: Right. I understand that, but right now, under potential health effects, you only have profiles in comparison to cigarettes, and profiles in comparison to other smokeless tobacco products, and nothing about the absolute risk.

DR. SAMET: No. I think that will be -- I think we did actually touch on that, and I think certainly that would be in the summary.

So next, onward to industry presentations.

And, again, what have we gleaned from those, remembering back to July, we actually had fairly substantial submissions from the industry.

[No response.]

DR. SAMET: Remembering back to July is a challenge, but -- and, again, I think here we have heard a little bit about what is in these, we understand. I mean, this is all overlapping around yield issues and so on. But is there something that we want to crystallize out of that set of presentations? And one possibility is that there is not.

Tim?

DR. MCAFEE: Jon, are you including with this the review that Dr. Southwell did of the industry-submitted documents, or are you only interested in the literal, oral presentations?

DR. SAMET: We can certainly lump -- I don't know how I did it on my slide, separate, but maybe that's an artificial distinction.

DR. ASHLEY: On your slide, they're separate.

DR. SAMET: Yes, they're separate. But why don't we just take -- I think maybe that would -- why don't we just take industry materials that we've heard? That would include the presentations by industry representatives and also the findings from the document reviews.

So for example, there, we heard about marketing, and I think there probably are some findings we should make, so let's just be a little more encompassing here.

Yes, Bob?

DR. BALSTER: I can offer one. It's certainly clear that the industry, in all the presentations that we saw, support restrictions on sales to children and support steps to prevent the access of these products to children.

DR. SAMET: Tim?

DR. MCAFEE: I would add that it seemed that, from Dr. Southwell's review in terms of the marketing, the emphasis was on dissolvable products as accessory items for current smokers, and as a mechanism to curb craving temporarily, and for

impression management.

DR. SAMET: I think that message came through quite clear, and I think it's an important finding.

Would everybody agree? Okay -- that dissolvables are accessory products for established smokers and used to deal with craving and for circumstances where social perceptions weigh against smoking.

Is that roughly it, Tim?

Yes, Bob?

DR. BALSTER: Again, it may be important to say what's not in there. It seems as if the industry is not positioning these products as smoking cessation products. I mean, they haven't done studies to suggest that. That doesn't seem part of their positioning. So they certainly are not being positioned that way.

DR. SAMET: We have been reminded by Dan several times that they couldn't be.

DR. BALSTER: Certainly not in terms of promotion and advertising, but one could imagine

they could do research on that.

DR. MCAFEE: But again, just to reiterate, they could be positioned as, for instance, Camel snus has sporadically positioned itself as a substituted product, not a cessation product, but you can do it. You can switch from cigarettes to dissolvable X. They could do that, and there's no evidence that they are trying -- any of the existing large commercial products are trying to position themselves that way.

DR. SAMET: Yes, Fred?

DR. PAMPEL: I don't think they presented any studies that showed that the products increased cessation, but they did present results. And there are some in the commercially private material -- I hope I can just talk about general findings rather than specifics -- that users of the products smoked fewer cigarettes. They didn't stop, but they cut down. At least, that's the evidence they presented.

DR. SAMET: Sandrine?

DR. PIRARD: Yes. When referring to

established smokers, it seems that some of the information we get was referencing to also snus user, MST user, so not just -- I would say not just established smoker, but also people using other forms of tobacco, as being potential target.

DR. MCAFEE: I had a question about those studies as well. The ones I recall -- but there may have been others -- were really not -- they're not looking at what was happening in real-world patterns of use. They were in situations where, basically, people were being instructed to use the dissolvables and even recruited with the idea that they might be wanting to cut down.

I think there was some variability in the studies, but I'm not sure the evidence is firm enough to say that, from those presentations, it's established that people who use dissolvables smoke less cigarettes.

DR. SAMET: Let me ask, do we want to comment on -- and I'm not sure I know where this goes, I'd say this under industry, but in fact there are different products. And they're quite

different, and they have different yields, different nicotine content. I mean, that seems to be noteworthy. And I'm not sure I have much more to say beyond that, but you have a stick, a strip, an orb, different amounts.

DR. BALSTER: Yes. I think, actually, this is a better place to put that than maybe where I suggested earlier, under health effects, where we don't really know whether the different constituents are completely associated with that, but we certainly know there are constituents with different products.

DR. SAMET: Okay. Anything else under this category? Dorothy?

DR. HATSUKAMI: I think it's also important to remember that we're not just talking about targeting cigarette smokers, but we're also talking about targeting smokeless tobacco users, too.

DR. SAMET: I think Sandrine made that point. Yes. So we've got that point.

So anything else on -- yes, Mirjana?

DR. DJORDJEVIC: I think it's important to

say that there are a variety of products with different nicotine and TSNA yields because we saw in the panel presentations, that Marlboro sticks and Skoal sticks have very remarkable amounts of TSNAs.

DR. SAMET: We captured that before, too, under the health risks.

John, are you poised?

DR. LAUTERBACH: I'm concerned about Mirjana's thing about remarkable amounts, when there are far less than typically found in most conventional smokeless tobacco products.

DR. SAMET: And we did make that comment.

Let me see. Mark, Arnold, any comments, if you're there?

DR. CLANTON: None from me.

MR. HAMM: Nothing useful.

DR. SAMET: Thank you. We even accept non-useful comments, as you know.

So why don't we go to our next big category? We've done industry. We've done peer review. So let's see. So we have the open public hearing and,

actually, there were a number of docket submissions, too, that we should probably include. So industry documents that we're going to consider, we've done that. So we just talked about industry.

So maybe make the next category open public hearing and, I guess, just docket submissions. Is that fair? Public submissions. And there were many, if you read through them.

So again, we heard a lot yesterday and, again, a sort of diverse expression of viewpoints in what we heard. So I'm not sure what do with N of 1 testimonials. For example, in relatively few of those, I think we already discussed, related to use of dissolvable products, per se.

So anything that we want to pull out of here specifically? I mean, I think we want to acknowledge the diversity of opinions we heard. I think that's important. Bob?

DR. BALSTER: I guess I was struck and not aware of the fact that there apparently is a concern by some percentage of the public that these products could be banned, or in some way removed

from the market. I thought that was -- I think that was a concern that I hadn't really been all that aware of. I don't know. It seems maybe to be more applicable to e-cigarettes than the dissolvables, but there was certainly something that we need to be mindful of, that there is a public concern about this.

DR. MCAFEE: I would add, the next layer down to that -- again, this is just attempting to catalog what we heard, but that there was essentially a sense the various governmental agencies at the state and federal level that have dealt with this should take a more proactive, positive approach towards providing information about individual risk to people; that is, not lumping all tobacco products together.

DR. SAMET: Ellen?

DR. PETERS: Just to make it explicit, and the reason they want that greater proactivity is because it is useful for -- their belief is that it's useful for smoking cessation. I'd also add that there's a belief that people may -- in their

health risk perceptions, that people may have exaggerated health risk perceptions of these products. That was the belief of the public speakers.

The other thing I'd add is that, in general, these products, including the dissolvables, aren't particularly liked in terms of the experience of using the products, with the exception, possibly, of e-cigarettes.

DR. SAMET: Tom?

DR. EISSENBERG: Yes. And I think, actually what you characterize as N=1 reports, they all kind of mash together for me. And the one message I got was that, to the extent that dissolvables were used to get people off of cigarettes, it was never dissolvables alone. And I think that matches exactly what we said from the peer-review literature, that these products, from what we heard from the public, from what data we see in the published literature, are not likely to wholly substitute for cigarette smoking.

DR. SAMET: So I think what we'll do is, in

our report, in our summary, reflect the diversity of opinions. And these, of course, are in the record along with all the submissions, so that documentation is there.

Let's go to our next big category, which was the -- okay. The Swedish experience, I think we had two main points, if I remember right, but that was Wednesday, which isn't as bad as July. So I think a major point was that context may generalize in the Swedish experience to dissolvable products difficult if not impossible. Is that a fair statement?

[No response.]

DR. SAMET: And part of that also was the distinction between the fact of the males and then the rising percentage of females who became exclusive snus users, which seemed to be an unlikely pattern, at least for the moment from what we know about dissolvables.

Yes, Neal?

DR. BENOWITZ: I think it depends on whether we're talking about the population impact or the

individual impact. I think we do have data from the Swedish experience on individual impact from exclusive snus users. So we do have those data. The context is more the population question.

DR. SAMET: Right. So when you talk about the individual data, the individual level, you're talking specifically about risks or beyond?

DR. BENOWITZ: Health risks.

DR. SAMET: Health risks. Yes.

Dan and then John?

DR. HECK: Mr. Chairman, I do think there is a lot of information on the populations, and behaviors, and dual use, and risk, embedded in that Swedish experience literature, which I know several of you served on one of I think about seven expert panels of various sorts that have considered this wealth of data in the past.

I think there's a lot of value there that we didn't hear necessarily in our very brief summary here, and there's been a lot of exchange in the literature on some of these topics.

So I think maybe, with reference to some of

these other expert panels that have very carefully and extensively looked at this database, we might draw additional value with all the caveats about the differences in population to the questions before us.

DR. SAMET: Well, I think the question -- I mean, I think again, we're not probably going to drill down real deeply into the Swedish data. I think Neal's comment about the lowered risk for individuals for tobacco-caused diseases I think is probably an important summary, isn't it?

DR. HECK: Yes, I would agree, but there are some additional questions that have come up, such as dual use. And the exploration of this Swedish dataset will reveal that dual use does not convey elevated risks relative to the single use of cigarettes in that population set.

So I think there's some additional information and insight that can be drawn from that dataset.

DR. SAMET: So from a procedural point of view, we really, in our discussions of the Swedish

data, did not go that deeply into the body of evidence related to dual use and risks to health. And I guess the question is whether we're going to find that relevant to our discussions here, since we're uncertain about future use patterns. So I guess what I would ask the committee is, do we need to go further on this particular point?

Let's see. Tom, did you have your hand up for that point?

DR. EISSENBERG: I'm not sure if I had it up for that point, but I think what I said before, I think, is critical, that what we heard was that for the Swedish experience, for the health benefit of Swedish snus to accrue, there is a requirement of complete substitution of cigarette smoking with Swedish snus use. And I think that's very important to keep in mind, that if there's any generalizability at all, it's going to require not partial substitution, not supplementation rather, but complete substitution. That's the message I heard, that, and that 50 percent of new users of snus in Sweden are naive to tobacco before they

pick up snus.

DR. SAMET: Dorothy?

DR. HATSUKAMI: I think the information on dual use is interesting, but it might not necessarily be generalizable to what you might see with dissolvables, just because of the characteristics of the products being so different. So I'm not sure whether the information from Sweden might be informative in terms of health risks associated with dual use.

DR. SAMET: John?

DR. LAUTERBACH: Two things, Dr. Samet. I want to take the latter one first about this dual use. Every time we have consumer tobacco products used, snus or dissolvable, instead of a cigarette, that reduces the concentration of secondhand and third hand smoke constituents in the environment, and therefore the benefit to public health.

Now, I want to go back to the other thing about the applicability of the Swedish experiment.

Remember the question I asked Dr. Rutqvist the other day about differences in warnings? Here,

we're considering products that essentially are meeting the GothiaTek standard. We're putting the same adverse health warnings on these things, not safer than cigarettes, when over in Sweden, the government is basically requiring health warnings that are much more reflective of the hazard of the product.

I mean, here, we're telling consumers that using smokeless tobacco, including dissolvables, including snus, that meets the GothiaTek standard, that that use of those products is just as hazardous as using cigarettes, and we all know that's not the case.

So if we're going to equate to the Swedish experience, we have to put something in there about the labeling and the fact that the current labeling is discouraging people to use a less hazardous product.

DR. SAMET: I think we might or might not come back to those issues when we begin to talk on the population-level issues. I actually think that what, in my mind, they've done is reaffirm the

importance of context, which is quite different in making the generalizations.

I think the qualitative conclusion about the difference in risk for snus users versus tobacco smokers is one we've heard quite firmly, and I think that we can make. I think, again, what we're trying to do is glean out of this what is relevant to our charge and not conduct an in-depth review of snus. I think I'm going leave it at that.

Bob?

DR. BALSTER: I just want to make clear that I think what we mean by context in that first bullet item there is that includes really the existence of a voluntary product standard in Sweden that yields a particular type of a smokeless product that is important to that context. So I think it's important that we acknowledge that context includes that standard.

DR. SAMET: I'm going to move us onto our last category, which was really the presentations about materials about youth, if I have this right. And that would include what we heard from our

colleague from Indiana and then the presentations this morning; and again recognizing the nature of where these products stand in their life cycle at this point, this is very early on.

So what are the key conclusions here? Bob, be brave.

DR. BALSTER: I'll take a stab at adding a bullet. As has been mentioned several times, Ariva and Stonewall have been around for a pretty long time. And in those data, there is a relatively low penetration of that in the youth market. I mean, it's supported by these data, that despite some of these products being available, specifically those two products being available, they haven't been taken up in an evident way.

DR. SAMET: From Indiana, we learned at least that the product availability led some youth to try that -- I guess, actually try it. It was what, 4 or 5 percent, 4 percent, 3 percent. I can't remember the exact numbers.

Other comments? Yes, Patricia?

DR. HENDERSON: I think packaging is very

important, as well, for this discussion, and how do we address that as we go forward.

DR. SAMET: So is that a general comment or the impact of packaging on youth is --

DR. HENDERSON: Among youth, absolutely.

DR. BENOWITZ: I think it's a theoretical concern. I don't think we've seen evidence yet that packaging does anything. It certainly could. But it's been hard to show anything about what packaging actually does in terms of consumption or uptake.

DR. SAMET: I think what we heard from the Virginia survey was the issue that the packaging comes with certain connotations, at least in the interpretation of those study participants. So I think it gives rise to your concern, at least.

Yes, Tom?

DR. EISSENBERG: Yes. I guess if I were to look at the decade-long experience with the Ariva and Stonewall product and the current packaging with a very jaundiced eye, then I could say that the current marketers of dissolvable tobacco

products have learned a very important lesson from the packaging of Ariva and Stonewall and are evolving their packaging to address the lessons that they've learned. And the Virginia data suggests that they're doing a very good job of making packaging that is, in fact, more appealing to youth than Stonewall and Ariva packaging has been.

DR. SAMET: So that's really an inference by assumption.

Other comments, John?

DR. LAUTERBACH: I'd like Dr. Eissenberg to clarify that statement. Are you saying the packaging of brands other than the Star Scientific ones are showing that lesson learned?

DR. EISSENBERG: Well, again, I was saying, if I looked at it with a jaundiced eye -- I guess what I'm saying is that Stonewall's packaging really hasn't changed that much, and Ariva's has changed a little since when it first came out.

If you look at the other products, especially the orbs and the strips, I'm seeing a

much more sophisticated, much more modern packaging. And it seems to have some appeal based on the limited data that we saw. And so that evolution of packaging is something that we need to be constantly vigilant of.

DR. SAMET: So if I pull the Indiana data, there was information there on use, so just as a reminder. And there was clearly some experimentation going on.

Dorothy?

DR. HATSUKAMI: I think also, it's suggestive that the way that these dissolvables are used is co-use among the younger population.

DR. SAMET: I think that's actually supported by the Indiana findings. Right.

Sandrine?

DR. PIRARD: Then with packaging, I think, one, being the fact that a lot of people seem confused, not only teens, but some parents also from the Indiana experience about what those products really are; are they tobacco or something else? And then other things we had heard from

Indiana's surveys leaves the impression that, well, it's great because even the cops won't know that I'm actually using tobacco, when they will see I'm using this little thing, those a little Altoid-like products.

DR. SAMET: Let's see. Mark and Arnold?

DR. CLANTON: Nothing here.

MR. HAMM: Nothing here, either.

DR. SAMET: Dan?

DR. HECK: Just a little comment on this packaging issue. Certainly, we've seen some sophisticated packaging in some of these products. And to the extent that they're somewhat fragile or hygroscopic, and may need some more protection than a more durable product, I can understand the packaging to be different.

But to be fair, I think, we've seen like with the mini-Nicorettes -- and we've seen pictures of those, too -- you're presented an image of a package of one product or another, whether that be a therapeutic over-the-counter drug, or a candy, or a tobacco product, an image of those different

packages, there may be confusion. But the context of the sale, behind-the-counter sales in the tobacco display, on the candy rack, or indeed in the drug store for the Nicorette product, I think real-life confusion at the point of purchase is I think pretty unlikely.

DR. BALSTER: I would add something that I think that we don't understand from this sort of work so far. And that is, I myself -- maybe others are not. But I'm confused as to what the public perception of individual risks is for these products. There's an assertion, for example, in the open hearing that people are overestimating the risk. But then we see data that people are actually identifying the risk as lower. I don't really think the data we have gives us a clear idea.

DR. SAMET: So actually, I would hold that because I think this fits under the recommendation category, because I think you categorize what we heard very well, very little evidence in sort of a mixed picture. So there are some very complicated

risk notions here, whether they are in the absolute risk framework or the risk comparison framework, that I think are very potentially challenging to anyone.

So actually think that we've been a pretty good committee to get this done.

DR. BENOWITZ: Jon, I'd just like to say, we missed one thing in the peer-review stuff, which is the childhood poisoning stuff.

DR. SAMET: Good point, good point.

So on the childhood poisoning, I think what we should say is that it has been tracked, that there have been some cases of ingestion apparently reported, very limited, and that there's not been an uptick, per se, in ingestion, but we have these very broad, non-specific categories, I think.

DR. BENOWITZ: Yes. And there have not been very many serious ingestions. Most of them have been quite minor.

DR. SAMET: Right.

Tom?

DR. EISSENBERG: Since we are not allowed to

talk about these things outside of the meeting, I have questions for Dr. Heck and Dr. Lauterbach that can help me understand.

Your point about packaging I think is well taken. It is behind the counter. Help me understand why it is that all the ads show the packaging. It seems that what the ads are trying to do is highlight the packaging to give people whatever impression the packaging carries before they get to the store.

DR. HECK: I think, not being a marketing expert, given that this is a relatively new product, or it is a new product, or a new product category for that matter, looking for impulse sales on the part of someone who goes into buy cigarettes, well, maybe they'll see this, and will recognize the product, and maybe try this alternate product. Your competitor is going in the store to buy a traditional smokeless product. Well, you want them to recognize your product as maybe something that they may enjoy as an alternative to traditional smokeless.

So presenting to the potential consumer the appearance of the product is, I think, part and parcel to introducing your product on the market.

DR. SAMET: Again, I think we've done a good job of pulling out the key findings from an awful lot of material we've been presented with. Our reward is lunch. However, lunch has been arbitrarily shortened to a half-hour at most because we have a lot of work to do. So dash over, and grab lunch, and let's come back and get to work.

(Whereupon, at 11:59 a.m., a luncheon recess was taken.)

A F T E R N O O N S E S S I O N

(12:34 p.m.)

DR. SAMET: I think we will go ahead get started, if everyone can take your seats. And I thank you all for eating quickly and getting back. And we're back to work.

So you've been handed the slides, and they include Caryn's notes on our conversations. I don't think we need to go back to that for now. I want us to push ahead. And don't worry about the wording or the wordsmithing at this point.

So I think the next thing we ought to do is probably take a brief look at the framework slide that was included with my note.

DR. DJORDJEVIC: Jon, may I just say something? Something fell through the crack here, because we started with the peer-reviewed literature and then we went into industry presentations. But we didn't really capture other presentations than industry, like what Irina Stepanov, for instance, was presenting, or Cliff Watson, which point out to the need for

standardization of reporting, so that we get consistent information on composition.

DR. SAMET: So that would fit under recommendations, I think.

DR. DJORDJEVIC: Oh, okay.

DR. SAMET: Yes, when we get there.

So this was something that was put together to help us think about our task related to impact. So this was sort of the population-level framework. And I think, by way of explanation, the intent here -- and we may want to change this. But the intent was to -- and somewhat similar to what we had with the menthol model was we have youth and adolescents over here, and the potential for tobacco-caused disease and premature mortality over here.

The idea was that the dissolvable products might be important around experimentation and initiation of tobacco products usage, that there are potentially two broad pathways, one to exclusive use of cigarettes and one to mixed use of tobacco products, that the dissolvable products

could figure in here. In terms of maintenance of addiction with a suite of nicotine products that allow access in circumstances where smoking is not allowed, these would be ways, as we've discussed, to deal with craving and so on. And then the question of what disease risk patterns are, depending on use pathway and how dissolvables would figure in. And by mixed use, that could include, I suppose, the pattern that we had not observed and we don't know whether will occur, which would be exclusive use of the dissolvable products.

So this is a very general framework and one where I thought, in terms of thinking about, again, impact, our population-level impact, we could use this to put together. So that's what this is, I think, and my note about this is some text description. And so I was proposing this or whatever modifications the group would like to make as a way to think about our impact charge.

Neal?

DR. BENOWITZ: I think this is a good start. And I don't know that dissolvables work in this

way, but for products like this in general, we should have something that also reflects the possibility for harm reduction, so that perhaps dissolvables might, although we don't see evidence, how people quit smoking or smoke fewer cigarettes per day. So there would be another harm reduction arm.

DR. SAMET: So the one possibility is, here, this number 3, referring to dissolvables, could go either way, I think, probably reflecting what you said. So the question is whether --

DR. BENOWITZ: It could increase harm by keeping people smoking longer or it could, in theory, reduce harm if it helped people quit.

DR. SAMET: Right. So I think probably in addressing this number three here on addiction, we should point out the two possibilities. I think that's important point.

Yes, Sandrine?

DR. PIRARD: Looking at this and the disease on this, we didn't -- I mean, we focused on physical disease. We didn't really focus on any

behavioral disease and, in particular, any kind of gateway effect. And I'm thinking, with those little pills, mints or whatever we called them, those dissolvable tobacco products, I know there's no data. But just to think in the context of the epidemic of prescription drug abuse, there might be a wonder if starting to use those oral products might kind of lead to an increased risk of using other -- like painkillers, and benzos, and all that. I mean, I'm just saying, within disease, we don't want to forget the behavioral health and other addiction.

DR. HATSUKAMI: Did you want to add smokeless tobacco to that particular figure as well?

DR. SAMET: I actually was trying to be inclusive here, but you would like a smokeless-only path?

DR. HATSUKAMI: Yes. I think so.

DR. SAMET: So we would have cigarette only, smokeless only, and mixed use.

Bob?

DR. BALSTER: I would also offer a friendly amendment. I mean, I think there are ways in which these products could alter continued use without directly altering the addiction process. So those boxes, it's already implied that addiction is the mediating factor for continued use. I could imagine these products altering sort of the broad risk perception, other things that wouldn't be so.

My amendment, to be specific, would be to change that box to say "addiction and regular use," because I don't know the addiction would be the mediating factor for every possible way in which these products could affect continuation.

DR. SAMET: So you would like to change the addiction boxes to label them addition and regular use.

DR. BALSTER: Yes.

DR. SAMET: Tom?

DR. EISSENBERG: I think the term "cessation" is complex now because maybe what you mean there is cigarette cessation. One function of these products is hypothesized to be continued

dissolvable tobacco use without cigarettes, and so that's continued tobacco use, but with cigarette cessation. So somehow, the box, cessation, needs to be labeled to make more clear what it is you mean.

Do you mean total tobacco cessation or cigarette cessation?

DR. SAMET: What would you like it to be?

DR. EISSENBERG: Personally, I think there needs to be more than one box.

DR. SAMET: So I think we want to flesh this out per your committee views. So we've heard so far addiction plus regular use. We've heard Dorothy suggesting to add a smokeless-only path to the diagram, which makes sense.

I guess the question, if we change addiction and regular use, what you would like to add, I think, Tom, is that coming out of this box that's labeled "addiction and regular use" now, there could be cessation of tobacco products or there could be a box which was labeled I guess "continuation of dissolvables." I'm not sure where

you think that's going to happen.

DR. EISSENBERG: Maybe "non-combustible tobacco use."

DR. SAMET: Right.

DR. EISSENBERG: "Exclusive, non-combustible tobacco use."

DR. SAMET: Under the mixed-product path. Okay.

John?

DR. LAUTERBACH: I was going to say actually something similar, where we come out of the addiction box number 3, for smokeless only, and go to a continue with essentially not the disease and death.

DR. SAMET: Yes. Actually, I think the disease and death is actually referred. We're all going to die.

[Laughter.]

DR. SAMET: But this actually was referring to risk of --

DR. LAUTERBACH: Tobacco related.

DR. SAMET: -- tobacco related. And I think

that's what the 4 is about, that there could be a modification of that risk. I think that's consistent with what you want.

DR. LAUTERBACH: Based on the number 4, based on the Swedish experience of snus, it would be basically continued use, and we basically have no evidence that for products meeting the GothiaTek standard, that they lead to chronic disease, so then would cause death from that particular use.

DR. SAMET: Actually, I think the point would be that we would indicate that that risk is substantially altered, and that's where the box is.

Mark?

DR. CLANTON: Yes. This is probably going to make this more complex, but if you look just at nicotine and nicotine alone, you don't have to alter the addiction box or the cessation box if you're just focusing on nicotine. If we need to mix nicotine and tobacco together to get to number 4, we may even have to have two conceptual frameworks, one looking just at nicotine and the other looking at both.

So we're running into the complexity issue again here.

DR. SAMET: So let me ask Bob's proposal for addiction and regular use.

Do you think that's too non-specific or oversimplified?

Mark, I just was trying to follow up with you.

DR. CLANTON: Well, I'm not sure I could answer that question. I'm just simply trying to get at, in this conceptual framework, what are we looking at? Are we looking at nicotine as it relates to its use, addictive potential, and need to stop nicotine use?

As we drift away from combustible tobacco products and get closer to this issue of more nicotine and less of the other byproducts of combustible tobacco, are we going to have a mixed model where we get in and alter all of these boxes at arms, or is it your preference that we look specifically at nicotine, which is what these products seem to offer in abundance and certainly

produce less nitrates and tobacco-specific nitrates.

So I'm trying to figure out, are we using the right model, or does it need to be modified?

DR. SAMET: Just a comment in thinking about the charge, the charge actually does not mention nicotine. Correct? Correct. So the charge does not mention nicotine. It mentions use, actually.

So in terms of a framework for dealing with that charge, I understand the complexity because addiction is embedded in it, but it's not the whole story I guess. I think that's your point.

Bob?

DR. BALSTER: I guess I would have concluded that since we are asked to be expansive in our consideration of the category, in my own mind, that does include products with nicotine only, even though that may or may not meet the definition of a tobacco product. I mean, we have an example of a product there that is not a nicotine replacement therapy.

So I think of this -- and can deal with

Mark's concerns, I agree with it. There is a path from nicotine alone through all of this stuff, including disease and death. I would disagree with Dr. Lauterbach. I mean, nicotine is not a harmless chemical.

So I just think we can just deal with this by essentially saying in our conceptual framework that what we're considering here is that whole table full of products over there, one of which is a nicotine-only product.

DR. SAMET: I understand the problem. Every time you simplify the world down, there are fewer arrows and boxes. It can't be exactly right. I think the question is whether we have things captured in a way that will prove useful for addressing our charge.

DR. BALSTER: I'm just saying, Dr. Samet, that if we explicitly state that the conceptual framework includes tobacco products -- or products that are containing nicotine -- for example, the product NicoSpan, that's a nicotine-only product. It's ambiguous with respect to its understanding,

with respect to -- but I think we were asked to be expansive and inclusive.

So I would think that we'd want to be able to say something about products that might end up with nicotine only. So if we explicitly state that that box, mixed use of tobacco products, includes nicotine-only products, then that carries -- I think that addresses the issue of nicotine's role.

DR. SAMET: Anyone else?

Tim, are you poised to say something? No. Okay.

Dan?

DR. HECK: I guess I'm kind of thinking maybe simpler is better here, but certainly if nicotine is worked into this in a graphic way, we ought to go ahead and satisfy the therapeutic nicotine medications because there's another world of complexity that's maybe not necessarily here.

DR. SAMET: I think I have heard three changes that need to be made, and let me list them: this addition of the smokeless only per Dorothy;, Bob's modification to addiction plus regular use;

the addition, I think per John, of something that allows for the possibility of going from mixed use to smokeless-only use; and then I think, as the fourth topic, that in text, describing this, we alluded to the fact that we think this is useful for dissolvable tobacco products and other products that might contain nicotine only.

I think those are the four points I've heard. So there will be a modification to the framework done by somebody more expert than me in PowerPoint.

Just give me one moment to write.

DR. BALSTER: While you are writing, I just would make a comment. I was not participatory to the menthol discussion. And I don't think we said it, but I find this framework very, very useful, and it does define, in my mind, the broader arena in which decision making about these products ought to be done. So I would commend the committee or those members of it who participated in the development of this framework for the menthol report, that this was a very useful thing to have

done, and I think it's helpful here as well.

DR. SAMET: Good. Thank you.

DR. MCAFEE: Jon, just one other quick point. One is, you're going to want to have a lot of arrows going back and forth between these boxes because some of these shifts from the different cigarette smoking, smokeless, and mixed use, where that goes, will be important.

But the other one, I've just been staring at the experiment and initiate. I'm not quite sure what we mean -- what our definition of initiate is versus experiment. This tends to be quite loose and varied from individual to individual.

But I would actually anticipate that, again, specifically thinking about the role of dissolvables, that they may actually play a role around if you increase the probability of experimentation, because we know that experimentation is an enormous risk factor for continuing on, so if they did nothing more than increase the probability that somebody would enter into the experimentation pipeline, that might be

very important.

DR. SAMET: I think that's meant to convey that, but what do you want different?

DR. MCAFEE: Maybe just you could -- I mean, unless there's a dramatically different difference, it could be that experiment and initiation are one box.

DR. SAMET: That's fine, too.

Does anybody have strong feelings one way or the other? We're not going to go into sort of offering a definition. This is more in the demand of others than mine.

Bruce?

DR. SIMONS-MORTON: Some distinction needs to be made. Experimentation is usually, did you ever try, whereas either initiation or routine use is measured by 30-day use, or even one-year use, or daily use, or number of cigarettes. So I think there's a need for some distinction.

DR. BENOWITZ: I know we are not going to be doing mathematical modeling of this, but the way it set up before, the continuing, and disease, and

death, it looks like that's related to smoking. And we talked about smokeless tobacco as a separate track. So I think it should be clearer that smokeless tobacco only has got a different disease.

DR. SAMET: Maybe that would be useful. So instead of having -- sort of brought things together with a box that says continue; instead have a separate health outcome --

DR. BENOWITZ: For each line. Right.

DR. SAMET: -- box for each one. I think that would work. And actually, it sounds like Swedish snus users are immortal? No.

[Laughter.]

DR. SAMET: Sandrine?

DR. PIRARD: So I think I will start to use those.

Just a comment on cessation. I think we all know that cessation is not just one outcome; usually, people tend to quit and then they relapse. So maybe you just want -- instead of having a straight arrow from addiction to cessation, which is to be like as it is; like when you quit, you're

just done. You won't have any tobacco-related diseases.

DR. SAMET: Tim made that -- yes. That was Tim's point I think in fact, that we should make these bidirectional. Yes.

So I think we could leave framework. Is that all right? Acknowledging no framework is ever perfect, but some are useful. So that brings us back then to other things that we need to do and discuss.

So it might be useful at this point, around sort of the flip side of what we did on the evidence, to list what are the key points of uncertainty. And that would really flow into offering a platform for mentioning what further information should be gathered, what surveillance might be done, what research might be done.

So let me suggest that we go now to address key uncertainties. We could do that around the framework. That might be a way to do it. And I think these would be -- I know we've identified an awful lot of gaps already, but I think what would

be useful is if we could list those that we see as most critical so that in the future, everyone will be better informed.

Maybe it'll be useful, maybe it won't. But why don't we start on the youth end and talk there about what we -- no. Let me amend that. Maybe we should start with the product first and see if there's anything else that should be listed as a major area of uncertainty around the products. We've been presented with a lot of information. And I guess this could also be thought of as, for future products, what information might be immediately useful.

So let's start there, with uncertainties around the product.

Yes, David.

DR. ASHLEY: I'm just going to remind the committee that when Irina Stepanov gave her presentation, there were a lot of questions that were asked that she did not have the answers to, if you all remember what those questions were.

DR. SAMET: Is that a question to us? Do

you remember what the questions were? I think we probably do.

Bob?

DR. BALSTER: I remember some of them. I remember very well that the information on youth would be very much on the -- poison control data, other data of that type, would be greatly assisted by having denominators in addition to the way it's presented.

So I don't know if it would raise the level of recommendation, but I could see asking the FDA to explore the opportunity to obtain denominators for various indices of toxicity that would be gathered from various measures like poison control and other places.

DR. SAMET: So this actually would be a surveillance need, I think. But I think we might as well get a list down. I think we can put it in the right spot. But I think it's beyond -- but what I heard goes beyond denominators. It's actually having some specificity in how the products that are ingested are captured. And

certainly those broad categories aren't useful; so denominators and specificity.

Neal?

DR. BENOWITZ: I think in characterization of human exposure, we have pretty good data on Ariva in terms of nicotine levels after single use, in terms of chronic nicotine levels, in terms of chronic biomarkers, but we really should have that for every one of the different products because they vary in terms of their nicotine content, their nitrosamine content, their pH. So every product should really have this fixed battery that's been done for Ariva.

DR. SAMET: Is it the Ariva battery that you feel is satisfactory?

DR. BENOWITZ: Yes. I think so.

DR. HATSUKAMI: I have a question. The level of exposure could be dependent upon what the instructions are to the individual. So do you think that it should be one in terms of using ad libitum or do you feel that it should be a specific number of doses that people should use?

DR. BENOWITZ: I think it's a good question because it brings up the fact that we don't know what the usual behavior is. So it would be nice to get data on the usual self-dosing patterns and be able to replicate those.

DR. SAMET: So is it a different recommendation, that there should be a better characterization of topography in actual use?

DR. BENOWITZ: I think so.

DR. HATSUKAMI: Yes.

DR. BALSTER: If I could amend that, I think we don't only want to know about the exposures, the usual use, or recommended use. There is the issue of swallowing, for example, prior to leaving the -- I mean, I don't know what the consequences of swallowing it are, but I would want to know that. So that may not be the usual or recommended pattern.

So I'm just saying, I would extend that to wanting to know about exposure with different topographies of actual mouth placement, or swallowing, or things of that type.

DR. SAMET: Yes, Sandrine?

DR. PIRARD: One thing that we have discussed also is the lack of understanding about product variability and content. It seems that -- I mean, most analyses were done on a few batches maybe from the same state.

DR. SAMET: Tim?

DR. MCAFEE: One other point that was raised yesterday, which was partially answered, and I think might vary from product to product, but it was the question of just to give one example of whether in vivo would make a difference is around pH and whether -- for instance, although we may know that for chew, the characteristics of the product overwhelm the oral cavity characteristics, I would wonder about something like a little, tiny, dissolvable strip, if the pH of the ingredients in the strip may not matter as much as the saliva. I don't know if that's known.

DR. SAMET: Let me ask this. If I understand the issue -- and I think we had a little bit of discussion about this yesterday. But would

this sort of fit into major uncertainties? It seems to me, in part, the answer comes from measuring the biomarkers as to what's getting in the people.

DR. MCAFEE: Yes, that would work.

DR. BENOWITZ: To me, I think we ought to step back to the question of engineering of dissolvable products because we've seen different types of products. We've seen compressed tobacco. We've seen the sticks. We've seen the strips and stuff.

The different engineering characteristics of the products may be related to different delivery characteristics, different pH. So it would be nice, ultimately, to have a classification of dissolvable products by type, and then engineering characteristics, including pH, and how that relates to human exposure because I don't think we have that kind of classification. We should. I suspect that the sticks result in a different absorption rate than a tablet and observed from profile, for example.

DR. SAMET: So let me ask -- I think I understand what you're proposing, but if each new product had a standard biomarker characterization and then topography was characterized in use, perhaps with some biomarkers under those circumstances, would you have what is needed from the public health point of view, regardless of whether you could relate that back to design?

I guess going with that would be the question of whether you felt that if you understood design characteristics, then you could begin to build a predictive model.

DR. BENOWITZ: But I think to follow up on Tim's point of view, the effect of pH may vary very much according to how the product is designed, whether it's a tablet, or a strip, or a stick, or whatever. So if we're going to go there to try to extrapolate from characteristics to delivery, then I think we should begin to develop a classification of types. That's all.

DR. SAMET: Any other comments on this point? Bob?

DR. BALSTER: I'm not quite sure how to word this, but in the course of the discussions, I've been relatively struck by the potential importance of product standards; now, what to say about that, I'm not quite so sure. I don't know that I would go so far as to say that we'd recommend product standards, but I think we should know more about how a product standard could be important here in terms of the long-term public health consequences of this product class.

So if you could help me, maybe, with wording, what'd we want to say about it, I think there's something to be said about trying to understand the potential value of a voluntary or some other type, or some type of a product standard.

DR. SAMET: I wonder if, David, you could comment on this point.

DR. ASHLEY: Yes. I'm not quite sure how that fits in with the discussion here. I mean, clearly, we could have an educational time talking about product standards and what that fits. But I

think what we're trying to get to here is, what are the questions that might be asked?

We will take the information that's gathered along with other information and determine what actions FDA might take. Product standards could conceivably one of those actions. And so I think the committee ought to be thinking very broadly and not worrying about recommending that FDA take specific actions. Well, you can do that. You can make that recommendation also, but don't limit yourself now.

DR. SAMET: Tim and then John?

DR. MCAFEE: Just to follow up on that a little bit, there are a couple of things -- and again, if we're leaning more towards questions related to the left side of this diagram, it may be that there are certain constituents that are currently not allowed, in cigarettes for instance, that one might want to consider, whether they would play a role around increasing or decreasing initiation. And one of the most obvious would be characterizing flavors. And then the most obvious,

of course, would be nicotine.

I assume at some point, we're going to have an interesting discussion about this complicated issue of the pros and cons of lower versus higher nicotine.

DR. SAMET: John?

DR. LAUTERBACH: I tend to agree with Dr. Ashley in one respect, other than that we have at least one government in Europe with standards for smokeless tobacco products. And maybe Dr. Proctor [sic] could enlighten us as to he thinks is going to happen in Europe if this goes on. Will there be a GothiaTek standard?

DR. SAMET: Yes. Interesting question, but I'm not sure we have the time to go there right now. I just want to refocus this because we were talking about key uncertainties, and key uncertainties that might be addressed through, as we said, further data gathering, research, and so on. And I had started this with discussion of the product. And so far, I have I think from Neal -- we had Bob's recommendation, which we'll

put under surveillance, about the poisoning, where we need better, more refined data; Neal's comment that in experimental settings, there should be a standard set of biomarker data on all products. I think we said there should be better characterization of topography in circumstances of actual use, within product variability needs better description. Again, these are all uncertainties.

The comment about some classification of dissolvable products as to type, that's sort of a -- not an uncertainty. That's a potential recommendation, and I think we should hold on that discussion. And the question of product standards, again, sits under the sort of recommendations as opposed to uncertainties.

So, again, let me just make sure we stick with the uncertainties. David?

DR. ASHLEY: There is one other that I thought you guys would remember, you didn't remember, from the discussion with Dr. Stepanov. And that was the stability, the stability of the products, whether they're changing over time.

DR. SAMET: We flunked our yesterday test.

[Laughter.]

DR. SAMET: Ellen?

DR. BENOWITZ: And environmental, I was going to say, like heat and moisture.

DR. SAMET: Stability and its determinants. Okay. Yes.

Ellen?

DR. PETERS: Just as there are an array of things to know about the product itself, there are an array of things to know about the consumers who ultimately use or don't use the product.

DR. SAMET: So, actually, hang on and we'll go there, but let me just make sure -- I want to close out the product issue first.

Going, going, it's gone. Okay.

So should we start with the youth side and talk there about key uncertainties? And I think part of what you were about to say fits in there; so maybe starting with youth and key things that we need to know at this point.

Ellen?

DR. PETERS: So this characterization of youth perceptions, I think we need to know more prior to actual use, when it's just simple exposure to the product through seeing the product in the advertisements, or seeing the package in a store, or seeing the package in their friend's hand, that kind of perceptions of the product prior to actual use.

But also, I think we need to understand more broadly what the categories of products are as consumers perceive them. It may be very different from how we lump everything together as smokeless, for example. And also, what are the perceptions of the attributes of the product that are important? That would include, potentially, risk perceptions and benefit perceptions, but also, how do they use those perceptions of attributes in deciding whether they may actually try to experiment or continue use of a product?

Then also, how are these various perceptions modified by the context, whether the package is there or not, whether there's a warning there or

not, whether it is at the point of purchase, or whether it's because a friend has something in their pocket that they're showing you? The perceptions may actually differ quite a bit. And those perceptions then can also influence the experience of the product once you actually try the product, and so an understanding of that as well.

DR. SAMET: So maybe to summarize, I think actually what you said applies probably to both youth and adults. And I think the uncertainty is that we have inadequate knowledge of perceptions of these products with regard to attributes, the risks; and risks could be construed broadly here, risk for addiction, risk for disease. I wrote down comparative risks, which I think is probably important. And then you wrote the importance of context and how that influences these perceptions.

So I think we can probably fairly say that those uncertainties are there for both youths and adults.

DR. PETERS: Yes. It might be different between those two groups, but also within the

group, there may be differences.

DR. SAMET: Right. But it would loom as a key uncertainty for both groups, I think.

Patricia?

DR. HENDERSON: Yes. Even before that is the exposure to fetals (ph), so pregnancy. We know very little about that.

DR. SAMET: So that would sit on the health risks side.

Yes, Bob?

DR. BALSTER: I would just add that in addition to knowing those things about the youth and adult, I think we need to know a bit more about how subcultural variation would be important in those perceptions.

DR. SAMET: Dorothy?

DR. HATSUKAMI: I think it would also be interesting to see how the consumer perception of the dissolvable products might affect perception of other products, such as cigarettes or even smokeless tobacco products.

DR. SAMET: In a way, that's something that

would have to be -- that's almost a surveillance issue as these products are rolled out.

Fred?

DR. PAMPEL: This is a very tough question to answer methodologically. But if there are kids adopting dissolvable tobacco without having smoked before, we can't necessarily assume that these kids would never have smoked. So are the adopters actually prone to adopt cigarette smoking anyway, in which case, it's a benefit? Or are they not likely to adopt cigarettes, in which case, it's a loss?

DR. SAMET: Actually, it's a great point that probably needs to be reflected in our discussion of impact. It's, I think, ultimately, unknowable, but I think it should figure into our discussion of population-level impacts.

So your question is, are there people who, but for the availability of dissolvables, would have been cigarette smokers? And I think that goes a little bit back to trying to get some understanding of who is adopting and using these

products.

Sandrine?

DR. PIRARD: Just to go back to the whole prescription abuse things, I think what youth tends to do nowadays is this farming thing with pH, where basically everyone kind of brings a bunch of pills, put it in a bowl, and everyone just grabs whatever is there.

So I think that there's this kind of attraction to any kind of oral product, and some of those kids might never touch cigarettes, but we can see that those little things, whatever you call them, could be kind of put with other things and kind of mixed in those farming parties. So I think there's this whole generation of using kind of oral tablets of pretty much everything they can find.

DR. MCAFEE: This probably goes without saying, but in addition to perceptions and some of these specific drilldowns, the bottom line is, we're very uncertain about how these products are -- who's using them, how they're being used, how they're being used relative to other tobacco

products. And this is just sort of -- we don't even really know the basics, and part of this is because they're so new and novel. But again, having reviewed, for instance, what's being asked in the surveillance questions -- which are literally just being started this year in our national surveys, and in some of our surveys, we have no questions -- the questions are quite high level; like, did you use? Did you use it once?

But all these kind of issues that we struggle with around the topography of use, how frequently people are using, I think it would be helpful if there were a little bit of guidance, and it was included in this; that we want to make sure we are actually collected data over the next year or two to carefully understand how and then, prospectively, what's happening with uptake.

DR. SAMET: So we certainly -- I mean, what you said is a major uncertainty now, but will become even more important for the future, on the assumption that the products we've seen are rolled out nationally. And then what you're saying is we

really need good surveillance to track, to use your words, "who is using the products and how they are being used?"

So I think that it's an uncertainty now. It's one that has to be addressed through ongoing data collection. It's a surveillance need.

DR. MCAFEE: Yes. But it's not going to automatically correct itself just because the products are used more. It's going to require a lot of proactive work on the various surveillance -- existing surveillance instruments to do this.

DR. SAMET: I think tucked away in our recommendations should be the relatively obvious one, that this will need to be done in a way that's sufficiently sensitive to track what could be fairly complicated use patterns, as we've learned.

Ellen?

DR. PETERS: I want to follow up on something that Dorothy brought up. I think Dorothy's point is actually a very important one; does the impression of one product change the

impression of the other product? And it's particularly important here I think because if, for example, FDA decided to change regulations such that dissolvables, let's say, can be advertised as smoking cessation, they're still a tobacco product. Tobacco's probably still going to show up on the package. If you can advertise them as a low-risk product, it's actually going to change perceptions of tobacco as lower risk. Oh, this tobacco product is okay. Maybe if I do just a little of that one, it'll also be okay.

So I just think that how these perceptions of one product influence perceptions of the other is actually really quite an important point.

DR. HENDERSON: Can I just follow up on that as how this also plays on policy-making? A lot of organizations -- for example this building is tobacco free. It includes all tobacco products; and what's going to happen to these communities that are moving that direction?

DR. SAMET: So let me take us back to uncertainties. You're a wandering group. In terms

of things, the gaps that need to be filled, we've talked about the need for this perception information. We've heard from Sandrine, from Dorothy, about additional aspects of perception that we might want to track or implications for use of either other tobacco products or other drugs, but we're just trying to highlight critical gaps now.

So we've talked about products, to an extent. We've talked about this understanding. There are other areas. I think Patricia highlighted a little bit the need for information around pregnancy, potentially, reproductive outcomes.

Other things, Bob?

DR. BALSTER: So I think another important area to try and obtain information about is how youths are obtaining the product; I mean, those that are using them, how they obtain them. Are they obtaining them through some type of accessing retail sales? Are they obtaining them -- through what means are they obtaining them? They're not

legally available to them, so I think we need to know more about how they get them.

DR. SAMET: Neal?

DR. BENOWITZ: I'm not sure this has been done, but again, following up on the Ariva story, why aren't youth trying them? Why are they not interested in them? There may need to be some focus groups to find out why these things have been marketed for 10 years; how come you're not trying them? I'd like to know why the penetrance is so low.

DR. SAMET: I actually think we probably have captured that on the perception issue, generally, because that would fit with the attributes of the product and why this particular group of products is not being used. I think we've got that covered generically.

Other things, Mirjana?

DR. DJORDJEVIC: Comprehensive chemical composition, like not only harmful and potential harmful constituents, but also those with constituent flavors, because we heard this morning

about some products being delicious, some products not. All that is important for attractiveness and acceptance.

DR. SAMET: Okay. And I guess that would, in turn, become a recommendation, that some standard set of assays would be needed. And we talked about the bioassays, but we did not talk about chemical composition assays.

DR. BALSTER: I think things like taste would not probably best be necessarily measured by measuring the product constituents, but might best be measured in some sort of perception test or things of that type. I'm not sure exactly how that's done, but folks in the food industry know a lot about how to do that.

DR. SAMET: Other uncertainties? So do we know enough -- again, I think we know very little about mixed-use patterns, implications for changing use, cessation, and so on. And I think we could certainly highlight that as an area of uncertainty, one where, at the least, observational data would be needed. Fair?

Let's see. Neal?

DR. BENOWITZ: This is not epidemiology, but I know we know some about abuse liability. Is that also a gap that we need more information about, abuse liability, especially in youth?

DR. SAMET: Dorothy?

DR. HATSUKAMI: I'm not really sure. In some ways, trying to get a handle in terms of how these products are being used might be really, in the long run, more informative than doing some abuse liability studies, but I'll defer to Tom.

DR. BENOWITZ: The reason I thought about this had to do with the flavor question, about whether flavoring in combination with nicotine changes the abuse liability of these products.

DR. HATSUKAMI: That might be important, to see whether some characteristics of the products might change its abuse liability. Maybe some of the strips have a more rapid rate of absorption. That might be more highly abused.

DR. SAMET: Bob?

DR. BALSTER: I think we clearly lack

sufficient information to make a firm statement about abuse liability. So if, in fact, such a statement was to be valuable, then we would need a lot more information to be able to make an evidence-supported statement about abuse liability.

DR. SAMET: Can I go back? I had made this comment before about needing to better understand heading out to the right of the diagram, for those who are using these products, what their impact is on use of tobacco products generally and on likelihood of quitting. So that's something where we need -- everybody's agreed. Okay.

Yes, Tim?

DR. MCAFEE: I think another area of uncertainty is we've heard two very strongly stated concerns about, number one, we can't really know what would happen because the tobacco companies have been precluded from essentially making any types of claims or that the current warning labels don't accurately describe the actual, individual risks associated with the products.

So as has been noted, I think this is a very

tricky area and one where we don't really know how youth would respond or users would respond. Could we create, could we craft messages that would change the product perception in a way that we felt was better for individual decision making or population benefit? That's something that I think is very important and we don't know whether we can do it or no or what the effects would be.

DR. SAMET: Let me ask, are you proposing a research topic, a policy-related need for research? I'm just trying to sort out, Tim, what you're saying.

DR. MCAFEE: Yes. I think it is something where I don't -- I'm not talking five years. I think there's stuff that could be done in the marketing-product evaluation research arena. That could be done; again, part of it looking at perceptions, testing of messages to see how people actually process the messages, if we were to say that these products have lower risk rather than the current one, it is not safe or something. If we tried to nuance that message, if we tried to nuance

a message about increased -- however, it increases your risk of becoming a smoker, all this. I think this is -- again, obviously, we're not going to do it, but I think it might be an important message to FDA.

DR. SAMET: So this is a research area. We had the corresponding I think discussed earlier when we talked about perceptions, and we talked about children and adults, following Ellen's comments. So I think this is an elaboration of a need.

Let me ask, around the risks to health, dissolvable products. So there in our diagram we have any number of possible use patterns, dissolvables alone; dissolvables as part of a smokeless mix that someone might be using, or dissolvables, plus smoke, plus whatever.

In terms of further studies that might provide an understanding of risk or comparative risk to health, there are certainly uncertainties. We can make some qualitative judgments on risk of dissolvables versus other products. But how

importantly do we view this area of uncertainty? And it seems to me, for one, it's something that needs to be tracked. And it's quite a difficult, challenging problem to sort out the consequences of changing use patterns for health in any real-time way. You have to resort to biomarkers and other intermediate outcomes.

But where do we highlight this? It's an uncertainty, and I think we acknowledge it and relay the recommendations.

Neal?

DR. BENOWITZ: I don't know of any short-term way that one could do this, without people using these products for 20 or 30 years. So I think we're just sort of left with extrapolating from low toxicity smokeless tobacco products. So I think there are gaps, but not ones that we can fill for quite a long time.

DR. SAMET: And comes with that, then, some thinking about how actually one would try and have information about long-term use and the future long after you and I are off TPSAC.

DR. BENOWITZ: I think some of the surveillance data would be useful for the mixed use in terms of, in people who are mixed users, what happens to their cigarette consumption? So if people cut their consumption down from 15 cigarettes a day to 3 a day, then it might make a difference. If they cut it down from 15 a day to 10 a day, it might not make a difference. So I think information about that would also be relevant to disease risk.

DR. MCAFEE: We had one study, the rat lip study. Are there any of these questions that you think we might actually be able to shed more light on with rapid cycle animal lab studies?

DR. BENOWITZ: The problem I see with those is it's very difficult to extrapolate those to humans. It certainly raises the potential, but there have been studies that showed pure nicotine as toxic in the oral cavity of rodents, yet the snus study, the snus experience in Sweden, suggests that it's not a major problem. So it's hard to know where to go with those. I mean, I think they

should be done, but I'm not sure how to use them.

DR. SAMET: Dorothy?

DR. HATSUKAMI: Jon, I just want to comment that there are some major challenges in the kinds of research that we're proposing because the packaging evolves. It's not as though we're going to be testing one package and that's going to be the process for the rest of the duration of the product. And so my concern is how do we get control of that, changing the package, even the changing in the product, in maybe slight ways?

DR. SAMET: I think we've seen the difficulty of the challenge before, if you look at the changing cigarettes over time, where I think the same issues come up. I think there's the change in context, which you allude to. There's a potential for changes in the product. There's a potential for changes in the way they are used; let's say a hypothetical scenario in the future, in which cigarette use goes down, but perhaps it's replaced by other types of products, how would one track the use of it?

I think that those challenges are definitely there, and they're certainly very difficult to study in population cohorts, and I think we know that. But I think we should acknowledge those challenges and wish FDA good luck.

DR. HECK: I think Dorothy and Dave can add to this as they feel necessary. Historically, we've seen some rapid product introductions in evolution, but now under the regulated environment, I think we'll probably see more stable product design and composition moving forward, and FDA will be well informed of those proposed changes.

DR. SAMET: Bob?

DR. BALSTER: Again, this is not the place to really go into this in any kind of depth, but it's really important to understand that there is an extensive literature on nicotine and its effects on health. I mean, there are a plethora of animal studies, some of which we saw here, in which there are known adverse effects of nicotine exposure. And I would like to highlight particularly those studies in which the developing brain has shown to

be particularly sensitive to effects of nicotine, which can have pretty long-lasting changes in brain and behavior, the significance for which public health are somewhat uncertain, but they're clearly there.

So there is a large literature on this. And I think that the relevance of that could be, of course, that these products could conceivably result in overall lower nicotine exposure, but that is really uncertain. And of course, that may not be true of future products of this type.

DR. SAMET: So what I'm going to do is, we have about an hour. I'm sensing a little bit of an energy lull here.

Yes. You're lulled?

I think what we need to do is take a look at the charge to us and just talk a little bit about what we might say about the key points in the charge.

So Caryn, if we could go back to the charge; so the nature and the impact of the use of dissolvable tobacco products on the public health.

And I think, in terms of thinking about public health, we have several indicators, the number of people using these products, the number of people using other products, including cigarettes and other smokeless products. We have -- I think Fred's very complicated, but important counterfactual, which is, are some people using dissolvable products who otherwise would be smoking?

So there are a variety of impacts, and then ultimately, the question of whether patterns of morbidity and mortality have been affected because of the existence of dissolvables. And in a way, I'm thinking about impact. Our challenge is roughly the same mental game as we had with menthol, where you have to somehow think about a comparison between a world with and without dissolvable tobacco products and what happens as a result of the existence and availability of dissolvable tobacco products.

That was what we framed in the menthol report, as a reminder, and actually in the

modeling, did sort of consider the counterfactual scenario. Now, we're not going to go to models quantitatively, but I think, qualitatively, we should certainly be using the same general idea when we think about impact.

Then, if we go to the next slide, it's impact on what. So we have risks and benefits to the population as a whole. And certainly, when you think about risks and benefits in public health at the top line, it would be premature mortality and disease. And then we have these additional points of indicators about likelihood that existing users of tobacco products will stop, and increased or decreased likelihood that those who do not use tobacco products will start using such products.

I think one question as we look at this is, do we know enough to answer these questions in a qualitative sense about which way risks and benefits might go, comparing our world with dissolvables to the world without dissolvables.

That's I think what we have to do in our minds and say, do we know enough? And we can say

yes, we do and we think the balance tips one way or another, or we could give some idea of the constraints in which the balance tips one way or another, or we could say not enough information in hand, more research is needed, and leave the answers to the questions for the future. So I think we have to be pretty open, given the lack of information, that we sort of wish we had, to dealing with our charge.

So I think that's what we have to do. And let me make clear first, is everybody comfortable with at least the scenarios that we need to compare?

Yes, Tim?

DR. MCAFEE: I guess the only thing that I think is a little different around this that I wanted to do a double-check on is, because as you earlier said, the committee's not being charged with answering the question of whether dissolvables should or should not exist, or be on the market. And I think the others -- I don't think some of these questions have -- it's not a yes/no,

black/white question. A lot of this, you could say, well, it depends on what happens with this. It depends on how the tobacco industry decides to market them. It decides on how the products evolve in terms of certain characteristics and it may depend somewhat on what action FDA might take around exercising its regulatory authority, what other parts of governmental and civil society do around education promotion.

So I would say one important thing that the committee could do is to try -- if there are elements that we can isolate and say we could markedly diminish the probability that adolescents will use this as a starter product by doing A, B, C, and perhaps we could increase the probability that more adults will use these products in a way in which would lead them to stop using non-combustibles -- can we isolate a few things like that? Those would be really helpful recommendations.

DR. SAMET: So I think I alluded to the fact that, in answering these, it could be that the

answers would go one way or another, depending on what plays out, which I think is what you just said. But let's look, and following up on what you just said, at the third point, the increased or decreased likelihood that those who do not use tobacco products will start using such products.

Now, I think a first question is, do we have enough information in hand to answer that question in even a qualitative way, which is to say that the likelihood is increased or decreased. And I'm not going to answer the question. I just throw it out as a rhetorical question for you to respond to, but we haven't heard very much evidence that speaks to this point.

Sandrine, did you -- no. Neal?

DR. PIRARD: I just wanted to say, I was thinking it's very hard to make any kind of definitive answer, just by the fact that early product definitively -- I mean, it seems, at least in my eyes -- that's just very subjective -- it didn't have the same appeal as the newer product.

So it's almost like when you say a world

with versus without dissolvable, it's almost like a world in 2010 versus a world in 2015 or whatever,

DR. SAMET: So we could anticipate some potential scenarios and say under what circumstances these might be likely to increase or decrease the number of individuals using smokeless. I mean, our framework is somewhat useful for that. I think the answer depends on all the things that Tim mentioned.

Neal?

DR. BENOWITZ: My comment was pretty much similar. I think, at the moment, these products have got no impact whatsoever because the penetrance is so low, and the use is so low. But that doesn't mean it might not; if it's marketed, the product's more attractive, if they change nicotine absorption. So I think we have to address both those things, what is the current status, which is probably nothing, no impact or virtually no impact, versus what it could be.

DR. SAMET: And the problem, of course, with what could be is there are many could-bes. And

whether we choose to say, well, what about a scenario of widespread use with aggressive advertising and promotion -- for example, at the extreme, which is probably something we need to -- at least boundary conditions would be probably useful, the right way to go, I think.

Yes, Dan?

DR. HECK: I'm not sure. I know we just heard briefly about the Environ model, but given the time and some experience to develop the inputs, I think, someday, we'll have, soon perhaps, the possibility to get at some of these questions that you've posed.

I might pose a quick question here. Should or how should the regulated tobacco industry stakeholders assist the committee in fulfilling its charge here?

DR. SAMET: I think the key issue, whether it's Environ or the industry, we have one more meeting in roughly 40 days and a report due in two months. So I don't think there's going to be too much opportunity, in terms of evidence digestion,

to go beyond where we are. Tools like the Environ model hopefully will be useful at points in the future, as the models are refined and data comes in that really will support some good guesses at what model parameters should be.

My own sense is, given our struggle even around qualitative directions here, that the Environ model is not going to rescue anybody yet. Sorry to Environ. But I think that's the case, and we need to acknowledge that. And we had some of that discussion yesterday.

John?

DR. LAUTERBACH: It seems we're almost in an impossible situation here in that there's no national distribution of some of the more controversial dissolvable products. And I guess, while the Star products are available in all states, there's not a great deal of market share of these versus total tobacco products or even non-combustible tobacco products. Perhaps, we're dealing with a situation where Congress reacted well before the storm.

DR. SAMET: But they acted.

[Laughter.]

DR. SAMET: And so that's probably the key issue. I take your point, and I think that's what we're all struggling with. I think Neal summarized no impact probably as reflecting the current state. You alluded to the limited penetration of the Ariva and Stonewall. And then I think the alternative is what could happen. And what could happen, I think, one thing we've agreed on, will depend on many things, the way the products are marketed, how they're packaged. I think we've touched on a lot of factors that will influence future scenarios.

At the least, in thinking about these questions, we can talk about the here and now. That's the trivial part of the task. And then we might at least I think give consideration to a future in which, again, we think about some potential boundary condition of a sort of roll-out of several of these products, future roll-out, perhaps, of more, and that they are marketed at the national -- sold at the national, level. It seems

like that's what we need to consider. And then we could say -- we could begin to say something or we could certainly say what we need to know to get better answers on these questions. Yes, Tim?

DR. MCAFEE: Maybe I'd just take a quick stab at some of the thoughts particularly relating to the third bullet there about the likelihood that they would start using such products that use tobacco products associated with these.

I think we've heard enough today to be worried about the potential for several elements of these products. And I completely agree with Neal. I'm not worried about the status quo or past history, but I think the fact that all the issues that we've struggled with around the shared characteristics of these products with other commonly-used and usually perceived as mostly safe products would lead to -- and to me, the scenario would be aggressive marketing to 18- to 24-year-olds that plays up the flavored aspect of it and is encouraging, just strongly marketed, and strongly encouraged.

I think there's very little question, based even on just what we've preliminarily heard, that this would spill over into the 12- to 17-year-old age group and that kids would -- there's no reason to think that they wouldn't be able to get access currently, based on our current experience with cigarettes and smokeless products, and that they would potentially -- if they experiment with these, because they have nicotine in them, which is addictive, they are likely to -- that will increase the probability that they will use more. And if they start using them -- I think everything we know about youth use of smokeless products, et cetera, would lead us to think that they would be more likely to use combustible products unless we figure out some very aggressive sorts of activities that would probably require -- because of the complexities of adherence to First Amendment rights of the tobacco industry to market to adults, would be very tricky to work out.

I think the fact that the same tobacco companies that are marketing combustible products

that are also marketing these could provide some benefits, but it's a big issue that's not present in Sweden, where it could be in their strategic interest, even if the products themselves are not taking off like gangbusters, that they would not be strongly incented, other than through goodwill and ethics, to take the steps that would be needed to stop the bleed-over into 12- to 17-year-olds. And frankly, we're very worried about 18- to 24-year-olds, too, because we know that this is a group that is still susceptible to combustible product evolution.

So again, we don't have quantitative numbers on this, but I think there's enough just pieces of a puzzle that would indicate that it's not a frivolous concern or just a paranoid concern to think that we need to think carefully about how this will affect initiation.

DR. SAMET: So just to paraphrase a little bit, what you're saying in answer to the third element is that while there are many gaps -- and we have not yet seen a scenario of widespread sales of

product by a large company -- that there is a basis for being concerned and watchful for the possibility that the availability of dissolvable products might increase cigarette smoking in the end.

DR. MCAFEE: Yes. I would probably go a little further and say I think, if there's aggressive marketing of these, particularly aimed at 18- to 24-year-olds, and "if they taste good," quote/unquote, instead of tasting lousy, and if they're co-branded with combustible products, it will familiarize 12- to 17-year-olds with the brand that's the same brand as the combustible products, I think it will.

I think unless there are aggressive countermeasures taken, the prediction would be that the net for initiation -- and I see no way that it would diminish initiation. That seems highly improbable, from what we know on this. So I think it's a significant concern.

DR. HATSUKAMI: I guess I share the same sentiment, that it is worrisome. And it's

worrisome because these are such discreet, convenient-to-use products that could be used anywhere without detection. And I can see that a younger population would be interested in using these types of products during school, which they obviously can't smoke during school, but they can certainly use these products. So I find it a little worrisome as well.

DR. SAMET: Patricia?

DR. HENDERSON: I have to agree with Tim. I'm thinking about just the history of what has happened. And there are certain vulnerable populations in the United States that have higher rates of smoking, and just how marketing really targeted these populations. And we've seen the example of menthol, what has happened to African-American communities.

It is worrisome, and I'm kind of thinking about Native American populations, too, where, if this gets into that population, the rates of initiation are already high for smoking. What's going to happen if this product gets in there?

DR. SAMET: Sandrine?

DR. PIRARD: Yes. I echo what is being said. And to me, I can't stand but thinking about those alcohol pops or flavored malt beverages, that basically are very similar in a sense to what we see here, which is branded product with a lot of flavor, clearly targeted to kind of a younger population, and looking like, basically, soda, and then you have -- I mean, out of all the surveys that have been done, basically, teens will say, well, it's great. If I drink this in front of my parents, they have no idea I'm drinking something alcoholic. They just think I'm drinking a lemonade or something.

So to me, it just seems to be so parallel that it's very hard not to be worried.

DR. SAMET: Let me check on the phone.

Mark, Arnold, do you want to weigh in?

DR. CLANTON: Yes. This is Mark. I want to offer a thought that our concerns, our worries, are very much a function of the availability of this product. And speaking in epidemiologic terms,

we're talking about exposure. Right now, the accurate (indiscernible) populations, 12- to 17-year-olds, et cetera, have very low exposure to these products. And as a result, we anticipate, if marketing works, they'll become more readily available. Then all of the issues we're concerned about, even in terms of the poisoning, may change based on how many households this product is in, and how often people open those products, and aggregate them into their containers, and it's more easy to access.

So whether you're a child, an adolescent, or adult, almost all of our concerns are a function of how many people are using these products and how often they're going to be available.

DR. SAMET: Okay. Thank you.

Let me draw us to the second point, increased or decreased likelihood that existing users of tobacco products will stop using such products. And again, our lines of evidence here are extremely limited. And so again, I guess the question is whether we want to -- no. Let's

discuss what we think we can say at this point.

Bob, were you about to --

DR. BALSTER: I've struggled with this particular one because I think we spent quite a bit of time earlier using the "could" word. And I think they could increase the likelihood that users of tobacco products will stop using such products. And there are certain features of them and certain data that are relevant to this from various locations that suggest that it could be.

But when I flip the question around and try to ask myself, well, what would I need to be able to conclude that they will increase on a population basis, then I have to start asking myself what's the standard of evidence that I would want to be able to make that conclusion as an individual, scientist, or as a committee. And I think then, we're getting into a question about what is the standard of evidence. And I think we're far away from meeting any sort of reasonable standard of evidence for drawing a conclusion in support of the no hypothesis and refuting the no hypothesis, that

they increase the likelihood.

So I just don't think that we can support, or I don't feel like there is enough evidence to support. There would be a pretty high standard of evidence needed to really draw a firm conclusion on it.

DR. SAMET: This will certainly be challenging. I'm just thinking about the recent paper, which I haven't read yet, but the NRT paper and long-term use at the population level. So again, this comes back to the question of what might be observed in clinical trials versus what happens in the population with long-term use. It's perhaps a little difficult. I mean, again, I think this is very challenging to answer based on what we know now, but that's in itself an answer.

Neal?

DR. BENOWITZ: I suspect that this may be product specific. For example, if you have a product that delivers a lot of nicotine quickly, it might be very helpful to help people quit smoking. If you have a low-nicotine delivery product, it

might be the opposite. It might just help kids get going and start using nicotine because it's less aversive.

So I think the answer to this question may depend on the product and how the product's engineered. I don't know that we can say that dissolvables will do this globally.

DR. SAMET: Dan?

DR. HECK: Somewhat related to what Neal said here, there are product-specific issues beyond just the product design. For instance, we've heard a lot of discussion of the Ariva and Stonewall products. And back in the original presentation by Star, we heard some business reasons, also, that may in retrospect have been related to the relatively low success of those products, limited distribution, a relatively small company, those kind of things.

But it occurred to me also -- and there probably is information on this that may be informative here -- are there data developed from the occasions when the NRT products went over the

counter, and then became more and more flavored and more appealing, that ties that ready availability and the relative appeal to maybe greater spontaneous quitting and the population. I don't know that such data might exist, but if it does, it may be useful.

DR. SAMET: Such data do exist.

Tim?

DR. MCAFEE: I think that is the exact concern that John was alluding to, that although this is an understudied area, where it has been looked at -- and there was a study done in the U.K., and there have been a couple of population studies, John Pierce's, about California, and then this very recent one, which I've only read the abstract to.

But the short answer is, despite the fact of the NRTs being used globally, having actually high utilization rate certainly among the general population of smokers, and at this point fairly high among people who are making quit attempts, in the 30 percent range, it has been difficult for

anyone to convincingly demonstrate a population-level effect on quit attempts. I mean, quit attempts are exactly what has been looked at. And there have even been paradoxical effects in the U.K. after one NRT thing.

I personally think there is probably explanations for this, mostly having to do with selection bias, but nonetheless, it would suggest that if we can't detect that with a product that was actually engineered, and designed, and approved for the purpose of helping people quit, and that now is actually being used at fairly high levels, our chances of being able to -- we certainly need to be skeptical about the probability that simply introducing another form of nicotine delivery will kind of magically result in increasing quit attempts in the real world, as opposed to being able to engineer it, which I would be quite confident could be -- can and to some extent has been, in clinical settings, where people are being recruited and encouraged to, who want to quit.

So I think this is a much more tricky

question, but I'm fairly hard-pressed with the current product characteristics, unless, as was said, unless as Neal said -- I think you could engineer a dissolvable product. I mean, there actually is one. It's called a lozenge. I mean, the lozenge I think functionally meets -- I mean, it's a dissolvable product with nicotine. But again, whether that's actually -- it clearly works in clinical environments, but whether it creates a population effect, there's really not evidence for that yet.

DR. HECK: I think, I guess, it's largely anecdotal, as we've heard at the testimony yesterday. But I guess we're beginning to accumulate, and I think there's probably some additional information you may have seen that I haven't. But there is some unique sensory contributions of tobacco itself and people familiar with tobacco use that may offer some advantage beyond just a simple nicotine and flavor delivery that characterizes the NRT cessation products.

DR. MCAFEE: Although I think John had

specifically said that his observation was that the gum flavoring was actually more appealing in terms of taste than most of the existing dissolvables.

DR. SAMET: Fred?

DR. PAMPEL: I tried to question some of the people commenting about the advantage of the dissolvables over NRT and didn't really get a clear answer. So I certainly don't know why the dissolvables would be that much better.

DR. SAMET: Bruce?

DR. SIMONS-MORTON: Yes. I guess it would be helpful -- I mean, I'm not sure how to phrase this. But for each one of these questions, if we had the caveat that the product's going to change, the social context is going to change, everything's going to change, and so you're constantly reevaluating this -- if you did that, and then we ask these questions with respect to the data that are available to us, I would think we'd be able to say some things about each of these areas. But as soon as you introduce all of the possibilities and the possible dynamics, it's impossible to answer

the question.

DR. SAMET: I think your point about the context is important and one that's been made before. And I think this relates back to how we answered these, going from Neal's two-word comment about now to what might happen in the future. And I think we're going to have to acknowledge that complexity.

I think the question here is whether we can make any statements about what the availability of a dissolvable product might to do cessation based on experience, whether it's NRT, or something else, or what we've seen around what people are saying about the products as they exist now, but that's as far as we can go.

I think what you're speaking to is the fact -- the need for very vigorous and comprehensive surveillance of tobacco product used in ways that will be informative on these questions. And it's going to have to involve probably following panels of individuals over sufficient periods of time to get exactly at these

questions.

DR. SIMONS-MORTON: Based on the few trials that we have, we can make some conclusions, that the products are pretty much not very well liked, that they have limited -- in terms of amount and time and duration of effect on the smokers who have been recruited, but that in some cases, there's been substitution. But we have very little -- there are few of these trials. But if you just look at the evidence, you can say pretty much that it's a mixed probably not-very-promising outcome.

DR. BENOWITZ: There is one literature that we haven't looked at that could be relevant, but it depends on how the products were marketed. And that is, in Europe, NRT has been used and approved for harm reduction. I haven't read the literature recently to see if it's effective, but it can be marketed for that purpose.

So NRT would be equivalent in many ways to having a dissolvable if that product were marketed for harm reduction or to help quitting.

DR. SAMET: Others on this point? Tim?

DR. MCAFEE: Just a quick point that we haven't talked about, I think there's one area where it's pretty predictable as to what the effect will be, and that's to the extent to which dissolvables are marketed to encourage people to use them as a bridging agent to allow them to keep smoking in their life, in situations where it's very difficult for them to smoke, that there's a high probability that that's going to increase the chance that they'll keep smoking. And I think that's pretty straightforward.

There's a lot of complex nuances about the NRT thing, which is quite controversial, but again, the other challenge around this is basically if you tell somebody that they can decrease their risk by doing something other than quitting, are you going to do something -- are we creating effects that are akin to what happened with filters, and light, and ultra-light? Which is, essentially, if you give a smoker a choice between quitting and cutting their risk partially by doing something that doesn't

involve quitting, a lot of them will opt to not quit. And again, unless carefully managed, we have the danger that this would be what would happen with dissolvables.

DR. SAMET: John?

DR. LAUTERBACH: I just wanted to make the point before to Dr. Pampel's comment about using dissolvables instead of NRT. It's basically a price differential. I mean, this pack of 20 pieces of gum in Florida last week was $10. The corresponding price of a pack of Ariva or Stonewall would be under $5.

DR. SAMET: Let me check on the phone. Mark, Arnold?

DR. CLANTON: Nothing to weigh in.

DR. SAMET: So let's go up to the top line item. And this is so highly integrative across the bottom two in future scenarios of use, mixed use, and so on. So I think we saw some of the numbers played out in different ways.

If the number of cigarette smokers were to drop -- or, potentially, the number of cigarettes

consumed were to drop because of the availability of dissolvables, then that would result in some potential collective reduction in population risk.

We won't go into the magnitude of it. We could speak to that. That really depends on the balance between the two below, as well as potential risks to health of the mix of products that people end up using. And I think we've heard this is not necessarily a simple matter of subtraction, that going from an average of 15 cigarettes to 10 cigarettes does not necessarily imply a proportionate reduction of risk, but at least, qualitatively, it would imply a reduction of risk.

So I think the answer to this around boundary conditions would be that risk of morbidity and mortality would go up if the number of tobacco users, including smokers, were to increase in a way that the collective risk increased.

I mean, it gets very complicated because you could have different mixture patterns of use, each with their own associated risk. But I could understand scenarios in which that might integrate

up, but on the other hand, there's very reasonable scenarios under which risk to the population goes down as well. And it seems to me that what we could do with this question is describe its complexity, and, I think, speak to the possibility that there are scenarios under which benefits could occur in terms of reduction of the tobacco-caused burden of morbidity and mortality, and that some of those are potentially plausible.

I'm not sure how much further we can go, but let me open this up for discussion.

Fred, are you poised to -- John?

DR. LAUTERBACH: Just one point. Let's say that dissolvables got 5 percent of the cigarette usage, which I think would be -- for those making dissolvables I think would be an overwhelming dream. Is even that effect measurable or significant in the overall health context?

DR. SAMET: I guess maybe there's a first question there, which is if there were 5 percent penetration of these into the market and then there was some associated reduction in cigarette use,

would there be some benefit, whether we could measure it or not? Presumably, from what we know, we could say yes. there would be a benefit. Could we measure it? That might be very, very challenging, particularly in a longitudinal context. But I think in a way, in the end, probably FDA will be left with using various sorts of models to try and understand the consequences for health risks of changing scenarios of use, whatever is driving them, whether it's dissolvables or other things.

Yes, Tim?

DR. MCAFEE: Just a quick amendment to that, I think the two other things that you'd have to have, whether it be measurable or not, is as was said about the Swedish situation, it would have to be that a very large fraction of that 5 percent was made up of people who were solely using dissolvables for which, again, we have virtually no evidence. So then you'd be left with the big question of, how do you get to that scenario because that doesn't look like what's happening.

I think the other one is you'd have to have a very, very small -- it would either have to be zero or in the negative direction -- impact on youth initiation because it would only take a fractional element of youth initiation to counterbalance even large switches probably in the adult population.

DR. SAMET: Other comments? I think we can all acknowledge the complexity of this aspect of our charge. Who wrote this charge? No.

[Laughter.]

DR. SAMET: Yes, Mark?

DR. CLANTON: Yes. You did a good job making it clear that we don't have an absolute correlation between cigarettes smoked and/or reducing, from some level, say, 15 to 10. We don't have an absolute understanding of what that means with risk. And so I appreciate that. But I also want to throw in, we don't want to make an assumption that diseases like cancer, for example, versus diabetes and coronary artery disease, sort of all equal when it comes to reducing the number

of cigarettes.

There isn't any threshold that we know about in terms of any nitrosamines in cancer. However, there does seem to be a fairly good correlation between reducing number of cigarettes smoked and your risk for coronary artery disease. That does tend to go down when you as the amount of cigarettes you smoke.

But in the case of cancer, since we don't know what that correlation is, it is best to maintain the advice that quitting altogether is the best way to reduce your risk to cancers related to cigarette smoking.

DR. SAMET: Thank you.

Other comments on this point?

[No response.]

DR. SAMET: So we've had a discussion of our charge and its complexity. And I think we've discussed at least qualitatively what might be said to each of these, ranging from, I think, the first, very difficult. And the answer is, what happens would depend on a number of things.

To the second, where there's the possibility that use would drop, there's a possibility that use would increase, it depends on marketing, the nature of the product, and so on. And then the third, where there was some concern, I think best expressed by Tim, about directionality based on what we know about introducing a tobacco product that may penetrate to youth, it gives them access to another way to get nicotine that might lead on, if I'm capturing what you said.

We've highlighted a lot of research needs. Before we wrap up in the next few minutes, we need to talk a little about process going forward. But I also wanted to see if there -- we've talked about research needs. We've talked about surveillance.

Are there specific items that anyone wants to bring up that we've not laid out? We've covered an awful lot of ground. I hope that, between Caryn and myself, we have captured all of this in a way that a summary can get written. But other recommendations for research, tracking, and so on?

Yes, Ellen?

DR. PETERS: I have just a modification to something you just talked about. When it comes to -- if marketing practices change, you may get a change to product usage. It's not just marketing practices of the tobacco companies. It's also any of our social agencies or the FDA itself. It's the changing information.

DR. SAMET: So I think that is an important point, the dynamics of the real world and these various factors.

Yes. Yes, Mark. Go ahead. Speak up. You're a little distant.

DR. CLANTON: Yes. I'm not sure how this comment fits, but it's just something that's been nagging at me. So for example, there are product warnings on, say, nasal decongestants that say if you have hypertension or other conditions, please consult with your physician before using this product. And this has to do with products that are currently available over the counter.

Given that we know, in fact, that nicotine has a similar vasoconstriction effect to other

stimulant medications, I'm wondering is there an opportunity here to at least discuss language that would be equivalent to what we see in nasal decongestants?

DR. SAMET: David, do you have any comments about that, the kind of specificity or recommendations that we might or might not make?

David's throwing his hands up.

DR. ASHLEY: And I don't really have a response to that.

DR. BENOWITZ: I don't think that there's evidence to support pure nicotine having cardiovascular effects like nasal sprays, for example. Nasal sprays have got some specific cardiovascular effects. They've got tolerance effects. It's different. But we just don't have the data for nicotine.

DR. SAMET: Sandrine?

DR. PIRARD: Yes. Reading, I think it's the NicoSpan, the one that's nicotine only, I was reading the warning. It's actually pretty interesting. There's something saying, like, don't

use if you're pregnant unless indicated by your doctor, which to me seems pretty much what you see on acetaminophen, when, obviously, everybody is using that when pregnant.

Then the other thing is, the risk to the fetus is not fully known. So when you read that, you're thinking, well, maybe it's not that bad, but actually I do not know if nicotine , a pure nicotine product like that would be risky. My understanding is that NRT is certainly not seen as a safe product for a fetus, but I think the NicoSpan product is very interesting in terms of a warning.

DR. SAMET: I wonder, maybe let's take our last 15 minutes or so and talk a little bit about process. So I think everybody has March 23rd pretty well engrained. March 1st, 2nd, we are meeting here. Remember that we discussed the form of our report. Part of our report is all that's gone on at this meeting and the meeting in July. It is the various materials that have been submitted. It is the presentations. It's the

peer-reviewed articles. It's our words sitting around the table, believe it or not. And that is the evidentiary body of the report.

Going with that will be a summary, since I can't imagine anybody reading what we just called the report -- but maybe somebody will -- and that there will be possibly a 20-page summary, distillation of what has been discussed; that a major task for our next meeting, at least the first day of it, would be to look at that summary and work on it, because clearly, we've laid out an awful lot of ideas, information, comments, that are going to have to be captured in that summary. And I think what words actually go into the summary will certainly be the most closely read part of our report.

So the proposal is that a summary will get written over the next several weeks, approximately, two weeks. Is that 14 days?

DR. ASHLEY: Fourteen calendar days, not 14 business days.

DR. SAMET: Fourteen calendar days, and this

summary will get written and then we would have it to look at.

Now, I would be happy to look around the table, and see someone raise their hand, and say, yes, I really want to write that summary.

[No response.]

[Laughter.]

DR. SAMET: Yes, just as I suspected.

DR. PIRARD: I have a question. I'm not volunteering. I actually just want to clarify, since it's my first advisory committee, what is the role -- is there a difference between the role of government employee versus special government employee on this report? That's something that I would love to hear.

DR. SAMET: Yes. We can explain that to you.

So I actually anticipated a lack of volunteers and have reluctantly agreed that I will write this summary in the next 14 calendar days, anticipating a huge reward for this or something.

[Laughter.]

DR. SAMET: So we would have this summary written that really I think particularly will focus in on our discussions today, but also on, I think, the key findings. But again, this will really be a summary for conveying what it is that is in the report, which reflects all the deliberations that we've had on the topic.

I think maybe we should hear from David and Sarah at this point, a little bit about how we might conduct the next meeting, but I would certainly see a large part of it as discussing this summary.

DR. ASHLEY: Yes. I'll make a couple of comments. Number one, I want to make one thing a little clear before you walk away and we don't clarify this. We actually need it by the 31st, so it's actually not 14 days; it's 11 days.

[Laughter.]

DR. ASHLEY: I just wanted to make sure that was clear. But there are two weekends in there, Jon, including this one.

DR. SAMET: There were two weekends.

DR. ASHLEY: I mean, the objective of what we're going to try to do, so that we have the report finalized, voted on, done before the deadline is, at the next meeting, the objective would be to come with the report. Now, the idea will be, the report will go out to you guys before the next meeting.

DR. SAMET: You mean the summary.

DR. ASHLEY: The summary. Excuse me.

Thank you, Jon. I appreciate you fixing that. The summary will go out at least some days before the next meeting, for you to look that over. We will come together during the next meeting. We will then spend the first day going through the report and getting the wording exactly like we want it.

FDA staff will probably spend the night cleaning that up and getting that correct so that, on the next day, there will be the opportunity to vote on the report and to have that finalized at the next meeting. Our objective is to have this done, and complete, and finished before the end of

the next meeting, and voted on, and final, and done.

DR. SAMET: Neal?

DR. BENOWITZ: If you are going to go ahead and get Jon's summary on the 31st, why can't you just send it down to us at the same time that Jon sends it to you?

DR. ASHLEY: If you want, ask Karen these details.

DR. TEMPLETON-SOMERS: I'm sorry. I missed that question.

DR. BENOWITZ: If we are going to give feedback, which I think we should, because we should help Jon, the question is, if Jon's going to send the report to you on the 31st, why can't we get it at the same time?

DR. TEMPLETON-SOMERS: That's actually what I was whispering to Caryn. The reason it's due so early is that we want to have it redacted as soon as we can. Those of you who are SGs and RGs will get the unredacted, but we want to have a redacted version that we can post. So it's due early, so

there'll be time to redact it, and post it, and still get comments from not only the committee, but also from the public.

Did I get that all?

DR. BENOWITZ: But we'll get it sooner so we have more time.

DR. TEMPLETON-SOMERS: You'll get it shortly after we get it, within a day or two, so like February 4th, something like that. And it should be posted shortly after that, barring no problems.

DR. SAMET: Bruce?

DR. SIMONS-MORTON: Does the summary include recommendations?

DR. SAMET: We certainly have recommendations that we've made so far around research and surveillance. I think, to the extent that we want to make other sorts of recommendations, I assume we could have further discussion, and we will have further discussion at the March meeting, and have the opportunity to shorten or lengthen whatever it is we've recommended.

DR. ASHLEY: Right, but you guys will not be able to leave the room that first day until that report is finished so that it can be cleaned up and voted on the next day.

DR. SAMET: Okay. So anything else? So David, on the first day, we look at the draft of the summary. We modify it, add, subtract, whatever, from the recommendations. The second day is essentially going to be a relook at the draft?

DR. ASHLEY: Yes. Obviously, when we come back the second day, the idea will be to look it over again and then vote on it. The theory is, when you come back the next day, it will have all the corrections, all the additions, all the changes. All of that will be incorporated. Obviously, we like people to look it over again before they vote on it, but it should be finalized. But yes, you'll have a chance to look it over, and it won't be a 200-page document like the menthol report.

DR. SAMET: So just a comment from Caryn and a reminder that if you have comments as you see the

draft, any comments should go directly to her and not to me. They'd probably just get buried in my e-mail anyway.

Anything else? I think we haven't done badly. We have five minutes to spare.

Any other thoughts? Dan?

DR. HECK: Just, again, quickly, Mr. Chairman, once again, if there's anything the stakeholder companies can offer you in terms of assistance, given your heroic task, we'd be pleased to do that appropriately, and good luck.

[Laughter.]

DR. SAMET: Thanks, Dan. It's going to take more than good luck.

Let me ask Mark and Arnold, first, thanks for hanging in over the phone. I can assure you that we're much better in person than by phone.

Any last words from either of you?

DR. CLANTON: Good luck as well.

DR. SAMET: Thanks.

MR. HAMM: I think the committee did a good job.

Adjournment

DR. SAMET: Okay. Thanks. So then I think we are close to adjourning. We actually had a lot of terrifically developed input from many, many people and I want to thank everybody. That's FDA staff, RTI, our public commenters, industry.

Our youth presenters this morning were very, very interesting. And I think we've certainly learned a lot over the last three days, applicable to our topic. I want to thank the committee for really hanging in and being very focused today in helping us get our job done. There's nothing like the incentive of going home to finish up.

So we'll be back together in March, I understand, so we'll see you then. Thanks. We're adjourned.

(Whereupon, at 2:30 p.m., the meeting was adjourned.)