FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

(TPSAC)

Wednesday, January 18, 2012

2:00 p.m. to 4:00 p.m.

Open Session

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

(2:01 p.m.)

Call to Order

DR. SAMET: Good afternoon. We're going to go ahead and get started. Welcome. I'm Jon Samet, chair of the Tobacco Products Scientific Advisory Committee. I'm going 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 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. I'll turn to Caryn Cohen, the DFO.

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 employees or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and conflict of interest laws covered by, but not limited to, those found at 18 USC Section 208 and Section 712 of the Federal Food, Drug & 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 USC Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts 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 when necessary to afford the committee essential expertise.

Related to the discussions at 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 USC Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves the nature and the impact of the use of dissolvable tobacco products on 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 & 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.

Thank you.

Introduction of Committee Members

DR. SAMET: All right. Let's proceed with committee introductions. And just so I don't forget, we should have two committee members on the phone. Let's see. Mark?

DR. CLANTON: Yes.

DR. SAMET: Why don't you go ahead and introduce yourself.

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

DR. SAMET: And Arnold, are you on?

MR. HAMM: I am, Dr. Samet. I'm Arnold Hamm, representing U.S. tobacco growers.

DR. SAMET: Great. And then, John, we'll start over on that side with you.

DR. LAUTERBACH: John Lauterbach, Lauterbach & Associates, LLC, consultants and tobacco chemistry and toxicology. And I'm here representing the interests of the small business tobacco product manufacturers.

DR. HECK: Dan Heck with the Lorillard Tobacco Company, representing the interests of the

tobacco manufacturers.

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

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

DR. EVANS: Sarah Evans. I'm with the Office of Science.

DR. ASHLEY: David Ashley. I'm director of the Office of Science here at CTP.

DR. DEYTON: Lawrence Deyton. I'm director here at CTP.

DR. SIMONS-MORTON: I'm Bruce Simons-Morton. I'm with the National Institute of Child Health and Human Development.

DR. EISSENBERG: I'm Tom Eissenberg. I'm with Virginia Commonwealth University.

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

DR. BALSTER: Bob Balster, Virginia Commonwealth University.

DR. HATSUKAMI: Dorothy Hatsukami,

University of Minnesota.

DR. PAMPEL: I'm Fred Pampel, at the University of Colorado Boulder.

DR. EMERY: Sherry Emery, University of Illinois at Chicago.

DR. SAMET: Good. Thank you.

So I guess we'll turn to Sarah.

Opening Remarks – Sarah Evans

DR. EVANS: Good afternoon, everybody. I'd like to welcome you back to this second meeting from TPSAC on the topic of dissolvable tobacco products. My name is Sarah Evans, and I'll be the lead scientist for this effort.

I'd like to begin by informing you that the information in these materials is not a formal dissemination of information by FDA and does not represent agency position or policy. The information is being provided to TPSAC to aid the committee in its evaluation of the issues and questions referred to the committee.

The Tobacco Products Scientific Advisory Committee is required to review and provide

recommendations to FDA regarding the nature and the impact of the use of dissolvable tobacco products on the public health, including such use among children.

TPSAC is to consider the risk and benefits to the population as a whole, including users and non-users of tobacco products; the increased or decreased likelihood that existing users of tobacco products will stop using such products; and the increased or decreased likelihood that those who do not use tobacco products will start using such products. TPSAC's report and recommendations are due on March 23, 2012.

A tobacco product is any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product, except for raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product. A tobacco product does not mean a product that is a drug, device, or combination product.

Currently, cigarettes, cigarette tobacco,

smokeless tobacco, and roll-your-own tobacco are subject to regulation under Chapter IX. FDA intends to propose a regulation that would deem products meeting the statutory definition of tobacco product, found at Section 201(rr) of the FD&C Act, to be subject to FDA's regulation under Chapter IX.

Smokeless tobacco is any tobacco product that consists of cut, ground, powdered, or leaf tobacco, and that is intended to be placed in the oral or nasal cavity.

There is no statutory definition of dissolvable tobacco product. Many dissolvable tobacco products may meet the current statutory definition of smokeless tobacco. Some dissolvable tobacco products may not meet the definitions of cigarette, cigarette tobacco, roll-your-own tobacco, or smokeless tobacco, and so may not be currently subject to FDA regulation under Chapter IX of the FD&C Act.

Meeting topics. The topic of this TPSAC committee meeting is specifically dissolvable

tobacco products. It is not smokeless tobacco in general. TPSAC is not being asked to address the use of dissolvable tobacco products as cessation aids, or whether specific products are substantially equivalent to products which are on the market as of February 15, 2007. At this time, TPSAC is not being asked to evaluate those applications, or to address use of dissolvable tobacco products as potential modified risk tobacco products.

In reviewing the nature and the impact of the use of dissolvable tobacco products on the public health, FDA requests that TPSAC be inclusive, without regard to whether they are currently regulated under Chapter IX, so not limited to products that meet the definition of smokeless tobacco. In providing recommendations to FDA, we request that TPSAC identify the types of dissolvable tobacco products to which the advice does and does not apply.

Right now I'm going to give you an overview of what we discussed during our July meeting. At

that time, FDA discussed our activities on dissolvable tobacco products. This included information available to FDA at that time. That included published peer-reviewed literature, submissions to dockets, responses to FDA's February 1st letter of 2010, and information from FDA-requested meetings with individual manufacturers.

At that time in July, we also discussed FDA's research activities, including consumer perception research and quantitative analyses. At that time we also discussed other FDA activities, including information requested from industry, or as we know it, the 904(b) letter.

FDA has responded to TPSAC requests for information from the July 21st meeting. Information on state and local level smoking laws in states where dissolvable tobacco products are thought to be marketed were included in your background materials. During this meeting you will hear presentations from FDA, RTI, and invited speakers on dissolvable tobacco products. And, in

addition, FDA has provided information submitted by the public in the background materials.

We began today's meeting with a closed meeting. At that time, TPSAC heard commercial confidential trade secret industry information. Also, there was a presentation, invited, from Altria. FDA requested information on design and marketing, storage conditions and stability, and the reproducibility of dissolvable tobacco products. We now continue with an open meeting, and we will be discussing this afternoon use of Swedish oral tobacco and related health effects.

With that, I'd be happy to answer any questions.

DR. SAMET: Questions from the committee? John?

DR. LAUTERBACH: Yes, Dr. Samet. I'm confused here about the definitions. When would a dissolvable tobacco product not be considered a smokeless tobacco product?

DR. EVANS: So we are asking the committee. We're taking a broad overview of dissolvable

tobacco products, and so we're looking for your direction and your discussion to help us solve that. But since there's no statutory definition of dissolvable tobacco products, we included definitions that were in the statute to aid you in that discussion.

DR. SAMET: I think this is a topic that we will be touching on. Actually, other questions for Sarah? I think it's just maybe important to point out that we're really beginning with, today and tomorrow, hearing a lot of information that will be relevant to our report.

I think you might remember March 23rd as the deadline for writing the report.

DR. EVANS: Correct.

DR. SAMET: Thank you for that reminder. We had not forgotten. But I think when we leave here on Friday, the day during which we do have time for discussion about the report and its formulation, we really do need to have a very specific plan coming out of what we've learned both from our July meeting, the materials that have been provided, and

the additional material that we'll hear both today and tomorrow. So I think the committee needs to keep in mind what our broader picture is over the three days. And I actually think that we do have a very full three days ahead of us.

So let me ask, any questions about where we're up to? So this afternoon, we do have something very specific we'll be looking at, and we have one, I think, charge question related to that. But anything else before we move on?

[No response.]

DR. SAMET: Thank you. Thank you, Sarah.

Then we'll move on to our first presentation by Dr. Lars-Erik Rutqvist from Swedish Match. His presentation is, The Swedish Tobacco Harm Reduction Experience. Yes, please, and thank you for coming.

Presentation – Lars-Erik Rutqvist

DR. RUTQVIST: Good afternoon, and thank you for inviting me.

At the July meeting of the TPSAC, many speakers referenced the Swedish data on snus when talking about health effects of dissolvables, and

that is obviously the background for my presentation here today.

I've been specifically asked not only to talk about the Swedish data on the switch from cigarettes to snus, but also to address the extent to which actions on the part of government, regulatory authorities, media, and industry contributed to the phenomenon.

Other central issues, of course, are the extent to which the data on snus is applicable to dissolvable products and whether the experiences from Sweden can be translated to the U.S. situation, but those are judgments that I leave to the FDA and to this committee.

I've submitted a brief review paper on the Swedish experience. I hope you've all received a copy of that. It compliments my presentation today, and includes selected references for those interested.

My key messages in this presentation is that, overall, tobacco consumption in Sweden is as high as in comparable countries. But Sweden has,

over the past three to four decades, developed internationally record low rates of smoking-related morbidity and mortality. Many researchers have concluded that the switch from cigarettes to snus that started in the early '70s, mainly among male smokers, has contributed to this development.

Snus is now the predominant tobacco product among males in Sweden. And the basis for the Swedish experience scientific claims is rooted in several published research articles, most of which derived information from a handful of key cohorts as well as national public health statistics.

The switch from cigarettes to snus was probably multi-factorial. Actions on the part of government, academia, and industry probably all played a part. But from the beginning, it was largely a grassroots phenomenon which was facilitated by the backdrop created by government and regulatory authorities and media.

It's important to remember that the Swedish experience is a rather fairly recent phenomenon. For most of the 20th century, Swedish tobacco use

was similar to other Western countries, with cigarettes as the predominate product of choice. It's only been since the last third of the century that snus has made a comeback. Remember that snus is the traditional product of Sweden and dominated the tobacco market back in the early 1900s.

The experience began in the late '60s, early '70s when the health effects of cigarettes became widely acknowledged. And many Swedish smokers turned to the traditional product, which was viewed as being more natural, so to speak, than cigarettes. But it took some time before the effects of the switch started to emerge in the public health statistics. It was not until the early 1990s that the experience was documented in published research articles.

This slide shows an example of the kind of data that have emerged. In the left panel, you see a comparison of smoking prevalence and snus use among males in three Scandinavian countries, Sweden, Norway, and Denmark. And in the right panel, you see corresponding incidence rates for

some common tobacco-related cancers. And as you can see, Swedish males have the highest snus use rate, the lowest smoking prevalence, and the consistently lowest rates of smoking-related cancer.

This slide shows similar data, but the comparison here is between Sweden and the rest of the European Union. But the conclusion is exactly the same: Swedish males smoke the least in the E.U. and have the lowest, or among the lowest, tobacco-related cancer rates.

To fully understand the Swedish experience, I think it's important to realize that Sweden is a highly regulated country. Personal habits are generally well-documented, including the use of various tobacco products. The government has a longstanding commitment, going back over a hundred years, to public health. And I would say Swedes in general are fairly well-educated and, for the most part, reasonably health-conscious.

There are national records of tobacco statistics that go back over 200 years. And for

the most part of the past century, the Swedish state was actively involved in snus production, either in the form of the state monopoly or a state-owned company. And this state involvement has facilitated collaboration between the industry, government, and regulatory authorities.

The Swedish experience scientific claims are rooted in a large number of research articles, which have derived information from a number of key cohorts. Like all cohorts, these have their strengths and weaknesses, but it's these data that are considered to be the most useful source of information for the study of Swedish snus.

Numerous scientific articles have been published based on these cohorts. The authors arrive at slightly different conclusions, even based on the same data set. But a common theme in virtually all publications on health effects is acknowledgment of a vast risk differential between snus and smoking.

Swedish institutions have a longstanding commitment to conduct and fund tobacco-related

research, and it may be of interest for you to know that at the moment, most of this research is focused on snus, which reflects the Swedish tobacco use patterns.

So how do Swedish public health authorities communicate about snus? I think an illustrative example is provided by the public health report for 2005 published by the Swedish National Board of Health. That report contains a section on snus, including detailed information on prevalence of use, time trends, health implications, and whether snus is a gateway to smoking.

The report noted that the health assets of snus are minor in comparison with smoking, and specifically mentioned that the recent studies showed no association between snus use and myocardial infarction. But they also cited data suggesting that snus may be associated with some types of cancer and may have adverse effects on pregnancy outcomes.

The report concluded that the scientific source material is not always strong, but the

assumption should always be that snus is not a harmless product. The report went on to state that many people apparently have used snus as a means to give up smoking. But as to the issue whether public health officials should actually suggest to smokers to switch to snus, well, the report formulated that question but left it unanswered.

Another important message in the report was that snus primarily acts as a gateway from smoking, not the opposite. This contributed to what many researchers and the public already had accepted, namely, that in Sweden, like in all other countries, the predominate gateway to smoking among adolescents is cigarettes, not snus.

The Swedish experience would not have been possible if there hadn't been, and continues to be, a public debate about snus as a tobacco harm reduction product. In the past decade, there have been more than 5,000 articles in Swedish print media about snus, and they have appeared in a wide range of publications.

This media attention, where different views

have been expressed, has undoubtedly had a significant risk communication impact. The exchange featured recently in the official journal of the Swedish Medical Association, Lakartidningen, is of special interest because it demonstrated the importance of the modified risk debate to the Swedish public health community.

Snus-related articles also appear in the business sections of newspapers, and the focus of those articles has been the Swedish government's work to overturn the current E.U. ban on snus. But they typically also address the relative health impact of snus versus cigarettes, which is a cornerstone of the present Swedish administration's position that the E.U. ban is disproportionate and ill-advised. The relative health effects of snus versus smoking is also a common topic among family and friends, and these conversations have been enhanced by the statements from government and academia.

In Sweden, snus is regulated as a food product since 1971, and I think this is

representative of how snus is viewed by the government and has definitely influenced how the product is perceived by the public.

Last year, the Swedish Food Agency developed a proposal for more comprehensive and precise regulation for snus products, which essentially codifies the ongoing relationship between Swedish Match and the agency. And this proposal has now been submitted to the European health authorities as part of the Swedish government's position on the E.U. ban.

The fact that snus came under the jurisdiction of the Swedish Food Act was also the starting point for a collaboration between Swedish Match and researchers at the agency, which eventually led to the voluntary quality standard called GothiaTek, which includes, for instance, requirements for maximum permitted levels of suspected harmful elements, requirements for the manufacturing process, and also a standard for qualified product information to consumers.

The goals of the standard includes a

commitment to continual quality improvement, to closely follow external research, and to conduct in-house research and cooperate with regulatory agencies.

Tobacco research governance and the interactions of regulatory authorities, industry, and academia is an important issue that was addressed in the recently-released IOM committee report on modified risk tobacco product applications. In Sweden, we've faced similar challenges; but I would say we made significant progress, for instance, with the development of the GothiaTek standard and the relationship between industry and regulatory authorities.

Just to give you a recent example, those of you who attended the mid-November international meeting for tobacco regulators sponsored by the WHO and the FDA may have noted that the presentation by a senior official from the Swedish National Institute of Public Health cited the GothiaTek standard, and also thanked Swedish Match.

The role of Karolinska Institutet, which is

a leading medical university in Sweden where I once worked, is particularly significant because of its seminal tobacco research and the impact of faculty on government policies. There is research from the Karolinska Institutet which I agree with and some that I question, but that's the nature of the scientific debate, and we're having that debate in Sweden at the moment.

To what extent has industry contributed to the switch from cigarettes to snus in Sweden? And when I say industry, bear in mind that Swedish Match has a more than 80 percent market share in Sweden for snus, which essentially means that Swedish Match is the industry.

The Swedish Match website is directed towards investors and employees. But I think this site, anyway, illustrates how the company has communicated with consumers in Sweden over the years. It features a combination of science and business-related information which is intended to compliment that provided by other sources, including government, academia, NGOs, as well as

family and friends. On the issue of health effects, the site presents factual, well-referenced information, and only presents analyses and conclusions from credible external sources.

The company takes great care to only present statements that are backed up by research and findings stated by government agencies and the scientific community. The site is definitely pro-snus, but it's science-based, not advocacy-based, which I believe is correct both from an ethical and business point of view.

Snus has never been marketed as a smoking cessation aid or harm reduction product. The fact that snus can function as an alternative to cigarettes is something Swedish smokers found out for themselves. I think this was facilitated by the deep-rooted cultural view as snus being a more natural, organic product, as it were, than cigarettes. This impression was later reinforced by acknowledgment from government and academia of the loss-risk differential between snus and smoking.

Snus has always been marketed as a traditional product under historic brand names, sometimes brand names that go back more than a hundred years, which is in contrast to the marketing approach by U.S. companies, that use cigarette brand names for their snus-type products, possibly implying that the two products coexist in a tobacco usage pattern. The health effect communication probably works best among educated consumers, who probably also are those who appreciate the GothiaTek goals of using best available production technologies.

So, in conclusion, Sweden has seen an earlier and more profound drop in smoking prevalence than any other country, so the Swedish experience is widely viewed as a positive public health story. I think the public's underlying sense of reasonableness behind the communication about snus has been an important factor to bring about this change, irrespective of whether the message has come from government, academia, or industry.

Public health representatives have been cautious and have continued to characterize snus as a potentially harmful product. But at the same time, they also presented the scientific facts, and have typically not equated snus with cigarettes. I believe industry, too, Swedish Match, can take some credit for the positive development in that the company's marketing has always been responsible and the communication has always been science-driven.

The Swedish experience is a complex and multi-faceted phenomenon that has occurred over several decades, and I'm happy to say that it is now being replicated in neighboring Norway.

I hope this presentation has been able to provide a context for future references to the Swedish experience. So thank you.

DR. SAMET: Thank you.

We have another presentation to follow, but why don't we take any questions specific to this presentation now, remembering that we'll have an overall discussion afterwards.

Sandrine?

DR. PIRARD: Yes. I have a question, and maybe it's almost impossible to answer. I don't know. But are the profits from snus in Sweden comparable to the profits that could U.S. industry derive from similar products? In a sense, is the profit as big as what we can see here in the U.S. in Sweden?

DR. RUTQVIST: Well, I have no experience from the cigarette business, so I couldn't comment on whether you can make a bigger profit on snus or on cigarettes. Please note that Swedish Match left the cigarette business many years ago. The company felt that cigarettes were a dead end from a scientific, ethical, and business point of view.

DR. SAMET: Tom?

DR. EISSENBERG: If I understand the data you're presenting correctly, in the 1970s folks in Sweden, particularly the males, started using snus and stopped using cigarettes. Is that correct?

DR. RUTQVIST: Yes.

DR. EISSENBERG: And so you would attribute the low rates of lung cancer now to the complete

substitution in those folks of their cigarette use for snus use; that is, they completely dropped cigarettes, and now they're using snus exclusively.

DR. RUTQVIST: For the most part, yes. There is, obviously, some dual use as well. But if you focus on dual daily use, which I think when it comes to smoking is the most troublesome from a lung cancer point of view, dual use is rather low.

DR. EISSENBERG: But those dual users, would they be captured in -- these aren't numbered. In the figure where it looks like there are somewhere around 11 percent of smokers in Sweden in 2008, male smokers in Sweden, would that include the dual users? I'm trying to get at the idea that it's exclusive snus use that underlies what we would call the Swedish experience.

DR. RUTQVIST: The figure that you see shows data on daily use.

DR. EISSENBERG: Yes.

DR. RUTQVIST: So that would be the total number of daily users. Some of those would obviously also be dual users.

DR. EISSENBERG: Okay. Thank you.

DR. SAMET: Sherry?

DR. EMERY: So the shift in use patterns that we see starting in the '70s, you're saying, was not a result of any marketing or promotional strategies, but just a grassroots reaction to the findings about cigarette smoking?

DR. RUTQVIST: I think the most important determinant was the increased widespread knowledge about the health effects of cigarettes. That is, I think, the main determinant of that. I know that it's been suggested that marketing had something to do with it. I have not been able to document that, and I have not seen any documentation as to what kind of marketing that would refer to.

The tobacco museum in Stockholm has a quite large collection of marketing material that goes back more than a hundred years. And I've looked at their collection from the '60s and '70s, and -- I mean, I think we have to accept that back then, when advertising was still allowed in print media in Sweden, the vast majority of the advertising you

saw was for cigarettes because that was the big product at the time. There was marketing for snus as well, but it was not very prominent.

DR. EMERY: I have a follow-up question to that, just about the nature of the cigarette advertising. Were the restrictions that were adopted on cigarette advertising also applied to snus advertising?

DR. RUTQVIST: Yes. Restrictions have always concerned tobacco products. It's not made as a distinction between cigarettes or snus.

DR. SAMET: Dorothy?

DR. HATSUKAMI: You had mentioned that the dual use is relatively low in Sweden. To what do you --

DR. RUTQVIST: Dual daily use.

DR. HATSUKAMI: Pardon?

DR. RUTQVIST: Dual daily use.

DR. HATSUKAMI: Yes. Dual daily use. I see. To what do you attribute that? Do you think it's because people in Sweden have an understanding that cigarettes are more harmful than snus, or the

fact that maybe the snus products contain high nicotine and could substitute for cigarettes? Any thoughts on that?

DR. RUTQVIST: I think the reason is multi-faceted. I think one important aspect is the nicotine delivery profile of the product. It's not a low -- the traditional types of snus that we have in Sweden is not a low nicotine product. It delivers nicotine quite effectively; obviously, not as cigarettes, but still, it would be classified as a high nicotine smokeless product. I think that could be one reason.

Another reason could possibly be that it's viewed as, as I said, a more natural, organic product than cigarettes. It could be because of the public's awareness of the health hazards of smoking. It's probably multi-factorial, and it's difficult to quantitate exactly how much each factor contributed.

DR. HATSUKAMI: Just related, you mentioned that you don't see dual daily use. But do you see dual non-daily use?

DR. RUTQVIST: I think the --

DR. HATSUKAMI: I think intermittent maybe snus but yet daily cigarette use, is what I'm getting at.

DR. RUTQVIST: If you have a situation where a large proportion of those who use snus are former smokers, I think you will see quite a lot of dual use. If you include, for instance, having a cigarette at the party once a month, if that's daily use, and you have a lot of ex-smokers among your snus users, you will see a lot of daily use.

I think the whole issue of dual use is difficult because it includes such a wide variety of behaviors. It could be those who use -- who smoke most of the week and use snus once a week. It could be those who use snus on a daily basis, who perhaps take a puff once a month. I mean, dual use is so varied. You can have so many usage patterns within that definition. So I think you need to really define what you mean.

DR. SAMET: Fred?

DR. PAMPEL: Whenever you get a big change

like this, lots of causes are involved. But it seems to me that somehow along the way, it was more than just the consideration of health effects because women didn't accept the snus the way men have.

It seems that there's some sort of norm going on about what's an acceptable kind of alternative behavior. For men, it's okay; for women, it's not okay. And maybe in Sweden it had something to do with traditional use of snus, and that sort of speeded the acceptance among men of the habit. We don't quite have that same background in the United States. And I just wonder to what extent that might make it difficult to replicate that acceptance of snus.

DR. RUTQVIST: I think you have a good point there. I think history played a big role in the fact that it was mainly the male smokers that took it up because, as you point out, it was historically mainly a male habit.

This is now changing because it's age-related. This conception of snus as being a male

habit is mainly among middle-aged or older women, because if you look at those under 45, young female smokers are taking up snus as well. And it's the same phenomenon that we see in Norway.

So times are changing, and history may not be so important any longer for young people.

DR. SAMET: I just want to go back to Dorothy's question. One issue with the introduction of dissolvables or other products into the marketplace will be surveillance on patterns of tobacco use. And you alluded to the challenge of tracking dual use patterns.

Do you feel that whoever does this in Sweden, your public health authorities, have they risen up to this challenge of understanding use patterns? And if so, how?

DR. RUTQVIST: Well, as I mentioned, much of the tobacco-related research that is ongoing at the moment in Sweden is focused on snus use because it's so prevalent. And this also applies to Norway. There are a lot of research projects that go on, and there are surveys that monitor use

patterns in the population. And I think whatever question you have on use patterns you can find in published statistics or research articles.

DR. SAMET: So just to follow up, then, you feel that the tracking that is in place is adequately monitoring the multiple different patterns of single use of tobacco and cigarettes and the various -- the spectrum of dual-use patterns you alluded to?

DR. RUTQVIST: Well, as a researcher, there are always extra questions that you would like to ask. You can always ask for something that people didn't collect information on. But apart from that, I would say that the surveys are quite comprehensive.

DR. SAMET: Good.

Let me check, before we move on to our next presentation.

Mark, Arnold, any questions?

DR. CLANTON: No questions here.

DR. SAMET: That was a no?

MR. HAMM: No.

DR. SAMET: Arnold, okay.

Tom, the last question?

DR. EISSENBERG: Yes. You've obviously studied the uptake of snus use in Sweden for quite a bit, so I wondered if I could get your expertise on two questions.

First, transitions in smokers, is the transition -- or do you have any data to suggest that the transition from being a smoker to becoming an exclusive snus user, is it you wake up one day, you try snus, and there, you're done, or how long does it take?

Secondly, what about uptake in non-users, that is, non-tobacco users? You mentioned just a second ago about adolescents switching to snus. But are adolescents also taking up snus when they were previously tobacco-naive?

DR. RUTQVIST: This depends on from which time the data derives. Back in the late '60s, '70s, almost 100 percent of those who came into the snus category were smokers because smoking was so prevalent.

This proportion, with the decrease in smoking prevalence, has gone down now. So at the moment, those who come into the snus category are somewhat different figures. Some say 50 percent; some say a bit lower than that, are not smokers.

So eventually, hopefully, the ideal situation would be that there would be no smokers in the population. So anyone who used snus would not be a smoker. So this changes with time.

Is that an answer to your question?

DR. EISSENBERG: Let me just make sure I understood what you said. Did you just say 50 percent of snus users were not using tobacco prior to their snus use?

DR. RUTQVIST: Those who come into the category now, yes.

DR. EISSENBERG: Then I didn't get anything about transitions in smokers, whether it's a gradual process --

DR. RUTQVIST: Ah, yes. Yes. No, obviously, it is a gradual process. The transition period varies from weeks to months up to several

years. So when you talk about dual use, a proportion of those individuals represent smokers in transition.

I have not seen reliable data that quantifies how large a proportion. I think we will be able to see such data in a few years because, obviously, it is a large research interest at the moment. So I know that people are looking at it. But their transition typically, I would say, takes several months, at least.

DR. SAMET: Last, last question.

DR. BALSTER: One of the obvious problems that we would have in applying information about snus use in Sweden to the U.S. situation is the existence in Sweden of this voluntary quality standard, which creates a particular type of snus product.

I don't know if this is fair to ask you, but is there a way to attribute the health-related changes over time to the fact of it being that particular snus product, versus just a switch to snus in general? How important was the standard,

in your view, as it might have attributed to changes in these health outcomes?

DR. RUTQVIST: I think the standard was very important, perhaps not because of the exact levels of the different constituents that it regulates. I think the standard was important and is important because of the fact that it symbolizes, or epitomizes, if you will, a commitment to quality development that has been there in the company since the 1960s. So there has been a continual quality improvement ever since. And today, if you look at the levels of nitrosamines and benzopyrenes, they are much lower than the GothiaTek limits.

So I think that has been important. I find it difficult to believe that a tenfold decrease in the levels of, let's say, polyaromatic hydrocarbons wouldn't matter. I find that difficult to believe.

DR. SAMET: Thank you, Dr. Rutqvist. And as we discuss, we may well come back with more questions, after the next presentation by Dr. Scott Tomar from the University of Florida.

Scott, thank you for coming.

Presentation – Scott Tomar

DR. TOMAR: Yes. Thank you very much for the invitation to speak here.

So my understanding of the charge to TPSAC is to really consider how the introduction of new tobacco products may affect the population, the health of the population in general, whether it increases or decreases overall population harm. Again, there isn't a tremendous amount of information specifically on dissolvable products. But I thought perhaps there are lessons we could learn from existing smokeless tobacco products.

So, perhaps dissolvable products could reduce population harm from smoking. If in fact these products would prevent smoking initiation, would help current smokers to quit smoking, or if it at least reduced cigarette consumption among smokers who continue to smoke.

On the other hand, the introduction of novel products could actually escalate population harm if in fact it recruits non-tobacco users into use of

these products, and particularly if they appeal to young people, who still make up the overwhelming majority of adopters of tobacco product; if in fact it delays smoking cessation; and if it promotes relapse among those who have already quit smoking. So again, I thought perhaps there are some lessons to learn from the available epidemiologic data on use of other products.

So I was just going to briefly review the epidemiologic data on patterns of smokeless tobacco usage and consumption in relation to cigarette smoking, a little bit from Sweden, a little bit from the U.S. I'll talk about some of the recent, very recent, randomized clinical trials on smokeless tobacco as a smoking cessation strategy. And I understand the previous speaker's point that the industry has not marketed these products specifically as smoking cessation devices or medications. On the other hand, they actually are funding some of these clinical trials. And finally, we'll talk about the implication of the findings from those studies.

So first, the question -- and this has come up a number of times in past years -- of whether the adoption of smokeless tobacco use might actually prevent smoking initiation. The theory is that if young people were to adopt use of smokeless tobacco, perhaps that would satisfy their need for nicotine dosing, and in fact maybe prevent them from becoming smokers. In fact, there are a number of publications out of Sweden that have actually made that claim.

So the hypothesis is that if smokeless tobacco use actually prevented smoking, increased the smokeless tobacco use, we would expect that to be associated with a decreased proportion of people under 25 who currently smoked. And the reason why I put that out there -- and all of these assumptions are highly supportable by available evidence -- nearly all tobacco initiation in developed countries, including Sweden and the United States, occurs by early adulthood. Very, very little occurs after age 25.

There's very little tobacco cessation that

occurs among young people. So in fact, because of that, trends in the prevalence of current use of these products generally reflects underlying trends of initiation because we're not seeing a whole lot of cessation at those ages.

So in fact, the data that were presented by the previous speaker on overall sales trends -- I unfortunately didn't include that slide here. But actually, there was a period of more than 20 years where in fact trends in both cigarette consumption and snus consumption were in fact parallel.

But in fact, where we're picking up, when you look at a 30,000-foot view, is a lot of birth cohort effects that are sort of mushed together. And in fact if we were to look just at the youngest cohort -- and these are official data from Statistics Sweden, trends in the percentage of males, age 16 to 24 who smoked or used snus daily. So as has been mentioned already, daily use of snus is more prevalent than daily smoking among these adolescent and young adult males.

However, if you look at the long-term

trends, going back to the late '80s -- and in fact, what I've plotted was the linear trend lines for both of those -- they're in fact fairly parallel and both declining. So at least in looking at the trends in daily use of either of these products, they both appear to be in decline. At least at this point, there does not appear to be a substitution or any kind of preventive effect from snus usage.

Another thing, we're seeing a little different pattern among females in this age group, the use of snus among young females, much, much lower than among males, and in fact, in the early part of these trends, almost zero. On the other hand, that was the period at which we saw the most rapid decline in the presence of daily smoking among adolescent girls and young women.

We're now up to about 4 or 5 percent prevalence of daily snus usage among young females, actually at the same time that the decline in smoking seems to have leveled off. But actually, as of the most recent data that have been reported,

the prevalence of daily smoking, it's within a percentage point or two for young males and females, not appreciably different at this point, although there's a very, very different trend in use of snus.

So again, there's just not a whole lot of evidence that the population level have any kind of major preventive effect from the use of snus on smoking.

Some data from the U.S. -- and unfortunately, the way that the data are collected in this particular survey -- this is from the Monitoring the Future survey. It was conducted by University of Michigan. It's been funded by the National Institute on Drug Abuse since the mid-'70s. They have consistently collected data on smokeless tobacco since the early '90s. So I've included all the years for which we have ongoing data on use of smokeless tobacco as well as smoking.

So as far as cigarette smoking, those lines are pretty much parallel for high school boys and

girls. This is for 12 graders in high school in the U.S., peaking in the mid-'90s. And then we've seen a pretty precipitous drop in the prevalence of daily smoking in high school seniors, in fact to the lowest point since it's been tracked. I didn't have all the data going back to the beginning of this particular survey, but going back to the mid-'70s, the lowest prevalence we've ever seen.

On the other hand, the use of smokeless tobacco -- and they don't separate snuff from other forms, although snuff is the predominate product used by young people in the United States -- we've actually seen a decline for most of this time; a little different trend line, but over most of this time, a decline in the prevalence of daily use of smokeless tobacco, with the exception of, the last few years -- and again, we'll keep monitoring that to see whether that's a persistent trend, but what looks like potentially an uptick in daily use of smokeless tobacco by high school males. Among girls through this whole period, almost not measurable. It's just about zero.

So in terms of whether these products are efficacious in getting smokers to give up cigarettes and move to this product -- and I'm not going to go through a lot of cohort studies although I can provide those to the committee afterwards if they'd be interested. But I thought the highest level of evidence that we have as of today are randomized clinical trials which specifically tested smokeless tobacco products for efficacy in helping smokers who want to quit in their attempts to quit.

To my knowledge, I could only find three randomized clinical trials. And the hypothesis, of course, is that if smokeless tobacco is an effective treatment or substitute for smoking, we would expect to see higher quit rates in the arm randomized to smokeless tobacco than in the control group.

So this first study came out a few years ago. It was done in Denmark. It's not a snus product, but it's what they call tobacco rolls. It's Oliver Twist pellets that are sold in Sweden.

It was a randomized open label trial, so in other words, the groups were randomized to either get the counseling alone or group counseling plus the use of this product. There was no placebo control in that.

It's six months, no significant different in either the six-month point prevalence of abstinence, about 23, 21 percent, not even close to statistically significant. And the continuous abstinence rate, very low and not statistically significant in either one of those groups. So that was the first clinical trial.

Two more recent ones. Both of these tested snus products, and both of them were placebo-controlled, both also funded in part by snus manufacturers. This one was actually a multi-site study done in the United States, randomized, double-blind, in which they were randomized to either get pouches with snus or with placebo.

At 28 weeks, it looked like a slightly higher point prevalence/abstinence rate in the snus group compared to placebo, although not

statistically significant. And again, the same patter for continuous abstinence, a couple percentage points higher, although again, quite low for both groups, and not even close to statistically significant in that particular study; and more recent study where they tested this in Serbia, also randomized, double-blind, really using the same protocol as the previous one. And I'd say pretty comparable findings: slightly higher point prevalence and continuous abstinence, although not reaching conventional levels of statistical significance; and overall, continuous abstinence rates quite low in both groups.

One of the other outcomes they looked at in that particular study was what was a reduction in mean number of cigarettes smoked per day among those who continue to smoke, which in fact was most of the participants. And, in fact, no statistically significant difference in mean number of cigarettes smoked between the two arms of that study.

So the other question is, what is the

evidence in terms of smokeless tobacco as a partial substitution? So I thought, well, if people continue to smoke, would their use of smokeless tobacco at least reduce their level of exposure to cigarette smoking?

So a couple studies that we've done looking at this. This is based on self-reported data from National Health Interview Survey. And in fact, in that study we found that adult smokers who used snuff only on some days were not significantly different from those who didn't use snuff. In mean number of cigarettes per day, both had about 18 or 19 cigarettes per day. On the other hand, those who used snuff every day did smoke, on average, about 7 fewer cigarettes per day in that particular study.

A more recent study that we did -- and granted, it's a pretty small sample size on this. These are data from a National Health and Nutrition Examination survey. This particular survey combines some self-report with some physical examination and laboratory assay for a number of

different things, including serum cotinine levels.

In this particular study -- and this is among daily smokers age 20 and over, and we looked at mean number of cigarettes per day and their mean serum cotinine levels as a function of their smokeless tobacco use. So this is daily smokers who had never used smokeless tobacco, those who used to use a form of smokeless tobacco but don't any more, those who also use smokeless tobacco but only on some days, and those who are truly dual daily users, users of both cigarettes and smokeless tobacco.

Again, with the caveat these are pretty small sample sizes, but really no difference in the mean number of cigarettes smoked per day among those groups, with the exception of those who are former smokeless tobacco users who in fact smoked significantly more cigarettes per day than these other groups. On the other hand, the dual daily use group had by far the highest mean serum cotinine level among these groups.

So again, based on this study, there doesn't

seem to be a whole lot of reduction in cigarette consumption as a function of smokeless tobacco use.

On the other hand, if you look at the prevalence of smoking as a function of smokeless tobacco use among adults, actually pretty dramatic differences among those. And again, cross-sectional data is sometimes difficult to interpret exactly what some of these things mean. But among men, who reported that they used snuff on some days, incredibly high prevalence of smoking, about 45 percent that were also smokers. Those who had quit using snuff, so they had reported that they at one time had been a regular user but no longer used it, also a very, very high prevalence.

But even among daily snuff users, the prevalence is not insignificant at about 15 percent, and really not all that different from those who never used snuff. And again, I know these are cross-sectional data. Sometimes it could reflect several different phenomena going on. But the bottom line is a very high prevalence of dual use among snuff users in this country.

One relatively recent cohort study that came out was done among a fairly large cohort of military personnel. And this was done among airmen in the U.S. Air Force. When they enter basic training, they go through a period of forced abstinence. They're not permitted to use any form of tobacco. And this actually was from a control arm of a much larger randomized clinical trial.

So to some extent, the behavior in this control arm I think of as somewhat of a natural experiment; what happened to these men -- and I say men; there were a small number of women, but it was overwhelmingly men, though -- what happened in this cohort of military personnel after they finished basic training and were allowed to either return to smoking, return to smokeless tobacco use, or some combination thereof.

So, in fact, they evaluated them at baseline, 12-month follow-up. What they actually found in this particular study was that those who were only smokers at baseline were actually much more likely to become dual users than they were to

switch completely to smokeless tobacco, by about a sixfold difference between those.

They actually found that those who were baseline dual users, those who used both cigarettes and smokeless tobacco at the baseline of this study, for one thing had the lowest rate of tobacco non-use at follow-up. So the overwhelming majority of them actually returned to using tobacco. But also, it was the least stable of the groups in that a larger proportion actually became cigarette smokers only than maintained that pattern of dual use; a quite significant difference. And actually, a much smaller percentage that went on to only use smokeless tobacco.

So at least in this fairly large cohort study, dual use really was most predictive of them going on to remaining a tobacco user, mostly moving back towards cigarettes.

But one of the things, and certainly that the FDA will need to grapple with, is how these products are marketed. It's one thing of the nature of the product itself, but who are they

marketing it to? What are the marketing messages? I'm an epidemiologist, not a dentist. I'm not a marketing expert. But I happened to come across this ad because I fly fairly frequently on both Delta and US Air. Delta has a policy of -- and they announce at the beginning of every flight. The use of cigarettes or smokeless tobacco products is prohibited. US Air has a little different announcement.

So actually, I found this ad in several issues of US Airways' in-flight magazine. I never found a comparable ad in Delta's magazine. But it's clear that -- and again, to me as a non-marketing person -- but to me, the message advertising this in an in-flight magazine, certainly with the images of windows on an airplane, promoting this particular product, at a time that -- for a time when they can't smoke, you could still have your tobacco flavor.

Then as these new products come out, and from the same manufacturer as the previous product that I just showed -- so these are some verbiage

from the website for Camel's dissolvable products. The quote here, "'I like to keep the variety pack in my car,' she says, 'or just handy in my purse. Then my options are always open.' Like many adult consumers we've talked to, Cynthia enjoys the anytime, anywhere benefit of Camel dissolvables." And again, it certainly appears to me to be targeting people to use at a time where maybe smoking is not possible or convenient.

So the bottom line, I'd say, at least based on the evidence that I've seen so far, no evidence for smokeless tobacco use in preventing smoking initiation. And in fact, I'd say the most recent data from Sweden suggests that it's possible to reduce the prevalence of both of them in parallel.

A small and not statistically significant efficacy of the use of either snus or those tobacco pellets as a smoking cessation method, although the rates of continuous abstinence were very, very low in both groups. The substantial prevalence of smoking among snuff users, particularly in this country, I couldn't find Swedish data reported in a

way that allowed me to present comparable data.

I'd say, based on at least the U.S. evidence, smokeless tobacco seems to be far more consistently associated with a partial substitution and dual use of these products than complete substitution. And I'd say that just based on some of the ads that I've seen just within the past couple months, the new U.S. dissolvable products and snus products that are now on the U.S. market are already promoted for situational substitution of smoking. And I'd say at least in my reading of the literature so far, a pretty weak and inconsistent body of evidence for smokeless tobacco promotion as a public health strategy for harm reduction.

So again, I know the charge to the committee was to look at the net effect of tobacco products on overall population harm. I'd say so far I'm just not seeing the evidence for promoting any of these products in terms of tobacco harm reduction.

I'd be happy to take your questions.

DR. SAMET: Thank you, Scott.

Let me open up for questions from the committee. Yes, John?

DR. LAUTERBACH: Dr. Samet, I'm quoting here from one of Dr. Hatsukami's papers, where it says here, "Results: General snus, parentheses, high nicotine, was not preferred by any smoker. No significant differences in preference were observed across the other tobacco products. During the smoking cessation phase, Camel snus was generally associated with greater craving relief and satisfaction, reduced use of cigarettes, and greater abstinence during follow-up compared to other products."

Can you comment on that, please?

DR. SAMET: I'm not sure who you're looking for a comment from. But we do have somebody here named Hatsukami.

[Laughter.]

DR. SAMET: And Scott, I don't know whether you want to comment.

John, that comes out of a clinical trial, I believe, or one of these panel studies, I think.

DR. LAUTERBACH: Yes.

DR. HATSUKAMI: So I guess the point that you're making is that Camel snus or a snus product might help in terms of cessation. For that particular study, we only looked at the effects over a period of two weeks. We only had them on a product for two weeks. So it's really difficult to generalize that to a larger population of smokers or whether in fact it would be replicated.

The primary purpose of that study was to determine what product that we would want to use for a much larger clinical trial, which we are conducting right now. So that's kind of a caveat related to that.

DR. SAMET: Just as a comment, if you remember, at the start, Sarah told us things we were not looking at, which did include, if I am correct, dissolvables as an actual therapeutic modality for smoking cessation.

That said, I mean, this still is broadly relevant to our charge, which has the word "impact," and that has to be considered largely.

And I think the reason we're hearing about the Swedish experience and the follow-up by Scott on smokeless tobacco in the U.S. is really to see what we can learn that may inform us, given the paucity of data on dissolvables per se that would be useful for our charge of impact.

John, do you have a follow-up?

DR. LAUTERBACH: Yes. Dr. Tomar, have you ever used Oliver Twist?

DR. TOMAR: No, I haven't.

DR. LAUTERBACH: Have you used any of the other smokeless tobacco products that were involved in these surveys you quoted?

DR. TOMAR: I've never been -- I mean, I've experimented with every one of them. I haven't -- I shouldn't say every product. But I have tried the traditional moist snuff products in the U.S. I've never been a regular user.

DR. SAMET: Actually, our report is not about Dr. Tomar.

[Laughter.]

DR. LAUTERBACH: Dr. Samet, what I'm trying

to make a case here for, having purchased some of the Oliver Twist products at my local tobacco industry in Volusia County, Florida, they are quite different in sensory effects. I want to sort out here the effects we're reporting on that deal with the sensory likeability of one smokeless product versus another that may be used in the surveys. That's all I want to point out here.

DR. SAMET: Let's see. Other questions? Bob?

DR. BALSTER: I guess I don't exactly understand the point of the slide you had with the US Airways magazine and an ad for the whatever, the Camel snus product. I didn't really think it was a question that the industry was essentially saying that these products and dissolvables could be used in situations where smoking was not appropriate or inconvenient or something like that. I never really thought that was a matter of question.

What is your point about that, exactly? That they're promoting it for use in first class cabins or --

DR. TOMAR: No. My point in both of those ads is that we have two products by the same manufacturer -- and, again the caveat, I am not a marketing expert, but certainly the interpretation I've had, and others that have looked at that, is that they are promoting dual use. They're not saying, stop smoking, in this particular ad. It's, use these products when it's not convenient for you to smoke.

When we're seeing an emerging pattern of dual use -- and in fact, dual use is most prevalent among younger people. When we're seeing a tobacco manufacturer who now controls both the manufacturer of cigarettes, a same name product in other forms, the same brand name, and promoting use of both of these products, if that's not promoting dual use, I'm not sure what is.

DR. SAMET: Tom?

DR. EISSENBERG: I guess I took a different message away from your presentation of that advertisement. I heard from Sweden that the so-called Swedish experience occurred in the total

ban of both cigarette advertising and smokeless advertising. So I thought you were trying to make the point that if we do indeed want to replicate that experience, we need to exercise those bans.

DR. TOMAR: And in fact, that particular ad in US Airways magazine -- and I in fact did write to US Airways because it's actually a violation of their own self-imposed policy on not accepting advertisements for tobacco in their publications.

DR. SAMET: Patricia?

DR. HENDERSON: Scott, did you find any data as it relates to snus and morbidity and mortality in Sweden, primarily looking at the rate of diabetes?

DR. TOMAR: There are a few studies. That's not something I reviewed for this particular presentation. There are some studies, not a large number. I don't know that we're at a -- I don't know that we have sufficient data to reach any causal conclusion on snus and risk. I know there are some studies that suggest an elevated risk, but it's only a couple studies that I've seen.

DR. SAMET: Fred?

DR. PAMPEL: Thanks for bringing this data together. It's handy to see the randomized controlled trials discussed together. But as your conclusion, the trials showed that ST was more consistently associated with partial substitution. So there were some benefits in terms of lowering the number of cigarettes among dual users. But then the conclusion is there's weak and inconsistent evidence for ST promotion as a public health strategy.

So wouldn't reducing the number of cigarettes be part of a useful public health strategy, or isn't the evidence strong enough to --

DR. TOMAR: No. Actually, in the randomized clinical trials, there was no -- at least the one that reported that as one of their main outcomes, there actually was no difference in the mean number of cigarettes smoked per day. Actually, the data I presented was from a cross-sectional study. It was not from the randomized clinical trials. And even

that, on the two U.S. studies, one looked like there was a substitution effect, the more recent data from the National Health and Nutrition Examination Survey -- in fact, it was virtually identical, a mean number of cigarettes smoked per day regardless of their smokeless tobacco use.

DR. PAMPEL: So the evidence isn't very good that it has a partial substitution effect?

DR. TOMAR: I'd say that there's some evidence from one of our studies, from the one randomized clinical trial. No, there isn't evidence in that particular study of a substitution effect.

DR. SAMET: Let me check. Mark? Arnold? Questions?

DR. CLANTON: No question here.

MR. HAMM: No question here, either.

DR. SAMET: Thank you.

Dorothy?

DR. HATSUKAMI: Scott, I'm asking you this question because I've forgotten or I wasn't really focusing on it. But in the randomized clinical

trials, do you know what the dose was of the snus products that people were assigned to? Do you remember what they mentioned? If not, I can just look at the articles, but --

DR. TOMAR: Yes. I don't know. In fact, I'm not sure if they even mentioned the specific brand or -- I assume it was unlabeled. But I don't know for sure what product was used.

DR. HATSUKAMI: What the nicotine dose -- yes.

DR. SAMET: Any other questions?

[No response.]

Committee Discussion of Question 1

DR. SAMET: If not, Scott, thank you. And again, we may turn back to you and Dr. Rutqvist in our discussions.

I think shall we unveil question number 1? And again, remember, we have a set of questions in part to help to structure our discussion and to, in a sense, get to the point. And again, thinking about our charge with the dissolvables and, as I voiced earlier, the relative lack of real world

experience, the question is, can we turn to experience elsewhere, Sweden or the United States with smokeless tobacco products in general, as outlined by Scott, to begin to get some help on our charge?

I think one point that both presentations made clear is that the context is important. And the context of Sweden in the 1970s is not now, and some of our experience with smokeless tobacco going back a ways is also not now. So things have changed over time. So I think we need to keep that carefully in mind.

So the purpose of this is really to discuss, and I think come to some resolution, around this question because we have many other issues we're going to move on to over the next couple of days. So I think you can all see this question regarding the data from Sweden.

What, if any, extrapolations can be made to use of dissolvable tobacco products from the impact of the use of traditional smokeless tobacco on oral health to the impact of the use of dissolvable

tobacco products on oral health -- I'm not sure we've actually heard very much about that, and we can, I think, for sure turn to Scott for some help on that issue. And then what factors may limit making these extrapolations?

So I think let's focus in first on the Swedish story. And I think we've had the long-run story, which was going back to that plot with declining snus use, rising snus use, and the tobacco figure that I've seen many times, and then I think, in fact, Scott's more recent coverage of what is happening at the I think it was 16 to 24 age range in terms of both snus and tobacco use.

I think the question that we really want to ask is what can we learn from this about the potential introduction of, really, another smokeless product into the tobacco marketplace. So dissolvables would be an addition to what is already there. And our charge related to impact, which does include youth in it, then I think our questions would be, what might be the impact of yet another product on tobacco product use generally,

cigarette smoking use, and then I think at the other end we have the cessation question.

So why don't we -- just to keep a little bit of focus, let's start with the questions around initiation of tobacco product use and the potential impact of having another smokeless product available, and I think take that one on first, and deal with the extrapolation.

What have we learned from the data we have seen? Have we gained something useful out of this? And it's not a fully rhetorical question since we have to write a report.

[Laughter.]

DR. HATSUKAMI: I guess I'll start. I think it's really hard to extrapolate the Swedish data to what's going on in the U.S., and there's several reasons for that. The most prominent is the promotion of co-use of cigarette smoking and the dissolvable products. So I think that's one thing that you don't necessarily see in Sweden.

Secondly, I think dissolvables are really quite different from snus in that you have such a

cultural -- as you said, Jonathan, a cultural context surrounding snus use. It was a traditional product, whereas these dissolvables are just a totally new product that's being introduced in the U.S.

Thirdly, I don't think we had the kind of educational campaigns that have been ongoing in Sweden that we do here in the United States. I think there's a lot of confusion as to the relative safety or the harm of cigarette smoking versus an oral tobacco product.

So for those reasons, I would find it very hard to extrapolate what we've seen in terms of initiation, uptake, even dual use in Sweden to a U.S. situation.

DR. SAMET: So I think just to crystallize what you've said, you really, I think, articulated the idea that we really should be very cautious in generalizing, if at all, from the Swedish experience around --

DR. HATSUKAMI: Initiation, uptake, pattern --

DR. SAMET: -- around initiation.

DR. HATSUKAMI: Not necessarily. Health consequences is another issue.

DR. SAMET: Health consequences is a different story. But on the --

DR. HATSUKAMI: Yes. Right. Right.

DR. SAMET: Sherry, were you going to comment?

DR. EMERY: I was also thinking about the limitations of generalizing from the Swedish experience. And my perspective comes from the uptake and the lack of marketing that was apparently involved in Sweden, and the completely different context for marketing tobacco products here in the United States.

DR. SAMET: Others? Fred?

DR. PAMPEL: I agree that the experience in Sweden is no evidence that the same thing will happen automatically here in the United States. There's too many differences to expect it to occur just because the product is available. Yet somehow, this remarkable experience in Sweden

suggests some potential, that if norms could be changed or if people started to think differently about cigarettes, something different might happen. So I wouldn't dismiss altogether the ability to extrapolate from Sweden to the United States.

DR. SAMET: Dan?

DR. HECK: Yes. I think, to Dorothy's comment, it is true enough. We don't have that same tradition here, national tradition of smokeless use. Traditional smokeless use here in the U.S., I think -- at least I always thought of as kind of a rural, outdoorsy novelty that -- and I didn't particularly know anybody growing up that used smokeless tobacco, I don't think.

So with the manufacturers -- well, we've seen the Marlboro and the Camel dissolvable products introduced, and snus is -- I think that with the dominant products here being traditional cigarettes, I think that the appearance of these products on the U.S. market, we kind of expect them to be done differently and perhaps paired, as we've seen, with the established brand names of

cigarettes.

Of course, that 600-pound gorilla in the room here that is off our agenda now is the relative comparative risk and the comparative exposures accompanying those two categories of products. I guess that's a subject for another day.

One other thing, just in keeping with the slide here, some differences with the Swedish products. I think we heard something about this at some of the previous presentations. But the traditional Swedish products, I think as we've seen some data presented perhaps at the previous meeting, are quite strong and quite alkaline. And I think some of these -- there are differences, and presumably some possible differences in the oral health effects that might characterize that type of product as opposed to these novel products in the U.S.

DR SAMET: Scott, let me ask. I think one thing that impressed me, back to your 16- to 24-year-olds, was two things. So in the males 16

to 24, there was decline in both smoked cigarettes and snus use. And yet in the girls, there was a rise in snus use, and if I remember right, a slight decline in cigarette use. Is that --

DR. TOMAR: Actually, there was a pretty precipitous decline in smoking that's kind of leveled off in recent years.

DR. SAMET: Microphone. I'm sorry, Scott.

DR. TOMAR: There was a pretty precipitous decline in the prevalence of smoking among girls 16 to 24, girls and young women 16 to 24. It's kind of leveled off in recent years. There's certainly been -- so we saw a pretty steep decline in the prevalence of daily smoking through about 2005, 2006 or so, and then it's kind of leveled off the last 5 years or so.

To some extent, the curve for snus is not smooth because they don't measure it every single year, so it's a little more jagged. But there certainly seems to have been an increase since the late '90s or so, although it's still only about 5 percent or so of prevalence of daily use of snus.

It's still a fraction of what it is among males in this age group.

DR. SAMET: And go back one to the males slide, I think. One slide back. That one, yes.

DR. TOMAR: Yes. So what we've seen long-term -- and back, I'd say, maybe seven, eight years ago, there was all this talk about there being this substitution effect because we were seeing this increase in the use of snus and a decline in daily smoking. And there were actually a number of publications out of Sweden at that time claiming a preventive effect when in fact when you look at it long-term, where we are today, at least over the past 20 years or more, there seems to be an almost parallel decline. Yes, snus is still more prevalent than smoking, but both seem to be declining in parallel.

DR. SAMET: So it's interesting. If you go back to the girls, and in sort of a relative steady state of product availability, there's suddenly this uptick in girls. And I'm just thinking about the U.S., where with few exceptions, prevalence of

smokeless tobacco is far lower in females.

I wonder, Dr. Rutqvist, do you have any explanation for the increment that we see here? Please come to the microphone.

DR. RUTQVIST: Excuse me, Dr. Samet. Did you mean why are young women taking up snus?

DR. SAMET: Yes. Why this recent increment in use of snus?

DR. RUTQVIST: I think it has to do with cultural tradition. In the old days, snus was, as I mentioned, a mainly male habit. But in younger age groups, differences between the sexes are becoming not so apparent any longer when it comes to use of both alcohol and tobacco. So I think it's a time trend. It reflects societal changes.

DR. SAMET: Thank you.

Yes, John?

DR. LAUTERBACH: A question for Dr. Rutqvist. Is the introduction or more prevalence of pouched or sachet snus being made more popular among the women as opposed to the traditional loose product?

DR. RUTQVIST: I think it's quite clear that both among males and females, pouched products are much more popular than the loose type of snus. And that is particularly the case among females, who do not favor use of loose snus for obvious esthetic reasons.

DR. SAMET: Dan?

DR. HECK: Just a quick question. I think it's maybe been made close on those slides. But is my recollection correct that Sweden is either unique or one of the few developed countries where the rate of smoking in adolescent females is higher than that of males? Is that accurate?

DR. RUTQVIST: That's correct. Smoking prevalence among females is higher, and I think we share this position with Norway.

DR. SAMET: Let's go back. Bob?

DR. BALSTER: So I think I was one of the people that suggested that we have a presentation on the Swedish experience. And I think it was partly --

DR. SAMET: Too late to recant?

[Laughter.]

DR. BALSTER: No, no, no, no. I'm not recanting -- I think particularly since that experience is being used to generate an awful lot of conjecture about American public health policy and how we ought to go forward.

So I would have to say, having now looked at the data and heard the presentations, I'm a little underwhelmed with the direct relationship between that experience and development of tobacco control policy in the United States for reasons that people have mentioned. I mean, I think there are some interesting things in there. I think it looks pretty clear. I suppose we should just be clear about the obvious. It looks like reductions in smoking is associated with health benefits. It's not only the Swedish experience that shows that. I believe there are data from other places that reducing cigarette smoking is associated with improved health outcomes. And I think that's evident in these data.

It's a lot less clear to me that the

reduction in smoking is causatively related to the snus situation. I mean, it could be partly related to that, but there are other things going on in Sweden that could account for that change in smoking, not the least of which was a pretty significant change in perception of risk. But at best, only a portion of change in cigarette consumption is potentially related to the uptake in use of snus. I don't believe it's been established to my conviction that all of those related changes in tobacco smoking are related to the snus.

Even more conjectural would be the tying of the relationship of smokeless tobacco use to improved health outcomes, as has been alleged. It's not even clear in Sweden exactly the extent to which snus contributes to the changes in health outcomes. And of course, it could be very specifically related to the specific snus that are available there.

So to extrapolate from a pretty tightly -- not so much regulated, but a voluntarily regulated situation with a very specific type of

product, to extend that to all of the range of smokeless products we have in the United States, and more specifically the dissolvables, which is getting to our point here, we're going pretty far away from, I think, what the situation was in Sweden to dissolvable products, which are different both in their character, different in the extent to which they have different constituencies in them.

So I would say there isn't too much relationship.

DR. SAMET: So I'm going to take that as a very long answer to 1(a).

[Laughter.]

DR. BALSTER: Yes, yes. I would say that's -- yes, sorry.

DR. SAMET: In which you are negative about making extrapolations.

DR. BALSTER: Just one further thing, that it seemed -- you began this with a discussion of initiation. It appears that if cigarettes were to go away, that there seems some likelihood that there would be initiation of tobacco use using

alternate products. And apparently, as I understand it, that's happened in Sweden, so that the new cohort of tobacco users in Sweden, because they didn't begin smoking, are now initiating with the smokeless product.

So I think it's reasonable to expect that if we were somehow to change the character of having -- of cigarettes' availability or use here, that we would begin to see initiation with alternative tobacco products.

DR. SAMET: So just to pin you down with your last comment, are you stating that's a lesson learned from the Swedish experience might be that the availability of smokeless tobacco products that are culturally -- that culturally fit, contextually fit, means that some people may turn to use of those alone at the time they initiate them. That's the suggestion from the Swedish experience of the more recent cohorts and, as we saw, with the 16- to 24-year-old data.

DR. BALSTER: I forgot the exact number, but I thought Dr. Eissenberg elicited, yes, a number of

50 percent of the current tobacco users in Sweden -- I mean, current initiators are initiating on snus, if that's the number I heard correctly.

DR. SAMET: Tom?

DR. EISSENBERG: Yes. I think Bob is questioning the role of snus in the Swedish drop in cigarette smoking. And I echo those questions. I would just say if we take it on its face value that snus did play a role in the drop in cigarette smoking in Sweden, and thus the drop of smoking-related disease, it was because snus -- and I think this is what I heard -- because snus completely substituted for cigarette smoking for a large portion of the population in Sweden.

I think it's important then to realize that when it comes to dissolvable tobacco products, I have not seen any systemically collected evidence that would suggest that dissolvable tobacco products that we have here in the U.S. will afford that complete substitution. Rather, they supplement cigarette use. And so if complete substitution is required, I'm not sure how we can

extrapolate to our dissolvable tobacco products.

DR. SAMET: Sandrine?

DR. PIRARD: So to follow up similarly on the health effects, so clearly we all know that if you see a reduction in cigarette use, you will have a significant public health effect like decreasing lung cancer and so forth.

Now, when you look at the graph showing the increase in snus -- I mean, increase and then decrease in cigarettes, basically what's compared is snus in tons versus cigarettes in million pieces. And I wonder, on a population level, at what point, basically, what kind of quantity of snus being used at a population level will lead to health impacts.

Also, I don't know if there's the same lag time as what you have with cigarettes, where you have to have about 20 to 30 years between uptake and then really when you start seeing the health effects. So what I wonder, especially with the comment made, that since cigarettes is decreasing, though you see more and more people initiating with

snus, that it might well be that 10 years from now in Sweden we'll in fact see like a re-increase in diseases like oral cancers and things like that.

DR. SAMET: Let's see. Are you wanting Dr. Rutqvist to respond to your question? I think there were a few questions directed at you. We can probably break them down and give them to you one by one.

DR. PIRARD: So I guess one was a comment saying that, indeed, it's hard to establish any causality between the fact that basically the substitution from cigarettes to snus is in fact the reason for a decrease in public health. And then the other, I guess, which is a question, is what is the lag time between an increase in snus use in the population that we'll expect it to then be translated in an increase in disease, such as frangible oral disease.

DR. RUTQVIST: I'll take the second question first. There is quite an extensive number of analytical epidemiological studies on health effects of snus. Take, for instance, the studies

on snus use and oral cancer. Among the snus users included, for instance, the case control studies, the mean duration of exposure is more than 20 years, and a substantial proportion of the snus users in those studies have used the product for more than 30 years. And still, there is no increase. There is no trend with duration of use. I think that essentially illustrates that exposure times in the available studies is quite considerable and much longer than the exposure times for smoking-related disease.

So unless there is a qualitative difference in induction time, I don't think there is reason to believe that any adverse effects would emerge after even longer exposures. It doesn't really make sense. Also, in the cohort studies, if you look at risk of lung cancer, risk of other type of smoking-related cancer, there is no trend with duration of use in the available studies.

The first question, could you please repeat that one?

DR. PIRARD: Yes. So my question was, when

we see the graph we have on one hand snus in tons and then on the other hand cigarettes in million pieces, and when we see a decrease, I mean, it's expected that if you see a decrease in cigarette use at a population level will lead to a decrease in lung cancers and so forth, which is what you see.

But when would you expect, at a population level, to really see a significant increase in some of the cancer -- I mean, what kind of threshold would you see? I'm not quite sure exactly what snus in tons and kind of -- I mean, I guess maybe I'm not phrasing this correctly. But clearly, what you see with cigarettes is that, as I said, there is not only a time lag, but also there is some kind of proportion, I guess, of the population. And then you start seeing the effect 30 years after.

So what I was wondering is that, now that it seems like people have an increased use in snus, somehow could you speculate on what will happen maybe 15 years from now or even 10 years from now as a result of this kind of increase that you have

seen over the last 10, 20 years or so?

DR. RUTQVIST: You mean in terms of health effects?

DR. PIRARD: Yes.

DR. RUTQVIST: Well, I would say that this type of ecological analysis serves illustrative purposes, at best. If you're really interested in health effects, I think you need to look at analytical epidemiological studies. I don't think this type of population level data really tells you very much. But it's illustrative for a presentation like this, but you really need to look at the epi data.

DR. SAMET: I would think, actually, the general point -- again, it goes back to the surveillance issues. In a marketplace of changing products and exposures, the question of how one tracks risk at the population level becomes very complicated. In Sweden, there have been diverse case control studies, cardiovascular disease, cancers, and so on, and a number of cohort studies. And some of them find links to snus use; pancreatic

cancer, for example, I think in the Swedish construction workers in one of the cohorts.

So the challenge, I think, is -- and I think that's what you're alluding to, is exposure at the population level changes, how does one really know what's going on. And again, I think that's part of the center's broader mission of surveillance, and one that needs to be thought through.

I think, Bob, you had a question.

DR. BALSTER: Well, I was just wondering: Are there any oral health effects that are widely attributed to snus use in Sweden?

DR. RUTQVIST: Well, particularly with the old type of loose snus, there is this problem with effects on the gingiva and gingival retraction and exposure to dental services. That risk is much decreased with pouch products.

DR. SAMET: Scott, do you want to comment on that question as well? This is certainly an area you've tracked closely.

DR. TOMAR: Sure. There's certainly evidence that use of snus products is associated

with, among other things, localized gingival recession. Yes, actually, there were a few studies that suggest a lower incidence of recession among those that use the pouch form.

The one caveat, though, is that so many of the Swedish studies were in fact industry-sponsored. Again, as somebody who teaches evidence-based dentistry to my students, it's a factor to consider in interpreting these. There's no doubt that these products are associated with oral mucosal lesions that are really of a type only found in snus or other smokeless tobacco products.

DR. SAMET: Thank you.

Dan?

DR. HECK: Just to follow up on the earlier question about the oral cancer, and I think Dr. Tomar has touched on that as well, one thing that's often forgotten is that the oral cancer risk, odds ratio as a relative risk for smoking, are in the order of 5 to 10. And even for the traditional moist snuffs, those studies mostly hover around 1.0 to 2. I just didn't want to lose

in the mix the fact that cigarette smoking is a rather significant risk factor for oral cancer itself.

DR. SAMET: Thank you.

Dorothy?

DR. HATSUKAMI: I wanted to ask a question to Dr. Rutqvist. Do you observe or do you have any data that would indicate that there's a graduation of the use of smokeless tobacco products where adolescents or maybe youth or young adults might start at a lower level of nicotine but graduate to higher levels of nicotine smokeless oral tobacco products?

DR. RUTQVIST: I am aware of the data here from the United States, where it's been suggested that there is this kind of graduation for first-time users to more experienced users. I'm not aware of any data to suggest that that phenomenon exists in Sweden. If you look at different age groups, what are the popular brands in different age groups, it's the same brands. It's the same brand that's most popular in young

people versus older people. It's the large, historical brands.

DR. SAMET: John?

DR. LAUTERBACH: Yes, Dr. Samet. I have two questions for Dr. Rutqvist. First question related to the reference to diabetes. What is the typical sugar content of Swedish snus?

DR. RUTQVIST: There is no added sugar in Swedish snus products. The only sugar that's there is the natural sugar that's in the tobacco leaves.

DR. LAUTERBACH: The second question, how does the labeling of your product in terms of government health warnings differ if you were to sell the product in Sweden versus selling the same product here in the United States?

DR. RUTQVIST: It's the European health authorities that determine the health warnings on snus products in Europe. And 10 years ago -- previously, there was a cancer warning on the snus cans, but that was removed 10 years ago because the European health authorities didn't find that there was any scientific evidence to link

Swedish snus to oral cancer. So now there is a more generic health warning, that it's a tobacco product, and that it may be addictive.

DR. SAMET: Patricia?

DR. HENDERSON: Just some general questions. How many people are in Sweden?

DR. RUTQVIST: Ten million.

DR. HENDERSON: Ten million. And then for the demographics that you provided on the graphs, is there other data that you have other than gender, like race or income?

DR. RUTQVIST: Race is normally not recorded is Swedish databases because we have -- the native population in Sweden is very, very small. So race is normally not recorded.

DR. HENDERSON: Income (inaudible - off mic)?

DR. RUTQVIST: Oh, yes. Oh, yes. If we're talking about other socioeconomic factors and so on, yes. That is available. Education, domicile, and so on. Oh, yes. That's available.

DR. SAMET: John?

DR. LAUTERBACH: I just wanted to have Dr. Rutqvist answer the second part of my question. He told us about the health warnings in Sweden. And the question I asked was if the same product was sold here in the United States, what would the health warnings have to be?

DR. RUTQVIST: Well, I'm sure you're aware that here in the United States, there needs to be rotating health warnings, including one warning for oral cancer.

DR. LAUTERBACH: Thank you.

DR. SAMET: Other committee questions? I do want to draw us back to question number 1. But we had the benefits of having two very knowledgeable individuals with us, and you've been very helpful to us.

Any other questions?

[No response.]

DR. SAMET: So let's just go back to questions we have to answer and stop asking questions. And I think I've heard a fair amount of consensus about being very cautious with

extrapolation. I think we've heard that. And I think, in writing a report, I think we could say why we are cautious. I think there's been enough voiced, I think both Dorothy and Bob and others were very good about making that suggestion.

Back to the usages, I think we've heard relatively little about this topic. I do think this is one we'll come back to. Let us ask, just is there anything else that we've heard today that we wanted to tuck away under lessons learned for our report? I'm not sure there is, but let's just make sure that's the case.

[No response.]

DR. SAMET: Let me check with those on the phone, Mark and Arnold, whether you have any additional insights or thoughts you want to add.

DR. CLANTON: No.

MR. HAMM: None for me, either.

DR. SAMET: All right.

Patricia?

DR. HENDERSON: I think it's just that the Swedish population is not as diverse as the United

States, and that's something that we need to take into consideration.

DR. SAMET: I think we've answered our first question. We have a lot to go. Let's see. And I'm not sure we have any other -- that's the end of our business for today.

So let me ask if we can break up early. I'll just remind everyone that tomorrow we're starting at 8:00 a.m. again, and just see if there's anything else before we come to a close for the day.

[No response.]

Adjournment

DR. SAMET: Okay. Then we are done. And thanks, everybody, and thanks in particular to our presenters.

(Whereupon, at 3:59 p.m., the open session was adjourned.)