FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

(TPSAC)

Thursday, March 1, 2012

1:00 p.m. to 7:00 p.m.

9200 Corporate Boulevard

Rockville, Maryland

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Meeting Roster

TPSAC Members *(voting, Special Government Employee)*

Jonathan M. Samet, M.D., M.S.*(Chair)*

Professor and Flora L. Thornton Chair

Department of Preventive Medicine

Keck School of Medicine

University of Southern California, Los Angeles

Norris Comprehensive Cancer Center

1441 Eastlake Avenue, Room 4436, MS 44

Los Angeles, California 90089

Neal L. Benowitz, M.D.

Professor

Chief, Division of Clinical Pharmacology

Departments of Medicine and Biopharmaceutical Sciences

Schools of Medicine and Pharmacy

University of California, San Francisco, Box 1220

San Francisco, California 94143–122

Mark Stuart Clanton, M.D., M.P.H.

(participating by telecom)

Chief Medical Officer

American Cancer Society, High Plains Division

2433-A Ridgepoint Drive

Austin, Texas 78754

Dorothy K. Hatsukami, Ph.D.

Forster Family Professor in Cancer Prevention and

Professor of Psychiatry

Tobacco Use Research Center

University of Minnesota

717 Delaware St. SE

Minneapolis, Minnesota 55414

Thomas Eissenberg, Ph.D.
Professor, Department of Psychology
Institute for Drug and Alcohol Studies, and
Director, Clinical Behavioral Pharmacology
Laboratories
Virginia Commonwealth University
Box 980205
Richmond, Virginia 23298

TPSAC Members *(non-voting Industry Representatives)*

Luby Arnold Hamm, Jr.
(Representative of the interests of tobacco growers -participating by telecom))
4901 Shallowbrook Trail
Raleigh, North Carolina 27616-6107

Jonathan Daniel Heck, Ph.D., DABT

(Representative of the tobacco manufacturing industry)

Lorillard Tobacco Company

A.W. Spears Research Center

420 N. English St., P.O. Box 21688

Greensboro, North Carolina 27420-1688

John H. Lauterbach, Ph.D., DABT

(Representative for the interest of small business tobacco manufacturing industry)

Lauterbach & Associates, LLC 211 Old Club Court

Macon, Georgia 31210-4708

Temporary Members *(voting)*

Robert L. Balster, Ph.D.

Director, Institute for Drug and Alcohol Studies

Virginia Commonwealth University

P.O. Box 980310

Richmond, Virginia 23298

Fred Pampel, Ph.D.
Professor of Sociology and Research Associate
Institute of Behavioral Science, Population Program
484 UCB
University of Colorado
Boulder, Colorado 80304

Ex Officio* Members *(non-voting)

Mirjana Djordjevic, Ph.D.
Program Director
Tobacco Control Research Branch
Behavioral Research Program
National Cancer Institute
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Timothy McAfee, Ph.D., M.P.H.
Associate Director for Policy
Centers for Disease Control and Prevention
4770Buford Highway NE
Mailstop K-50
Atlanta, Georgia 30341

Sandrine Pirard, M.D., Ph.D., M.P.H.
Medical Officer
Division of Pharmacologic Therapies
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Administration
1 Choke Cherry Road, Room 2-1079
Rockville, Maryland 20857

Consultants *(nonvoting)*

Sherry Emery, M.B.A., Ph.D. (*participating by telecom)*
Senior Scientist
Institute for Health Research and Policy
University of Illinois at Chicago
1747 W. Roosevelt Road, Suite 558
Chicago, Illinois 60608

Bruce Simons-Morton, Ed.D., M.P.H.
Branch Chief and Senior Investigator
Division of Epidemiology Statistics and
Prevention Research
National Institutes of Health
Bethesda, Maryland 20892

Ellen M. Peters, Ph.D.
Associate Professor
The Ohio State University, Psychology Department
235 Psychology Building
1835 Neil Avenue
Columbus, Ohio 43210

FDA Participants at the table (non-voting)

David L. Ashley, Ph.D.
Director, Office of Science
Center for Tobacco Products
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850-3229

Cathy L. Backinger, Ph.D., MPH
Deputy Director for Research
Office of Science

Sarah E. Evans, Ph.D.
Social Scientist
Office of Science

C O N T E N T S

P R O C E E D I N G S

(12:59 p.m.)

Call to Order

DR. SAMET: Let's go ahead and get started with our meeting of the Tobacco Products Scientific Advisory Committee. I'm Jon Samet, chair of the Tobacco Products Scientific Advisory Committee. Thank you for joining us. I want to make a few statements, and then the committee will introduce themselves.

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

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

we ask that the advisory committee members take care that their conversations about the topics at hand take place in the open forum of the meeting. We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion.

Also, the committee is reminded to please refrain from discussing the meeting topics during breaks. Thank you.

Caryn?

Conflict of Interest Statement

MS. COHEN: The Food and Drug Administration is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act of 1972.

With the exception of the industry representatives, all members and nonvoting voting 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

the 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 and Cosmetic Act, is being provided to participants in today's meeting and to the public. FDA has determined that members of this committee are in compliance with federal ethics and conflict of interest laws.

Under 18 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 discussion 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 impact of the use of dissolvable tobacco products on the public health, including such use among children. Discussions will include such topics as the composition and characteristics of dissolvable tobacco products, product use, potential health effects, and marketing.

This is a particular matters meeting, during which general issues will be discussed. Based on the agenda for today's meeting and all financial interests reported by the committee members, no conflict of interest waivers have been issued in connection with this meeting.

To ensure transparency, we encourage all

committee members to disclose any public statements that they 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 might have with the firms at issue.

I would like to remind everybody present to please silence your cell phones if you have not already done so. And if you are calling in, please

keep your phone on mute unless you are speaking. And I would also like to identify the FDA press contact, Michelle Bolek.

If you're here, please stand up. Thank you very much.

Introduction of Committee Members

DR. SAMET: Let me ask the committee to introduce themselves. Tom, we'll start with you.

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

DR. CLANTON: Mark Clanton, representing pediatrics and oncology. Oh, I'm sorry. Go ahead.

DR. SIMONS-MORTON: I'm Bruce Simons-Morton, NICHD.

DR. CLANTON: I think you got me.

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

DR. PETERS: Ellen Peters from Ohio State University.

DR. BALSTER: Bob Balster from Virginia Commonwealth University.

DR. BENOWITZ: Neal Benowitz, University of

California San Francisco.

DR. HATSUKAMI: Dorothy Hatsukami from University of Minnesota.

MS. BACKINGER: Cathy Backinger, Office of Science, Center for Tobacco Products. I'm sitting in for David Ashley.

DR. EVANS: Sarah Evans, Office of Science, Center for Tobacco Products.

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

DR. MCAFEE: Tim McAfee, Centers for Disease Control.

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

MR. HAMM: Arnold Hamm, representing U.S. tobacco growers.

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

DR. LAUTERBACH: John Lauterbach, Lauterbach & Associates, representing the small business tobacco product manufacturers.

DR. SAMET: Thank you.

Sarah?

DR. EMERY: This is Sherry Emery. I'm from UIC. I'm remote today.

Opening Remarks – Sarah Evans

DR. EVANS: Good afternoon, everyone. Good afternoon, and welcome to the third and final meeting of TPSAC on the topic of dissolvable tobacco products. I'm Sarah Evans from the Office of Science, and I'll be the lead scientist for this effort.

As you know, 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.

So right now I'm going to talk about what to expect with the report on the nature and impact of the use of dissolvable tobacco products on the public health. The language right here comes directly from the Act. In terms of referral and considerations:

"The Secretary shall refer to the TPSAC committee for report and recommendation under section 917(c)(4) the issue of the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children. In its review, the Tobacco Products Scientific Advisory Committee shall address the considerations listed in subsection (a)(3)(B)(i)."

Report and Recommendation: "Not later than two years after its establishment, the TPSAC shall submit to the Secretary the report and recommendations required pursuant to paragraph 1."

Final report: The report and recommendations will be deliberated on and finalized at the conclusion of this meeting. The report will also be made available to the public on FDA's website once it has been reviewed for redaction of any commercial confidential or trade secret information.

FDA actions: Once the report from TPSAC is received, FDA will consider the report and recommendations of the committee, as well as other scientific evidence concerning dissolvable tobacco

products, and make a determination about what actions, if any, are warranted. There is no required deadline or timeline for FDA to make such a determination. Any sale, distribution, restrictions, or product standards are implemented through notice and comment rulemaking.

Today's meeting, we will start, actually, with the open public hearing, and then we will have what we hope is a robust discussion of the TPSAC report summary. Finally, we will vote on the TPSAC report. And right now I'm just going to discuss for everybody or announce the questions to the committee for today's discussion.

Number 1. Regarding the summary of the TPSAC consideration of dissolvable tobacco products, what changes should be made to any part of the document? In particular, do you have any disagreements or concerns regarding the key findings from the evidence review? What changes would you make to this assessment of the available evidence? In particular, do you have any disagreements or concerns regarding the recommendations for further information-

gathering, surveillance, and research? What changes should be made to these recommendations for further information-gathering and study?

Number 2. The TPSAC report on dissolvable tobacco products will include the summary document as well as the background materials, transcripts, presentations, and minutes from the three TPSAC meetings on dissolvable tobacco products. Would you like to provide any clarification for or dispute any information provided to the committee or resulting from the committee process, such as meeting transcripts, that will become part of the committee report?

Finally, for number 3, we have our voting question today. Do you agree with the report, which consists of a summary from the committee as well as background materials, transcripts, presentations, and minutes from all three TPSAC meetings on dissolvable tobacco products?

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

DR. SAMET: Are there questions for Sarah?

[No response.]

DR. SAMET: Thank you. And I think we, in going around, missed Sherry Emery on the phone.

Are you there?

[No response.]

DR. SAMET: All right. So we do have Sherry Emery on by telephone.

DR. EMERY: Oh, hello. I'm on. I'm sorry. I was muted.

[Laughter.]

DR. SAMET: You're unmuted now. Welcome, and now we know you're there.

DR. EMERY: Thank you.

DR. SAMET: And as we move along, if I'm ignoring you, unmute and get my attention. Okay?

DR. EMERY: I will. Thanks.

Open Public Hearing

DR. SAMET: All right. Thank you.

So we'll move on now to the open public hearing portion of the meeting.

Both the Food and Drug Administration, the FDA, and the public believe in a transparent process

for information-gathering and decision making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the committee of any financial relationship that you may have with the sponsor, its product, and, if known, its direct competitors. For example, this financial information may include the sponsor's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting.

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

The FDA and this committee place great importance on the open public hearing process. The

insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many topics there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way, where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore, please speak only when recognized by the chair. Thank you for your cooperation.

So we have four public commenters today. You've each been allocated 10 minutes for your presentation, and you will receive a warning when you have two minutes left in your presentation. I think the lights are up on the podium for you to see. And at the end of 10 minutes, please end your presentation.

Our first presenter is Elaine Keller, president, the Consumer Advocates for Smokefree Alternatives Association. Please.

MS. KELLER: Good afternoon. My name is

Elaine Keller, president of CASAA, The Consumer Advocates for Smokefree Alternatives Association. I have no conflicts of interest.

Before I address TPSAC's draft report on dissolvables, I have a true story to share with you. During the last several years that I smoked, I was being kept awake by my own loud nighttime wheezing, I had a productive morning cough, and laughing would trigger an embarrassing coughing jag.

On March 27, 2009, I finally smoked my last cigarette. Within a month, the wheezing and the morning phlegm were gone. Best of all, I was able to enjoy a good belly laugh for the first time in years.

Now, how many of you believe that these health improvements would have happened if I had continued smoking for the last three years? Anyone? Me, neither.

Why didn't I stop smoking earlier? It wasn't for lack of trying. The problem is that every medically approved smoking cessation method requires complete abstinence from nicotine. When my inability to concentrate, pay attention, and remember became

unbearable, I would relapse. I'd try it again, only to experience defeat time after time.

Don't think for a moment that I'm the only victim on this wheel of misfortune. The vast majority of today's smokers will never be able to quit if nicotine abstinence is a requirement.

How did I finally manage to stop inhaling smoke? I switched to what was then a brand-new product called an electronic cigarette. The device vaporizes a liquid solution that contains a small amount of nicotine. Imagine my dismay when I learned the FDA wanted to ban these products.

I used to believe in science and in the honesty and goodwill of scientists, researchers, and doctors. In July 2009, I lost my credulity and my innocence. The FDA's Center for Drug Evaluation and Research issued a news release headlined, "FDA and Public Health Experts Warn about Electronic Cigarettes."

The press statements cleverly employed classic propaganda techniques with the goal of making the public believe that these products are much more

dangerous than smoking. "They contain carcinogens and toxic chemicals such as diethylene glycol, an ingredient used in antifreeze," announced the lead paragraph.

The words "carcinogens" and "antifreeze" were carefully selected, aimed at creating feelings of fear and loathing on the part of the public. CDER failed to mention that conventional tobacco cigarettes contain nearly 16,000 times higher levels of the so-called carcinogens. The FDA found 1 percent DEG in a cartridge that holds half a milliliter of liquid. CDER failed to mention that even a small adult, weighing in at 50 kilos, would need to drink the contents of a thousands cartridges in a single day to reach a lethal dose.

Unsupported conjecture was expressed with all the conviction of proven fact by a host of experts who had no firsthand knowledge whatsoever. The goal of the campaign was to make the public believe that these products are much more dangerous than conventional combusted cigarettes. To a large extent, the campaign was effective. Smokers who had

been considering trying e-cigarettes announced, "Man, those things will give you cancer or poison you. I'm sticking with my smokes."

Numerous foreign countries banned sales of e-cigarettes based on the press coverage of the FDA's testing. Millions of smokers across the world were denied the opportunity to switch to an alternative that might have saved their bodies from further smoke damage.

I have seen some of the same hidden persuader techniques applied in the testimony and reports presented to this committee regarding dissolvable tobacco products. I commend the committee for looking past the hype and recognizing that dissolvable tobacco products reduce exposure to TSNAs and do not increase nicotine intake.

The important issue is not that some potentially harmful substances have been detected in the products. We have these in our drinking water. The issue is whether these substances are present in large enough quantities to endanger health. Are they? The peer-reviewed literature failed to reveal

this important information.

It isn't enough to say that TSNA yields of dissolvables are lower than those of cigarettes. The public should be informed that levels are more than 100 times lower. If switching to snus results in the same life expectancy as becoming completely abstinent, it stands to reason that switching to a dissolvable form of tobacco could provide similar lifesaving benefits.

TPSAC's draft report states the 50 percent of snus users in Sweden are new tobacco users. The report needs to acknowledge that increased use of snus has lowered both the smoking rates and the total use of tobacco. In 1981, 47 percent of males used tobacco and 34 percent were smokers; 27 percent of women used tobacco, and nearly all of them smoked. The percent who were snus users grew modestly, but total tobacco use among men dropped to 31 percent and among women to 20 percent.

It isn't enough to state that labeling in Sweden differs from the U.S. It's important to point out that labeling in Sweden doesn't mislead tobacco

users into believing that switching to smoking won't increase their health risks.

Why is the FDA concerned that availability of products with much lower health risks than cigarettes might lead to increased used? Even if every single adult in the U.S. took up use of a tobacco product that was 90 percent less hazardous than smoking, there would be 171,000 fewer deaths from tobacco each year. But it is probably more likely that snus, e-cigarettes, and dissolvables are 99 percent less hazardous than smoking, which would save over 400,000 lives every year.

The Institute of Medicine's 2001 report, "Clearing the Smoke," mentioned something that really should be obvious to everyone in this room. The faster you can help smokers to stop inhaling smoke, the less irreversible damage will be done to their bodies. Conventional smoking cessation methods and products are not working fast enough.

One tool to help smokers halt the damages is to encourage them to switch to non-smoked sources of nicotine such as snus, e-cigarettes, and dissolvable

tobacco products, even long-term use of NRTs. It boggles my mind that some people in tobacco control believe that if only they can discourage smokers from switching to something safer, those smokers will suddenly quit altogether.

This type of magical thinking is dangerous. Even if someday they do quit altogether, someday will be too late for many smokers. Let's stop insisting on the perfection of complete nicotine abstinence. It isn't working. Let's strive for the good of harm reduction. Thank you.

DR. SAMET: Thank you. And are there questions or comments from committee members?

[No response.]

MS. KELLER: I left them speechless.

DR. SAMET: Thank you.

We'll move to our next speaker, Bill Godshall, executive director of Smokefree Pennsylvania. Please.

MR. GODSHALL: I'm Bill Godshall, founder and executive director of Smokefree Pennsylvania. Since 1990, we've advocated local, state, and federal

policies to reduce indoor tobacco smoke pollution, reduce tobacco marketing to youth, increase cigarette tax rates, hold cigarette companies accountable in civil court, and to otherwise reduce cigarette consumption. For disclosure, neither Smokefree Pennsylvania nor I have ever received any funding from any tobacco, drug, or electronic cigarette company.

Once again, I urge TPSAC to cite in its report the extensive and consistent evidence that smokefree tobacco products are about 99 percent less hazardous than cigarettes, that more than 99 percent of all tobacco diseases and deaths are attributable to daily inhalation of tobacco smoke, and that several million smokers in the United States have already quit smoking cigarettes by switching to smokefree alternatives.

It was wrong for cigarette companies to mislead the public about the risks of cigarettes for decades, but it is far worse when public health agencies deceive the public about the comparable health risks of cigarettes and noncombustible tobacco

products.

Ever since Congress mandated the three inaccurate and misleading warning labels on all smokeless tobacco products in 1986, federal health agencies have been committing public health malpractice by deceiving the public to believe that smokeless tobacco products are just as hazardous as cigarettes and by discouraging smokers from switching to far less hazardous smokefree alternatives.

Until recently, however, federal health agencies correctly stated that cigarette smoking is the leading cause of disease and death. Unfortunately, during the past several years, federal health agencies have begun to claim that tobacco use is the leading cause of disease and death in another deceitful attempt to confuse smokers and the public to believe that all tobacco products are as hazardous as cigarettes. Federal health agencies also have begun to falsely claim that the cigarette epidemic is a tobacco use epidemic to further deceive the public.

Last year, the FDA falsely stated on its modified risk tobacco product web page, entitled

Health Fraud, that, "No tobacco products have been scientifically proven to reduce risk of tobacco-related disease, improve safety, or cause less harm than other tobacco products." That is a lie.

Since 2009, the FDA has misrepresented its own laboratory test findings on electronic cigarettes to scare the public and falsely claim the products were target marketed to youth. These and other false and misleading health claims are still on FDA's website.

Smokers have a human right to be truthfully informed that smokefree products are far less hazardous alternatives to cigarettes. Consistently, health agencies, organizations, and professionals have an ethical duty to truthfully inform smokers that smokefree products are far less hazardous than cigarettes.

The good news is that during the past decade, in the United States cigarette consumption declined 32 percent, including a 20 percent decline in just the past three years. Meanwhile, moist snuff consumption increased 54 percent the past decade,

with adult smokers accounting for the majority of new snuff users.

During the past five years, snus consumption has increased by double digits annually, with adult smokers accounting for most new snus users. And e-cigarette consumption has experienced triple-digit annual increases, with adult smokers accounting for virtually all e-cigarette users.

In the past decade, smokefree tobacco products have increased from 10 percent to 20 percent of total tobacco consumption in the U.S. My goal is to get it to 50 percent.

Since several million smokers in the U.S. have already switched to smokefree tobacco alternatives, it's mathematically impossible for smokefree products to increase tobacco-attributable mortality, even if every single American began using a dissolvable and/or other smokefree tobacco product.

A 2010 national survey on drug use and health found that nearly 70 million Americans reported using a tobacco product in the past month, including 58 million cigarette smokers, 13 million cigar

smokers, 9 million smokeless tobacco users, and 2 million pipe smokers. And a recent CDC survey just found that 2.7 million Americans had used an e-cigarette in the past month.

But only half of the nation's 70 million tobacco users -- that is, the 33 million daily cigarette smokers -- will suffer the overwhelming majority of tobacco diseases and deaths. That is why the only effective way to reduce tobacco disease and death is to continue reducing daily cigarette smoking and cigarette consumption.

In contrast, tobacco mortality reductions will be negligible, even with huge declines in the number of smokefree tobacco users, cigar smokers, and even non-daily cigarette smokers, which now account for 30 percent of all cigarette smokers.

Dual usage of cigarettes and smokefree tobacco products is a necessary prerequisite for smokers to switch to less hazardous smokefree alternatives, and dual use can occur for weeks, months, or years. While complete cessation from cigarettes provides the most health benefits, smokers

who don't quit smoking but instead substitute smokefree alternatives for many or most cigarettes also reduce their health risks.

Smokeless tobacco opponents have long claimed that smokeless tobacco is a gateway to cigarettes, but survey data has consistently found the exact opposite. In September, SAMHSA released the most comprehensive assessment to date, and found that two-thirds of U.S. residents who had reported using both cigarettes and smokeless tobacco in their lifetime had used cigarettes prior to using smokeless tobacco, and that fewer than one-third had used smokeless tobacco prior to using cigarettes.

Since surveys have consistently found that more than 75 percent of Americans inaccurately believe that smokeless tobacco is as hazardous as cigarettes, the most cost-effective way, actually free way, to reduce the number of smokeless tobacco users who switch to cigarettes is for health agencies, organizations, and professionals to begin truthfully informing the public that smokeless tobacco products are far less hazardous.

For more good news, according to the Monitoring the Future survey, during the past 15 years cigarette smoking has declined by 75 percent among 8th graders, by 67 percent among 10th graders, and by 50 percent among 12th graders.

The Monitoring the Future survey also found declines in smokeless tobacco use among youth during that time, while the 2010 National Survey on Drug Use and Health found that the past month use of cigarettes, cigars, smokeless tobacco, and pipe tobacco among youth between the ages of 12 and 17 have all declined between 2007 and 2010.

Illegal tobacco sales to minors have also declined dramatically in this country, as the Food and Drug Administration's recent inspections found just 4 percent of retail stores willing to illegally sell to a minor. And that is a huge reduction from the 50 percent sales rates that we were finding 25 years ago when we urged Congress to pass the Synar Act, and 18 years ago when we convinced then-Commissioner David Kessler to include what is now called the 1996 rule to assert jurisdiction over

that, which requires compliance inspections.

In regards to the committee's draft summary report on dissolvables, I recommend eliminating Figure 1 because no evidence was presented indicating that dissolvables cause disease or death, case nicotine addiction, reduce the likelihood of smoking cessation, or are a gateway to far more hazardous cigarettes.

In sharp contrast to Figure 1, the evidence indicates that all smokefree tobacco products are far less hazardous than cigarettes, that most new dissolvable tobacco users are adult smokers, and that smokers are far more interested in trying dissolvables than are non-tobacco users.

Mark Wolfson's survey on college students found that smokers were 13 times more interested in trying to use a dissolvable than were non-tobacco users, and less than 1 percent of all non-tobacco users indicated any interest in using any of the smokefree tobacco products.

In the Peer-Reviewed Literature section of the draft summary, the proposed statement claiming,

"One study showed that Ariva was perceived as being a non-tobacco product" should either be eliminated or be changed to state that one study found that Ariva tasted better than Commit lozenge. The proposed statement that, "Consumers have not responded positively to current products" should be deleted because it is inconsistent with actual consumer purchasing behavior.

All references in the draft summary to the Indiana experience and to the Y-Street presentations should be eliminated because deceptive propaganda campaigns that demonize products cannot be considered objective scientific evidence. Y-Street's push poll only found that some youth can be manipulated to agree that some tobacco products look like candy, and that they might be willing to try to use the product, only after being shown photographs of never-before-seen tobacco products that were strategically placed beside selectively chosen and easily recognizable candy products.

Y-Street also found that some adults can be deceived to believe that the push poll is scientific

evidence. Although it would have received an F in any basic research methods course, its authors were invited by FDA to present their findings to this committee, and several TPSAC members couldn't even recognize the built-in bias of the so-called survey even after I repeatedly informed them. Besides, it is unethical for anyone, especially health agencies, to deceive youth into believing that tobacco products are candy, as doing so only encourages youth to use the products.

I also urge the committee's report to recommend eliminating three mandatory warning labels on smokeless tobacco products, at least for the dissolvables. There is no evidence that dissolvables have ever caused mouth cancer, tooth loss, or gum disease, and by claiming it is a not-safe alternative only discourages and confuses people to believe they are just as hazardous as cigarettes.

Thank you very much. I'll be happy to answer any questions.

DR. SAMET: Thank you.

Questions or comments?

[No response.]

DR. SAMET: Sherry, just not to forget you?

[No response.]

DR. SAMET: Thank you. We'll move on to our next commenter, Dr. Michael Ogden, senior director of regulatory oversight, R.J. Reynolds Tobacco Company.

DR. OGDEN: Thank you, Mr. Chairman.

Good afternoon, ladies and gentlemen. Reynolds appreciates the work done by the TPSAC during their review on the nature and impact of the use of dissolvable tobacco products on the public health. While we agree with a number of the draft summary report conclusions, we also believe there are a number of findings that merit further consideration and comment.

First and foremost, though, we do agree with the finding that dissolvable tobacco products are likely to be associated with far lower disease risks than cigarettes. RJR strongly believes that the disease risks associated with smokeless tobacco use have been demonstrated to be substantially lower than those for cigarette smoking, and that the risks for

dissolvable tobacco would also be lower. This is consistent with findings from TPSAC's draft summary report.

The evidence for these types of noncombusted tobacco products must be viewed as unequivocal, as detailed in RJR's citizen petition to FDA requesting that one of the warning labels required for smokeless tobacco products be amended from "Warning: This product is not a safe alternative to cigarettes," to "Warning: No tobacco product is safe, but this product presents substantially lower risks to health than cigarettes."

Unfortunately, TPSAC's second draft summary report now includes a new statement that continues to perpetuate the half-truth of the currently mandated warning statement. It says, "No tobacco product is safe, and DTPs are not a safe alternative to conventional smoking products." We strongly urge TPSAC to reconsider this proposed new statement in the report and align it more correctly with the evidence that clearly shows regarding smokeless tobacco products in general.

Support for this request, which again is summarized in RJR's citizen petition, includes findings from more than 100 epidemiology studies demonstrating that the use of smokeless tobacco is associated with substantially less risk for disease compared to cigarette smoking, and that for nearly all smoking-attributable diseases, the associated risks are not significantly increased compared to never tobacco users.

For example, among the 14 appropriately controlled U.S. studies conducted since 1990 that examine oral cancer risk among smokeless tobacco users, not a single study indicates an increased risk for oral cancer compared to never tobacco users. Moreover, smokeless tobacco use is not associated with an increased risk for developing lung cancer, respiratory disease, or heart disease.

RJR agrees with opinions expressed during the open public hearing and the public submissions that government agencies, including TPSAC and FDA, should be more proactive in educating the public on the comparative disease risks associated with the various

tobacco product categories; that is to say, the pronounced continuum of risk from those products associated with the greatest risk for disease, cigarettes, to those associated with the least risk, smokeless tobacco products, including dissolvable tobacco products, without combining all tobacco products into a single category of equal risk.

RJR respectfully disagreed with TPSAC's narrow consideration in the first draft summary report of whether the Swedish experience is generalizable to the U.S., as summarized. To TPSAC's credit, that position has been moderated slightly, and more appropriate statements now appear in the second draft summary.

The Swedish experience should be viewed as an example of what is possible if smokers switching to using a tobacco product associated with significant less risk for disease do so in significant numbers. Such a change in tobacco use behavior would provide substantial individual and population-level benefits regardless of the unique characteristics of that population.

TPSAC members were provided data on the Swedish experience, suggesting that both daily smoking and daily snus use among males age 16 to 24 years have declined during the past data. While those data were intended to suggest that product substitution was not occurring among Swedish males, these data instead indicate that younger males are initiating cigarette smoking, snus use, and total tobacco use at declining rates, which in turn represents a significant population-level benefit.

TPSAC members heard evidence that the Swedes are well-informed with regard to the lower disease risks associated with smokeless tobacco compared to smoking, which in turn likely impacts their tobacco use behavior.

To be clear, peer-reviewed studies from Sweden have consistently demonstrated that during the last decade, daily smoking among males aged 16 to 84 years has decreased by about 50 percent as daily snus used has increased by about 50 percent. This product switching or substitution has, for example, led to significant reductions in lung cancer

mortality to the lowest levels of any developed nation.

The TPSAC initial draft summary report made two notably incorrect statements: one, that females are more likely to use snus and continue to smoke, and two, that complete substitution of snus for cigarettes is needed to achieve health benefits.

The first statement has been appropriately corrected in the second draft, as there is no evidence in Sweden that females are more likely than males to be dual users of snus and cigarettes. The second statement has been moderated in the current draft report, but we believe warrants additional clarification.

While complete substitution of cigarette smoking with snus use would provide a maximum benefit in terms of both individual disease risk and population-level harm, decades of epidemiologic research has demonstrated that disease risk is influenced significantly by cigarettes per day and years of smoking. In fact, corresponding dose responses have served as a primary basis for

establishing causality.

For example, data from the 1989 U.S. Surgeon General's report indicates that lung cancer mortality ratios for both male and female cigarette smokers increase in a dose-dependent manner based on number of cigarettes smoked per day. The suggestion in the draft report that 50 percent are new tobacco users requires additional qualification.

The psychological and social risk factors for initiating tobacco use are well-established; for example, family peer group tobacco use, poor academic performance, risk-taking behavior in general, et cetera. And a small proportion of never tobacco users will be at an increased risk for initiating tobacco use each year. However, Swedish studies consistently demonstrate that young males who are at increased risk for initiating tobacco use are preferentially choosing to use snus instead of cigarettes, and that those who initiate snus use are significantly less likely to become, ever, cigarette smokers.

This change in behavior represents a

population-level benefit that has resulted in Sweden being the only country whereby the male smoking prevalence is substantially lower than that for females.

Ultimately, TPSAC concluded that dissolvable tobacco products are not having a meaningful effect on any of the potential mechanisms that could impact public health, as specified by the proposed conceptual framework.

While we agree that there is currently insufficient epidemiologic data specific to dissolvable tobacco use to support unqualified conclusions, Reynolds would argue that there is sufficient evidence for the category of smokeless tobacco products to indicate that increased use of dissolvable tobacco is more likely than not to decrease population-level harm.

The disease risks associated with smokeless tobacco use are, at a minimum, significantly reduced compared to cigarette smoking, with sufficient evidence to indicate that the associated risks are unlikely to be significantly increased compared to

never tobacco use.

RJR believes that dissolvable tobacco products present the same or lesser risks. Thus, public health concerns regarding these products are effectively narrowed to the potential for dual use, to increase tobacco consumption and/or decrease smoking cessation, and the potential for these products to increase smoking initiation.

Even if the data from a substantial number of Swedish studies, which consistently demonstrates no adverse population-level effects associated with increased smokeless use, are not considered, the industry has identified a sufficient number of U.S. studies -- has identified a number of these studies that indicate that dual use of smokeless tobacco and cigarettes is not associated with increased cigarette consumption or decreased smoking cessation. To the contrary, dual use would appear to instead be associated with reduced cigarette consumption and increased cessation of smoking.

Thank you very much.

DR. SAMET: Thank you. Just as a comment or

perhaps a clarification, there's not really a first draft and a second draft. There was a draft created for discussion, and then individual commenters have provided their -- so there's not been any group process leading from a first draft to a second draft.

DR. OGDEN: Fair enough.

DR. SAMET: I just want to make that clarification.

Questions or comments from the committee?

[No response.]

DR. OGDEN: Thank you.

DR. SAMET: Thank you.

Our next presenter is James Dillard from Altria Client Services.

MR. DILLARD: Good afternoon, Dr. Samet. Thank you. And good afternoon to the advisory panel. Welcome to the end of your journey on dissolvables. My name is Jim Dillard. I'm senior vice president for regulatory affairs at Altria Client Services, and I'm here today on behalf of Phillip Morris USA and U.S. Smokeless Tobacco Company.

We've been actively engaged with both the FDA

and the TPSAC on the issue of dissolvable tobacco products, including submitting comments to the docket and making presentations during both public and the closed session at some of the earlier TPSAC meetings. And as you, the TPSAC, finish your work relating to the dissolvable tobacco products, I'd like to make just a few brief points relating to the draft report.

First, we too, as the last speaker mentioned, are encouraged that the draft acknowledges that available evidence supports the conclusion that dissolvable tobacco products are likely to be associated with far lower disease risk than cigarettes. We believe that dissolvable tobacco products can play a role in reducing the harm from cigarette smoking.

We want to be clear. A harm reduction strategy must compliment, and not compete with, proven strategies to discourage initiation and promote cessation. Everyone must stay focused on these core strategies to reduce tobacco-related harm.

We also recognize that despite focused efforts to discourage initiation and promote

cessation, many adults will continue to use tobacco products. In fact, you heard from some of those adult consumers during the public comment period at the January TPSAC meeting.

Our research tells us that about 30 percent of adult smokers are interested in smokeless alternatives to cigarettes. For these adult smokers, products that are lower on the continuum of risk should be made available, with the goal of reducing tobacco-related morbidity and mortality.

Second, TPSAC's draft report correctly acknowledges the importance of how communication to adult tobacco consumers can impact use patterns for dissolvable tobacco products. We believe that adult tobacco consumers have the right to receive, and manufacturers have a right to communicate, complete, accurate, and non-misleading information about tobacco products, including dissolvable tobacco products. This includes information that certain tobacco products are associated with reduced risk of disease compared to other tobacco products.

Such communications are important because

studies show that the vast majority of smokers continue to believe that smokeless tobacco is as harmful as cigarette smoking. For example, a 2005 survey by O'Connor et al. of over 2,000 adult U.S. smokers found that only 10.7 percent correctly agreed that smokeless tobacco products are less hazardous than cigarettes, while 89.2 percent disagreed, and 6.4 percent didn't know.

More recently, Reagan et al. published the results of the 2009 general population survey of awareness and beliefs about tobacco use. Among respondents aware of snus, 49.9 percent thought that snus was as harmful as cigarettes, 8.3 percent thought that snus was more harmful than cigarettes, and only 4.5 percent thought that snus was less harmful than cigarettes.

Generally, similar findings were observed for dissolvable tobacco products. Among respondents aware of dissolvable tobacco products, 6.6 percent thought they were more harmful than cigarettes, 39.2 percent thought they were as harmful as cigarettes, and only 3.8 percent thought dissolvable

tobacco products were less harmful than cigarettes. And a large proportion, 50.3, were unsure.

Complete, accurate, and non-misleading communications about dissolvable tobacco products should be a priority for both the FDA and manufacturers.

My third point relates to TPSAC's discussion of what it calls mixed-use patterns involving multiple tobacco products, including dissolvable tobacco products. As we've shared previously, cigarette smoking is the most hazardous type of tobacco use. That harm can be reduced from greatest impact to least impact by not smoking, decreasing the number of years smoked, decreasing the number of cigarettes per day, and finally, decreasing smoke exposure per day.

As FDA studies the issue of so-called mixed-use patterns, I'd like to remind TPSAC and FDA about a September 2010 paper by scientists in our company, Altria, published in the Nicotine and Tobacco Research, entitled, "Does Dual Use Jeopardize the Potential Role of Smokeless Tobacco in Harm

Reduction?"

In that article, we reviewed the available literature on health effects and trajectories of use among dual users from a variety of U.S. and European epidemiologic studies. The data suggested that there are not any unique health risks associated with the dual use of smokeless tobacco and cigarettes, which are now anticipated from smoking cigarettes alone.

Further, studies show that dual users smoked fewer cigarettes than exclusive smokers, and studies of tobacco use patterns over time indicate that dual users are more likely than exclusive cigarette smokers to cease smoking. We urge the FDA to review this information as it considers the issues surrounding so-called mixed use.

My final point was going to be about the Swedish experience, but I think the previous speaker did a nice job and raised the same points that we would and wanted to raise. So in the interest of expediency, I'll end there. And I appreciate the opportunity to address you today, and would take any questions.

DR. SAMET: Thank you.

Questions or comments? Tim?

DR. MCAFEE: Thank you very much. I just have a very quick question.

Given that you've acknowledged that a lot of this will boil down to a couple of issues relating to initiation and dual use patterns, cessation, et cetera, one possibility, it seems, would be that there's not some immutable characteristic of these, the physical elements of these products, that would make it so that they would or would not do some of these things. And some of this is going to relate to, functionally, how they are marketed, promoted, et cetera.

Is Altria willing to engage in further efforts to ensure that anything that might happen around the messaging, the regulation of dissolvables or other similar products, where there would be restrictions and/or specific elements around the messaging, to make absolutely crystal clear not just that people understood the issues associated with individual use if they only used that product, but

they understood the more nuanced issues associated with how this may impact their likelihood of quitting or starting, et cetera?

MR. DILLARD: Dr. McAfee, I think that's getting to a larger question, which is, I think, claims and modified risk tobacco products. Certainly, if a manufacturer were to make a claim about a product -- and I think that would be in any sense an engagement that, by statute, we have to have with both the agency and likely with this TPSAC. So I think it includes all the things that you listed, and probably others as well.

DR. SAMET: Other -- yes, Mark?

DR. CLANTON: Mr. Dillard, forgive me for having my back to you, but I'll turn around in a second. As a segue to that question, it seems in some of the presentations there was a desire -- I'll characterize it as a desire -- to have FDA educate the public to statements about potential safety or improved marginal safety of these dissolvable tobacco products.

Is there an intention, or do you have any

knowledge, that various members of the industry are planning to actually submit claims of lesser harm or greater health to the FDA? Because I don't think we've seen that yet.

MR. DILLARD: At least from my perspective, that would be something that would be competitively sensitive on any activity that we have. But I could just in general say I'm sure the industry is looking very closely at this. We're very well aware that the modified risk tobacco product guidance document will be coming probably in April, and we're awaiting that anxiously.

DR. CLANTON: Thank you.

DR. SAMET: Any others? Sherry? Just to make sure we don't forget you.

[No response.]

Committee Discussion

DR. SAMET: Thank you.

The open public hearing portion of this meeting has now concluded, and we will no longer take comments from our audience. The committee will now turn its attention to address the task at hand, the

careful consideration of the data before the committee, as well as the public comments. So thank you for your comments.

Now, I think just to reorient ourselves to the task, I want to go back to the slides that Sarah showed us. The first, I think, two or so essentially said, discuss the report. And that's what our job is. And then we do end with a voting question.

So what changes should be made to any part of the document was the first. And the second, do you have any disagreements or concerns? You might even have some agreements, perhaps.

Let's see. What comes next here? And again, my reading of this is we need to have a full and open discussion of the draft. And I think -- is the next one our voting question? Yes. And then we end with a voting question about the report.

I want to remind you that what was written was a summary of our discussions and a distillation of where I thought we were at the end of our January meeting, that this report, as modified based on discussions at this meeting, along with a larger set

of materials, including the transcripts, the presentation materials, other materials gathered on dissolvables, will constitute the report.

Some of you may have seen on the website that there is a compilation of what we have heard at our prior two meetings and the materials submitted to TPSAC. So I just want to show you that, in fact, there's been fairly substantial material that has both been found by FDA through literature searches, presented by various parties in both our open and closed sessions. And if we can pull that up, we will; and otherwise, I will tell you that it's a long list.

[Pause.]

DR. SAMET: So really, as a reminder, this is a compilation of the materials from the various sessions. And I think you can just thumb down through this. There's the July materials, and continuing on to January.

So we've seen a lot. And again, this set of materials is part of the report on dissolvables. So this, of course, fortunately is different in form

from the menthol report, for those of you who are menthol report survivors.

So our job today is to go through the draft. As you remember, I "volunteered" at the end of our last meeting to write a summary that I thought captured our discussions as we had put them together, particularly on the last day of the January meeting. You have in your folder the document that contains that report, with editorial comments as well as -- editorial changes as well as comments.

So what we need to do is to move through this and reach a document that the voting members will be able to vote on. And that is the goal for the meeting. I'll just remind you that once that is done, we actually get to go home. So just keep that in mind as you think about how much time you want to spend on the details.

I think what we don't need to do here is wordsmith. And I don't know how many times I've been at meetings and said, we're not going to do wordsmithing here, and somebody goes, you know, just let's make this little change. And so I'll try and

keep us from doing that, and that we will make certain that grammatical things are fixed and so on.

So I think what we should do is plow into this and get going. I of course found the first comment to be something I particularly agreed with.

[Laughter.]

DR. SAMET: There may have been other comments in green that I did not find quite so friendly.

DR. HECK: I'm standing by that comment, Mr. Chairman.

[Laughter.]

DR. SAMET: But I will say that I appreciate positive feedback. But all I was really trying to do was capture the spirit of our discussions.

So I think we have this in front. I think that this is going to be a somewhat challenge to me to keep everybody here in line. So Caryn will help me keep track of who wants to speak and comment. And let's try and do this essentially panel by panel with the hard draft, and I think that will keep us organized.

I think what I'd like to do is, as we go through this page by page, when we think a page is done, we'll just go on to the next page and comment through. So let's do this, then I'll just call out pages, and anybody who wants to comment, to do so.

I suspect there might be some general comments overall. But perhaps maybe just hold those. Let's go through the details here, and then if we don't cover points that you think are overarching as we go through them, let's come back to that at the end.

Yes, Neal?

DR. BENOWITZ: Well, there's one overarching comment that I think relates to the speakers that we've heard and our past discussions, which I think is important to deal with. And that is the use of the term "smokeless tobacco" and "dissolvable products."

We've heard about all the safety issues with smokeless tobacco. Those are based on snus. Those are based on modern U.S. tobacco. But we know that old smokeless tobacco that was used in the '30s or

'40s caused oral cancer in the U.S. We know that Indian smokeless tobacco causes a huge epidemic of oral cancer. We know that smokeless tobacco is not a single thing.

So it's hard for us to talk about safety of smokeless tobacco or dissolvables without knowing what we're talking about or without having some product regulation. And that's to me a big overriding theme that needs to be addressed.

DR. SAMET: Do you mean product definition?

DR. BENOWITZ: Yes. Well, not just that. There's no answer to this because this really depends ultimately on regulation. So we can say a regulated smokeless tobacco product, that is like Swedish snus or better, does not cause risk or causes little risk. But we can't say smokeless tobacco is general is safe. And we could say that some particular dissolvables look to be safe, but we can't say that all dissolvables are going to be safe without knowing what they are.

So to me, it's an issue that has to be addressed somewhere up front.

DR. SAMET: Two comments. So one is, we have an actual charge related to something called dissolvable tobacco products. And it is left undefined -- that is correct -- in the Act.

Second -- and I think this is where -- I understand what the public commenters are saying, and I understand what we are charged to do. And I think it's a little hard to fence off dissolvable tobacco products from other smokeless tobacco products and from the potential role of these products in harm reduction strategies, which is what we have heard about both in today's public comments and in prior public comments.

But to the extent that this is covered in the conceptual framework, I think it's implicit. I actually think that this report itself is not the place to begin to address harm reduction strategies generally. And I think we, at least in my mind, need to fence ourselves off a little bit and say what this report is about and what it is not about.

I appreciate the concerns you're raising. But, in fact, in the evidence that we have considered

in developing this report, we have only seen one sliver of the general literature that's relevant to the broader issue. I mean, I can appreciate why you are bringing this up, and I don't know whether we need to in this report say dissolvable products are what have been presented to us as dissolvable tobacco products, period. And this category may be fluid over time.

It is not defined except by us, except as how it has defined itself by what has been put in front of us as dissolvable tobacco products. And we recognize that there are broader implications of these products as other smokeless products in harm reduction. But this is, again, not the task for us as prescribed in the Act.

So maybe we need language to that effect. But I actually think, given what we have seen and heard, this is how we should define our task. And maybe we haven't done that with sufficient clarity. So I'm sure others will want to comment on this.

DR. BENOWITZ: I think it's fine. I just think we need a caveat up front saying that this

discussion is based on the limited products that we've looked at, which does not include the full potential range of dissolvable products, and same thing for smokeless tobacco.

DR. SAMET: Right. The task that we were given might have been defined differently, but we actually have a specific task, I think.

Dan?

DR. HECK: I think, maybe extending on what Neal said, there are some occurrences later in the text somewhere that we'll come to where there's some sentences around where smokeless tobacco, SLT, and cigarettes are referred to. And I think what Neal says is absolutely true, particularly worldwide. There are huge differences in the smokeless products.

I'm just going to suggest maybe we park in the back of our minds the concept of maybe striking out those references to smokeless in those sentences because the real thrust was really comparing the cigarettes. But those are somewhere later in draft. We can discuss those when they come up.

DR. SAMET: So I'm going to suggest, as we go

through the report, that we see if we are sufficiently clear with this I think important point raised by Neal and by others.

Any other comments to this point?

[No response.]

DR. SAMET: How about page 2? And again, obviously, this is just introductory material. And page 3? Again, here is our charge as given to us, so just a reminder.

Page 4. So this is a description. So page 4 and on to page 5, maybe perhaps we make a mental note, at least, that we may want to return, perhaps on page 5, before we go to the committee framework, to insert several sentences, Neal, that speak to your comment. That might be the appropriate place to do it. So let's leave a placeholder there.

You can write "Neal's comment placeholder"?

All right. And then, moving to the bottom of page 5, there's a comment here by John, and one of our public commenters commented about Figure 1 as well. So Figure 1 is there as a conceptual framework for thinking about the problem. It's not there to

say this is what we know about.

So I guess I would raise the question of whether its theoretical nature and use in the report is explained adequately. John Lauterbach had a comment here. You may or may not want to amplify on it at this point. But I think it's in that same kind of vein.

DR. LAUTERBACH: Dr. Samet, as I pointed out, there's no evidence out there -- the committee has received no evidence to support the disease/death in the bottom box on page 4 for dissolvable product use.

DR. SAMET: Yes. Tom? And then Mark.

DR. EISSENBERG: Yes. I had some comments about that, too. It seemed to me that there might have been one thing meant by whoever drew Figure 1 and another thing on the interpretation of Figure 1 with regard to the three boxes on the far right-hand side, all of which say disease and death.

My interpretation of that, after some thought, was that whoever drew the figure was intending to point out that everybody dies, and not that, for instance, dissolvable products only causes

disease and death.

My suggestion, with that understanding -- although it may not be true -- was that each of these disease and death boxes should actually be two separate boxes, one that says, "Tobacco-caused disease and death," and another that says, "Non-tobacco-caused disease and death," with the idea being that at some point we would like very much to know what the probability is of, for instance, tobacco-caused disease and death if you used dissolvable products only. It may be vanishingly small, but we would like to know.

Certainly, I don't think the implication here is that dissolvable tobacco products only cause disease and death.

DR. SAMET: Well, I know the person well who drew that framework.

[Laughter.]

DR. SAMET: Sadly, it is true that 100 percent of us will die. It's the timing, of course, that is of interest.

The point, I think, actually, Tom, you

captured in a way really is the comparative rates in the end of tobacco-caused disease and death, at the end of those three separate arrows. And I think the modification you suggest, or text to that effect, one or the other, is appropriate.

I think, again, this is a conceptual diagram, and one that was used to, in a sense, organize thinking and to capture what we know and really what we would like to know in the end.

Mark?

DR. CLANTON: Dr. Eissenberg's thoughts actually captured what I was thinking, so I won't add to that.

DR. SAMET: Neal?

DR. BENOWITZ: I think some minor wording changing on page 5 might deal with the idea that this is really a conceptual analysis. And so on the very last line, if we said "risks and benefits to health," that would make it clear that we're really looking at the impact. We're not saying in particular that this is causing risks, but we want to say, these are the ways that dissolvables could influence health.

I have to say that our charge was to look at the risks and benefits.

DR. SAMET: So if we were to modify the figure per Tom's suggestion -- and, actually, a benefit is that the rate of tobacco-caused disease is lower in that bottom versus other pathways.

So I think the proposed modification of the figure seems appropriate, and then with a text insertion that says that the comparative risks are of importance and that a benefit is a reduction in rate of morbidity and mortality for one line versus the cigarettes-only line, essentially.

Let's see. So I think the challenge we're going to face is doing this in real time, which is how we have to do it. So the modification would be that each of those boxes to the right -- and I don't think you're going to be able to do this because I think that's a -- can you? Okay. Each, at the top, it will say tobacco-caused or --

DR. BALSTER: Tobacco-caused.

DR. SAMET: Tobacco-caused. Tobacco-caused disease and death. And that will go into each.

John?

DR. LAUTERBACH: Dr. Samet, I have one concern here. We really haven't -- if we say that the risks of the dissolvable tobacco as presented by the products this committee was exposed to, the question I have, is the risk of long-term use of this any different than the long-term risk of use of these? That happens to be a nicotine lozenge from Equate, 4 milligrams. This happens to be a 4 milligram dissolvable.

I think the real question here is, are the risks of long-term use of these equivalent, one up, one down? I think that's really the big question facing this committee on the whole issue of dissolvables

DR. SAMET: I actually don't think that you're going to get agreement, certainly not from me. That's not the charge that was given to us. I understand the question you're raising, but again, that is off our charge.

Bob?

DR. BALSTER: I think without a change in the

language to risks and benefits to health and changing the boxes -- I mean, this is not a path analysis with weights that only go in one direction. This is a conceptual model in which the changes in those end boxes could go in either direction, or no direction.

So I don't think it's implying that we know the answer to what the weights of those arrows are, or even the direction. So I think it's fine as presented.

DR. SAMET: Right. This again was for organizing us, and I think probably leading to the recommendations. I guess, again, I think in the spirit of John's comment, I guess the question is whether we are explicit enough; is the secret code of conceptual -- TPSAC developed a conceptual framework for describing the potential roles. So this is quite guarded.

Now, whether there needs to be another sentence that says, we have adopted this framework for the purposes of this report, acknowledging that evidence to support this framework specifically is not there. I mean, I'm happy to put another caveat

in to keep John happy.

But I think for the committee's purposes, and I think particularly for pointing to what research gaps there are, this kind of formulation is useful, and I wouldn't want to abandon it. But I'm happy to make certain that readers understand that this is something we have constructed, and that evidence to support this particular model is not necessarily there. But we are drawing on some realities of what we know about tobacco.

Mark?

DR. CLANTON: This probably won't help at all. But if this were a logic model, I could understand the concern because the logic model would be drawing you to a particular population conclusion. This is not a logic model. This is a simple way of categorizing the data and showing connections between different outcomes and relationships.

So, again, I'm perfectly happy with the modifications, and it is a conceptual piece that does help us organize our thoughts. But it's not a logic model.

DR. SAMET: Tom?

DR. EISSENBERG: Yes. I don't want to belabor the point. I get the idea that this is a conceptual model. I think that the amendment that was just made doesn't address the misunderstanding that several people have about this figure.

What I had suggested was two boxes at the end of each line, one that said tobacco-caused disease and death, another that says non-tobacco-caused disease and death, because that captures the two possibilities. Right now it just looks like dissolvable products only cause tobacco-caused disease and death, which I think is the misunderstanding we're trying to avoid.

DR. SAMET: So, Tom, if I understand correctly, you want two boxes at the end of each of the --

DR. EISSENBERG: That's correct. Or you could bring them down into two boxes.

DR. SAMET: Ellen?

DR. PETERS: I think a much simpler change, I think, would still address what you want. Just make

it the probability of tobacco-caused disease and death, and that takes care of tobacco and non-tobacco at that point in the risk boxes.

DR. SAMET: Risk for --

DR. PETERS: Risk for probability of, likelihood of --

DR. SAMET: In each box?

DR. PAMPEL: I guess that would work.

DR. EISSENBERG: It works for me.

DR. SAMET: Risk for. Okay. Fred?

DR. PAMPEL: I guess that would be a good idea. I just didn't see the issue because clearly, the language to follow says does the availability of DTPs affect the likelihood of experimentation? It doesn't imply that it would only increase. It would affect.

So I read that as a framework in which the DTPs could have a direct effect in either direction, and therefore was not implying some sort of negative effect. That wording is on the bottom of page 6 and the top of page 7.

DR. EISSENBERG: You're right. The

likelihood is an important word there. That's referring only in the figure to the little number 1, which is at the far left end of the model. We're talking about the far right end of the model.

DR. PAMPEL: I'm talking 4 as well. It says the risk of tobacco could be affected. It doesn't say harmed or increased. The effect could be in a positive direction.

DR. SAMET: I will say that here is the danger of any model. It just can't be perfect. So the question is -- I'm about to invent a new word, model-smithing --

[Laughter.]

DR. SAMET: -- and let's just talk about how far we want to go.

I think, Dorothy, did you have a comment along the way?

DR. HATSUKAMI: Yes. My comment is not necessarily related to what's been discussed. But one tobacco product that's missing is smokeless tobacco, the conventional smokeless tobacco. We don't really acknowledge that in this particular

framework.

DR. SAMET: Well, I think that's the mixed use.

DR. HATSUKAMI: I guess I'm not really sure. What about smokeless tobacco only? It's possible that smokeless tobacco users might use dissolvable products as well. So we can either just acknowledge that smokeless tobacco should also be considered, or put cigarette smoking or smokeless tobacco --

DR. SAMET: Yes. So if we put a line in that says specifically that this model does not include smokeless tobacco products, which would add a further complexity, I think would that --

DR. EISSENBERG: And e-cigarettes, and any other tobacco products not depicted on the model.

DR. SAMET: It could be many, yes. Yes, so we could end up with a lot of lines here, I think.

Neal?

DR. BENOWITZ: Have we distinguished dissolvables from smokeless tobacco anywhere? Because that's one of the issues, is certainly you could consider dissolvables to be a form of smokeless

tobacco.

DR. SAMET: So the wording is "other forms of smokeless tobacco." Right?

John, do you have further comments here?

DR. LAUTERBACH: Dr. Samet, I have two comments. My first concern on the whole thing is the analogy to the menthol report because that basically deals with cigarettes. And I think the issue here we should be trying to point out is the great difference in risk to the user between cigarette smoking and use of U.S. and Northern European-made smokeless tobaccos in general, and dissolvables in particular.

I pointed that out in some of my comments to say that, hey, we're not including the smokeless tobacco products of the far east of Africa, which have a tremendously hazard index than do the particular products in the U.S. and modern, contemporary smokeless products, even to the point of the standard chewing tobacco product, which other than dental caries has had no adverse epidemiology.

So I think the thing is, we need to try to be either, is this going to help us in terms of this

conceptual framework, or are we going to get too complex in it and is it not going to be helpful?

DR. SAMET: Well, I think we can come back to that at the end. But I actually think that this turns out to be helpful for getting the report organized, and I think we should stick with it. I think we all recognize the complexity of these products. I mean, when you begin to consider them globally, as you just did, we recognize that there are many, many, many forms of smokeless tobacco.

What I think we've heard -- so let's go back to page 5. So I want to bring up a few specifics now. You're going to be challenged today. So first, do we want a sentence -- where does the comment go, John's comment about -- the bottom of page 5? Yes.

So do we want a further sentence, as a reminder -- so beyond the sentence in Figure 1. So the first sentence, is our first sentence sufficiently descriptive of the theoretical nature of the model, and that it's conceptual, and that we have developed this purely for the purpose of this report?

Do we need any other caveats, in part, to

address John's concern? Are we happy with our introduction of the model as it sits there now?

DR. MCAFEE: One quick thing you could do, that the third sentence down says, "The framework represents three potential patterns of tobacco use, product only." You could put, "only three potential patterns of tobacco product use." So you're further indicating that you're not trying to cover the entire universe in this model.

DR. SAMET: Yes. So he wants to add, "represents only three potential patterns." And we might actually begin that sentence by saying, "For simplicity, the framework only represents."

Now, continuing, so page 6, we've made modifications in the figure that we may want to further explain. So let's see where that might be done. So not page 6, but let's go to page 7. And I think we want to get to where we describe what happens at the end.

So maybe we're -- let me just see here. Hang on one second. We may want to go --

[Pause.]

DR. SAMET: So I think if you go to page 7, yes, where it says, "Further, the framework acknowledges that risk for morbidity and premature mortality caused by use of tobacco products could be affected by use of DTPs," we could say, "In this model, rates" -- I guess we need the word "risk" --

DR. PAMPEL: Increased or decreased.

DR. SAMET: Yes. So go back. "Could be affected by use of DTPs, either increased or decreased." And then we could say that a benefit -- I mean, just to get this out on the table -- "A benefit of availability of DTPs would be a reduction in risk for morbidity and premature mortality compared to that in users of cigarettes only."

DR. CLANTON: Is it a benefit or potential benefit?

DR. SAMET: Well, it's a potential benefit.

DR. HECK: Yes. Maybe we should say "could" instead of "would," just to be neutral.

DR. SAMET: So you want to say a potential benefit, would be.

DR. HECK: Well, could.

DR. SAMET: I like would, but -- yes. That seems -- would be a reduction in risk of morbidity and premature mortality.

DR. CLANTON: Risk of tobacco-caused morbidity and premature mortality.

DR. SAMET: I told you, you were going to be challenged, Caryn.

Morbidity and premature mortality in comparison --

DR. MCAFEE: Just to be -- I guess I'm not clear why we're pointing out that there could be a benefit unless we're also going to say that there could be -- it would be better to just say it could go either way.

DR. SAMET: Well, we say that in the other sentence. And I think, since our prior is probably moving towards the possibility of benefit, I think this is probably reasonable to say how this would come out.

DR. BENOWITZ: I've got a problem with this. It's not really in comparison with cigarette smokers.

It's comparison with the scenario that these products were not available because it could involve cigarette initiation, all kinds of things.

So this doesn't really make any sense to say comparison with. It would be in comparison with a situation that the DTPs were not available, or just not put it there at all. I don't think you need to say anything. I just think you stop with mortality.

DR. SAMET: What do you want to do? You don't want to put the comparison in?

DR. BENOWITZ: No. Because it's not a comparison of --

DR. SAMET: All right. Why don't we do that, and then -- okay.

All right. On page 7, let's go up. We also have to deal with -- these are comments from committee members. So we have -- let us see the top of that sentence, Caryn.

So, in this framework, availability might affect the likelihood of initiation and also affect progression to regular use. So again, we need to decide about these proposed modifications.

So is this okay? Bob?

DR. BALSTER: This was my suggestion. It's just basically repeating what you say in the very first sentence. But I'm just concerned that having only "addiction" there, given all the recent data suggesting that current regular users of tobacco may not always meet definitions of addiction, by just having regular use and addiction is a broader categorization. And I would also suggest that you put "regular use/addiction" in the box, too. But this could be wordsmithing, but --

DR. SAMET: I think this is fine. So we will accept that. And "would influence the maintenance of tobacco," so the same comment, really.

All right. And then, let's see, going to the bottom of page 7, we have a comment from you, Bob.

DR. BALSTER: Well, it's just --

DR. SAMET: It's the same.

DR. BALSTER: It's the same. It's just adding that to the box, then; instead of just having addiction in the box, putting "regular use/addiction." It's a small thing.

DR. SAMET: So go back to the model. So you would have "regular use/addiction."

DR. BALSTER: Yes.

DR. SAMET: Is that okay with everybody? Yes. Okay? Yes.

So let Caryn finish her work here.

[Pause.]

DR. SAMET: So last chance on the figure. Figure-smithing? John?

DR. LAUTERBACH: Dr. Samet, could we come back and look at this again after all the changes are made before a final vote?

DR. SAMET: Of course I'd like to say no, but of course you're going to.

So page 10. John, do you still want to comment further about Figure 1?

DR. LAUTERBACH: Again, we get back to the situation as some of the speakers mentioned, in terms of dose or whatever. It appears that Figure 1, at least as originally conceived, assumes that all dual use is bad. Maybe I'm misreading that, but that's what it appears to be.

DR. SAMET: No. It really does not. I think -- Tom, do you want to comment?

DR. EISSENBERG: Well, I'm not sure of the right verb, dismayed or amazed, to find that I'm addressing John's concerns independent of having heard them. But I also had that same thought, I think. And I didn't know when we were disposing of the figure we were done with the caption because I think a lot could be done with the caption. And one thing that could be done is addressing that concern.

So you see the number 2, where it says, "Experimental use leading to an established pattern of mixed use of tobacco products," I think we could add to that to make it a little more clear what we're talking about. And I have some text. So I'm down here. I'm going to skip what's in parentheses.

DR. SAMET: Let us get our wisdom saved.

[Pause.]

DR. SAMET: We're successfully saved?

We're saved.

DR. EISSENBERG: So I think the point that John is raising is that people walking into this

figure have different ideas of what we mean by mixed use, some of which is worse than others or, looked at another way, some of which is better than others.

So I added to the number 2, the explanation of the number 2, to read, "Experimental use leading to an established pattern of mixed use of tobacco products" -- skip what's in parentheses for a second -- "that might include regular cigarette smoking supplemented with the occasional dissolvable smokeless product, regular dissolvable smokeless product use supplemented with the occasional cigarette, and all the variations in between."

DR. SAMET: Okay. So that is in addition to number 2 on page 10.

DR. EISSENBERG: Do you want it?

DR. SAMET: So does anybody want to hear that again, or did you -- everybody's got it? Okay.

So I'm giving this to Caryn. And I think what you could do is perhaps, rather than king it now, write "Eissenberg modification."

DR. EISSENBERG: Well, there's another one, so I need my sheet back, or I can bring it up here.

DR. SAMET: Here. Let me give this back. All right? Here.

DR. EISSENBERG: So, then, at the end of -- well, I was confused, I guess, why the number 3 is pointing at addiction when number 3 is a point about cessation, about how the availability of DTPs could influence cessation. That's what number 3 is depicting, and yet for some reason, it's not pointing at cessation. It's pointing at addiction.

DR. SAMET: I would be happy to see the number 3 moved, or moved on the arrow between addiction and cessation.

DR. BENOWITZ: It's complicated because the idea is if you provide nicotine, you're sustaining addiction, and therefore an effect on cessation. So it could go either way.

DR. SAMET: Yes. Would it be -- actually, that was sort of the spirit of why it is where it is.

Are you happy with leaving it there?

DR. EISSENBERG: I'm not wedded to it. That wasn't the major thing I wanted to bring up.

DR. SAMET: All right. Keep going.

DR. EISSENBERG: This is the last point on the caption. There's a point made much later in the document with regard to the possibility of DTPs lessening the risk of tobacco-caused disease. And as I say, it's much farther in the document, whereas it is worth bringing up here.

So for number 4, I was suggesting leading with what's there, "Differing risk profile for tobacco-caused diseases and premature mortality," but then clarifying it such that, for example, "Exclusive use of dissolvable tobacco products may lessen the risk of some tobacco-caused diseases -- for instance, lung cancer -- relative to exclusive use of cigarette smoking."

I think we made that point later on in the document. It's just worth making here in the figure.

DR. SAMET: So let me disagree, only because this is the point where we're introducing the model and not findings that come later. So I think that we should reserve that for later while introducing the model as the model, and just leave it at that and not put it in the caption. So if that's okay.

But the other Eissenberg modifications -- this is the first one?

DR. EISSENBERG: Yes.

DR. SAMET: Anything else here?

John, you made a comment that I really didn't understand, this classification of dissolvable products as new. I don't think there's any assumption that they're new or not new in this figure.

DR. LAUTERBACH: Perhaps I put that in the wrong place, Dr. Samet. I had originally rewritten your report, and then Caryn urged me to change my comments into additions or modifications to your report. So some things may have gotten misplaced.

DR. SAMET: Then I think at this point, then, we have page 10 behind us. Page 11, I think we have now made some modifications to those, the Eissenberg modifications. Oh, okay. Thanks. And then the red. So again, I'm not sure whose red this --

DR. PETERS: This is actually mine. I may have mistyped. What I was trying to point out was that we talked about 3 being a decreased likelihood

of smoking cessation. But an increased likelihood of smoking cessation is also possible. I think I either mistyped or it was mistyped into there.

DR. SAMET: I mean, again, I think acknowledging that this is the figure, not the place to present evidence, if you want to say decreased or increased likelihood of smoking cessation, at the start of number 3?

DR. PETERS: That's all. Yes.

DR. SAMET: Decreased or increased. And that one, I think that's okay. It's kind of the spirit of what we talked about, I think, with Tom's wording, so I think that's okay.

Let's see. Dan, you have a comment there.

DR. HECK: It may, with these revisions, have been captured elsewhere. But I was just thinking, with a few words here, the exclusive use, partial or complete replacement, that we could capture the possibility, at least, as we've seen from the Swedish experience with snus, that maybe the smokeless products could assist -- even in dual use, partially displace cigarette use.

DR. SAMET: I think --

DR. HECK: We may have captured this now with other revisions. I'm not sure.

DR. SAMET: Yes. I actually think that the addition maybe gets a little bit of the spirit of what you were trying to do. And again, I don't think this is the right place to introduce findings. It's just a conceptual model. So if that's okay, I think what we'll do is move on.

Page 11 gone, if that's okay?

DR. HATSUKAMI: No.

DR. SAMET: Yes, Dorothy?

DR. HATSUKAMI: Actually, I have a comment. So number 3, you indicate an increased or deceased likelihood of smoking cessation. But if you go back to number 1 that is on page 10, you have increased experimentation.

So I'm wondering whether you need to add the increased or decreased experimentation/initiation of cigarette smoking as well, just to be consistent.

DR. SAMET: Well, let me ask. I mean, I think on this number 1, do we want to give way to the

possibility of decreased experimentation? It seems to me that at least the public health concern is increased. And we say, "Hypothesized mechanisms by which dissolvable tobacco products could have impact on public health." And then we say, "Increased experimentation and initiation."

I mean, if we want to put all of these in let's say, a neutral, non-directional stance, we could say "Changes in experimentation" or something like that. And this goes back a little bit to Neal's comment. I mean, this is all in the hypothetical of availability versus non-availability; at least from the public health point of view, the concern is increased experimentation. So I think this is a question of how we want to present the framework.

DR. HATSUKAMI: Sure. But then on 3, isn't the public health concern decreased likelihood of smoking cessation? You've changed number 3 to say "increased or decreased" on page 11. So I guess I'm just saying, for consistency, maybe you should indicate that public health could be positive or negative.

DR. HECK: Mr. Chairman, I agree. I think, although the public health concern is the negative effects on public health, but with the charge being risk or benefits, I think the kind of neutral or encompassing descriptor here would be maybe be more appropriate.

DR. SAMET: Then I will suggest that number 1 be changed to "effects of experimentation and initiation," which is non-directional. So "effects of."

DR. HATSUKAMI: Is it "effects of" or "effects on"? It should be "effects on," yes.

DR. SAMET: On. Sorry. You knew what I meant.

DR. HATSUKAMI: Yes. And then, just to go back to page 11 -- well, I guess this is maybe wordsmithing, actually. But it seems number --

DR. SAMET: Watch out.

DR. HATSUKAMI: I'm sorry. Number 4 seems a little repetitive. If there's exclusive use, and then it says, "or partial or complete replacement of cigarette," I think you can just take out "from

exclusive use or." I think that could be taken out.

Does that make sense?

DR. SAMET: Okay. That's fine. Exclusive use.

DR. BENOWITZ: But I think 4 raises just a question, which we don't think is a concern with current products. But is there any direct effect of dissolvables on death or disease, and is there a possibility that when you combine dissolvables with smoking, it might influence the risk of smoking? Not by cigarettes per day, but by some intrinsic biological effect. That's my interpretation of what this means, in which case this is relevant, as stated.

DR. HATSUKAMI: What? No, I think it retains the -- you want to keep the "from exclusive use" in there? Is that what you're saying?

DR. BENOWITZ: Yes. Yes, both.

DR. HATSUKAMI: But isn't "complete replacement of cigarette use," isn't that exclusive use?

DR. BENOWITZ: Oh, I see. Yes. Yes, that's

fine.

DR. HATSUKAMI: Yes.

DR. BENOWITZ: That's fine.

DR. SAMET: Let's see. We're moving forward. Okay. Page 12, Key Findings from the Evidence Review. This was an attempt -- and let me just say, to summarize what I thought we had agreed to was what we said at the end of the last meeting about the literature review findings.

Now, I think we want to be very careful. This is not an attempt to write a referenced document. Okay? So the references sit in all the materials that Caryn showed you on the compilation. So this is not going to be reference 1 to 300, or whatever it might be. This is going to be our report of what we found. So just remember that.

So, let's see. I think there's an initial comment from John. I don't know whether we need to say the obvious, but we do not make any effort to differentiate one product from another. I don't think we need to state that, but I think that's what your comment is about here, John.

Dorothy?

DR. HATSUKAMI: I do think that maybe a sentence should be added after the first sentence, pointing out that, in general, the resources are limited in the types of products that have been examined. For example, few studies are -- I don't think any studies looked at the effects of sticks and strips.

So I'm wondering if we can just add that in just to acknowledge that there have not been any studies conducted on -- or limited studies conducted with strips and sticks.

DR. SAMET: So you want to make a comment that essentially would say, reviewed a variety of sources of evidence on DTPs, and then add something that says -- perhaps saying that there were -- maybe just say, "reviewed a variety of sources of evidence," and then just say something like, "On the whole, the evidence was limited and also did not provide any information relevant to evaluating individual products," or something like that. I think that's John's concern.

DR. HATSUKAMI: Or something like that.

DR. SAMET: Yes. "Any individual products," probably. "Any individual dissolvable products."

MALE VOICE: No. Some individual dissolvable products were, though.

DR. HATSUKAMI: I think it's "some," because there are some on --

DR. SAMET: Okay. Well, "some individual products" or "some things." I mean, I think it gets a little tricky here because it's -- right.

MALE VOICE: Some individual products.

DR. SAMET: All right. That's fine.

DR. BENOWITZ: I'm not sure if this is wordsmithing or not. But in the first sentence, do you want to just state that these are products that have been marketed up to this date, or something?

The reason I say that is because I don't want to generalize between the evidence we've looked at now with all potential dissolvables that might be introduced in the future. And they could be quite different.

MALE VOICE: That was your point earlier,

too.

DR. SAMET: That's fine. And by the way, if you want a definition of what wordsmithing is, when I say it's wordsmithing, it is.

[Laughter.]

DR. SAMET: But I think this is good.

Okay. Page 12, anything else?

[No response.]

DR. SAMET: Let me check. Sherry, I don't want to forget you. Anything to now?

[No response.]

DR. SAMET: She may be muted.

So that was page 12.

Let's see, Page 13. Let's see. Bruce, you have a point here.

DR. SIMONS-MORTON: Yes. I just thought that this was a good place to throw in a reference about what's known about current prevalence.

DR. SAMET: So I agree. We probably should have a little bullet somewhere that says, "Prevalence of use," or something. I mean, this is not actually out of the peer-reviewed literature per se. We heard

different data sources on both prevalence from different surveys of use and sales, at least for the Star products.

So I don't know whether this belongs somewhere else, but it's probably a point that we should make. Hold the thought because I think we need to make that point because that clearly is important, the kinds of information that are actually available to us. So let's see. Don't delete his comment, and let's figure that out.

Then, John, your comment, I mean, again, just in terms of style, we're just simply not going to put in individual references. It won't work. But the reference body that we use will be clear.

So, let's see. There's a red comment here. What is that?

Dorothy?

DR. HATSUKAMI: I guess I would disagree with that comment, particularly where it says, "DTPs are not a safe alternative to conventional smoking products." I don't think that that's correct. So I would disagree, at least with that segment.

The "No tobacco product is safe," I guess there's no demonstrated -- there's no studies that have demonstrated that no tobacco products are safe.

DR. SAMET: I'm not sure whose comment this is. I actually would probably just prefer to delete it, I think.

DR. BALSTER: I'll 'fess up to putting it in there. I was really basing it on what I had said at the last meeting. There's an awful lot of published data on the toxicity of nicotine per se. And as a constituent of these products, nicotine is not a safe product, or a product containing nicotine. And certainly, products containing tobacco are not safe.

But I'm not sure -- it could be misleading in the context of putting it there. So I wouldn't insist on it. But I believe, actually, the sentence is correct as stated, but I'm willing to give it up.

DR. SAMET: If you're happy to give it up, I think I'd prefer to see it go. I mean, in part, some of it relates to what I think our charge is and what evidence is available at present. So let's delete that guy. It's gone. Okay.

DR. PETERS: Jon?

DR. SAMET: Yes, Ellen?

DR. PETERS: I actually thought that there was some usefulness to the comment, at least the first part of it, about "No tobacco product is safe." But perhaps it just needed to be moved after abuse liability and after health risk because we don't have anywhere in here, I don't believe, anything about the absolute risk of the product. We're only focused on the relative risk with cigarettes. And I think both are important.

DR. SAMET: Let me propose that we delete it here. This question of "No tobacco product is safe," I think we should look at that as we come to the end of it. I actually think this was not something we were asked to judge and that it was not part of our charge, and will quickly get us into issues such as what is safety and how would one even define it, which, since I want to go home, I don't think we should take on.

Mark?

DR. CLANTON: Yes. I agree with taking it

out here, and maybe if there's an appropriate place later, coming back to it. But the central issue has to do with nicotine versus tobacco products. The first part of that sentence is absolutely correct, but the second piece actually deals more with safety of nicotine. So it's a mixed kind of statement.

So again, I don't know that it has a context in this part of the report, and I think taking it our here is probably the right thing to do.

DR. SAMET: So it's gone, and we will tuck it away in our memories to come back to.

Oh, yes. So constituent yields. All right. So if you look, page 13 on to page 14, the comment is, "There is variation across products in yields of nicotine and tobacco-specific nitrosamines. Heavy metals are present also in variable amounts. The yields of nicotine and TSNAs are lower than those of cigarettes."

Now, this was a summary of data that we heard. I don't quite understand, John, the reference to the GothiaTek standard. That was not the consideration. This was about constituent yields and

not particular interpretation of those yields.

So I see what you're saying in your comments, but I just don't think that we're trying to have that degree of specificity here.

Did you want to say something?

DR. LAUTERBACH: Yes, Dr. Samet. As I think everybody knows, when you start doing trace analyses, generally, the lower the level of the analyte, the higher the variability in the value you get. And we say this thing, this warning, as you put it, could be perceived as being these things are all over the map, from high to low, when they're all very low and just the inherent variability of doing trace analyses is likely for the source of the variation as opposed to rapid changes in the product formulation, et cetera.

DR. SAMET: But I think the statements are correct. And then the qualitative, or semi-quantitative, statement that follows, "The yields of nicotine in TSNAs are lower than those of cigarettes," does provide a context for interpreting the values in the variability.

So if cigarettes are up here, we say these

products are down here, and there's variation, which personally I think was okay. And again, remembering that this is the high-level summary, and I'm going to keep us there because I think that's where this report should be.

So let me see if others want to comment here. Tom?

DR. EISSENBERG: I was just -- I don't have a problem with what I think is the intent of the statement, but I'm very confused by the word "yield" with respect to DTPs. And someone can correct me if I'm wrong, but when I talk about cigarettes, I talk about the content of the nicotine in the cigarette, the yield in the smoke, and then the delivery or exposure to the person. So there is no yield in that respect with a DTP. There's either a content or a delivery/exposure.

DR. SAMET: So you would like to change this, which I think sounds appropriate, "the contents of nicotine." Is that --

DR. EISSENBERG: Well, I'm not sure what we want to compare it to in that sense.

DR. PIRARD: Or "concentrations."

DR. EISSENBERG: And then, so what would we compare it to?

DR. SAMET: I see.

DR. EISSENBERG: If we're talking about the content, are we talking about then the content of the cigarette or the yield of the smoke or the delivery to the smoker?

DR. SAMET: I see your concern.

Neal?

DR. BENOWITZ: Well, I had exactly the same concern. I think we have content on most products. We have biomarkers of exposure on a few. And so I would just say, "Content," and in a few cases, "exposure," or something like that, but content and exposure, but separate. Indicate that both are important.

DR. SAMET: Dan?

DR. HECK: Yes. I think I agree with what Tom said. Maybe we could do this by starting the sentence, "There is variation across products in content of nicotine, TSNAs, metals." And then in the

latter sentence, "The deliveries" -- implying deliveries to the user -- "of nicotine and TSNAs are lower than those of cigarettes." That way we would get the composition and the dosimetry.

DR. BENOWITZ: Well, but I would just say that we have content for most all the products. We have delivery for only a very few. So I'm against generalizing delivery to all of them. So you could just say, "where measured," or, "in a few products," or something like that, just to qualify that.

DR. SAMET: But the first suggestion made by Dan, that sentence, "There is variation across products," I think we would replace "yields" by "contents" there.

Then let's agree on some wording for this other sentence, that Neal, you would like to say, "The contents of nicotine and TSNAs" -- or, no.

DR. BENOWITZ: Or you could say, "Human exposure, as assessed by biomarkers, in the few cases where it has been measured, has been lower than cigarettes," or something like that.

DR. CLANTON: Can we talk about amount?

DR. BENOWITZ: Well, but we want to separate content from actual human exposure. Human exposure can be looked at with biomarkers, but it's only been done in a very few studies.

DR. HECK: Maybe something like, "Available data for biomarkers" --

DR. SAMET: Yes. So perhaps, "Available data for some products" --

DR. HECK: -- "indicates that they are lower."

DR. SAMET: -- "show delivery to users of lower amounts of nicotine and TSNAs than are provided by cigarettes."

DR. BENOWITZ: But then I also have a question from John's comment about Stonewall. I haven't seen the data, but is there evidence that Stonewall actually delivers more nicotine --

DR. LAUTERBACH: I should have had "nicotine content" there.

DR. BENOWITZ: So there are no biomarker studies on Stonewall indicating that it provides more nicotine than the cigarette; is that true?

DR. LAUTERBACH: Not to my knowledge, sir.

DR. EISSENBERG: No. The ones that exist show that it's less.

DR. SAMET: So to help Caryn out, it's going to say, "Available data for some products show delivery to users of lower amounts of nicotine and TSNAs than are delivered by cigarettes."

Okay. So that's page -- yes, the final sentence comes out. That was, I think, important changes.

Let me make a suggestion. It's 3:00.

DR. BENOWITZ: I was just writing you that note.

DR. SAMET: We're going to take a break. So how about a 10-minute break? I think we're doing not bad. And remember not to discuss what you're not supposed to discuss.

(Whereupon, a brief recess was taken.)

DR. SAMET: Ladies and gentlemen, the meeting has begun. I'm learning here.

Let me give you a little portent of what we might do, which is to try -- if we continue to make

progress, to get through our task today. If we have big issues pending and really need to come back and discuss, then we will do so. But if we continue to move along, let's see where we end up because I sort of like the idea that we're going to just focus in and get this done.

Neal's not here. I did write a couple of sentences to put in for Neal's comment, but we'll come back to it, then.

So I think when we went out of the room, we were at like page 35 or 40.

[Laughter.]

DR. SAMET: Oh, 14. All right. We had fixed the bit about delivery and yields, and I think now we're on to page 15, so at abuse liability. And, let's see, we have some editing here.

Does somebody want to take ownership? Dorothy?

DR. HATSUKAMI: I don't take ownership of this, the modifications that have been made, but I'd like to just make some changes in the abuse liability statement. It should read, "Abuse liability in

current smokers should be lower for current DTPs than for conventional cigarettes and for most conventional smokeless tobacco products." That's how I'd like to change it.

DR. SAMET: And should that be "current smokers" or "tobacco users"? That doesn't make sense with "in current smokers" to me, at least. Shouldn't that --

DR. HATSUKAMI: Yes. Is that --

DR. SAMET: Shall we just say, "Abuse liability should be lower," and just take that out?

DR. HATSUKAMI: Yes. I think that that's fine, to take it out. Don't you, Bob? I mean, abuse liability should be lower for current DTPs.

DR. BALSTER: All we have data on are smokers.

DR. EISSENBERG: Are we talking about particular abuse liability studies?

DR. BALSTER: We're talking about all data is smokers.

DR. EISSENBERG: So what are you considering an abuse liability study? Are you talking about

laboratory evaluations that included -- no. There was at least one where Stonewall was compared to usual brand smokeless tobacco use.

DR. BALSTER: Oh, sorry. Take it out.

DR. HATSUKAMI: Yes.

DR. EISSENBERG: I'm confused by the word "should." Are we saying, the data indicate that -- or, "The limited amount of data that we have indicate that the abuse liability is"? The should seems confusing to me.

DR. HATSUKAMI: I think "is." It should be "is," not "should."

DR. EISSENBERG: Yes.

DR. HATSUKAMI: Yes, that's right.

DR. SAMET: So do you want -- "The limited data available," I think that's probably useful to -- "limited data reviewed"?

DR. HATSUKAMI: "Available." Yes. Sorry.

DR. SAMET: Wordsmithing.

DR. HATSUKAMI: Oops. So "is." Yes.

DR. SAMET: Okay. Is everybody happy with Dorothy's modification?

DR. EISSENBERG: Until we get to SMTs, like Ellen and John, I was confused about SMTs. And I don't even know where that abbreviation came from.

DR. SAMET: John?

DR. LAUTERBACH: Dr. Samet, on these dissolvable tobacco products, the use of liability is pretty much limited by the effect of the body of nicotine in the stomach. You can even have these things in a candy dish on the table and start taking these things, and you're going to be basically self-limiting.

DR. EISSENBERG: That's an empirical question.

DR. SAMET: Are you happy with the text as written?

DR. LAUTERBACH: Yes.

DR. SAMET: Thank you.

DR. HATSUKAMI: Could we just take "other" out? Instead of "for other most conventional"? It seems --

DR. SAMET: Most.

DR. HATSUKAMI: Yes. "For most," yes. And

I'm not really sure, Bob. Why did you put "because of lower nicotine content"? It could be -- did you add that there? Was that you?

DR. BALSTER: At this point, I can't remember.

DR. HATSUKAMI: Because I don't think that's necessary because it could be --

DR. BALSTER: Yes. Okay. I don't remember what I did.

DR. SAMET: And I don't know where SMTs came from, although I did write this.

DR. EISSENBERG: Yes. I think this would be the first I've ever read that talks about SMTs as opposed to either ST or SLT.

DR. HATSUKAMI: Yes, that's right.

DR. SAMET: I'm not sure I know where that -- so can we just leave it at smokeless tobacco products? Why don't we just leave it spelled out, and whatever SMT is and whoever wrote it, which I don't think it was me, but --

DR. EISSENBERG: Yes. It comes repeatedly throughout the rest of the document.

DR. SAMET: So let's kill it.

DR. EISSENBERG: So we have to have an abbreviation.

DR. SAMET: You what?

DR. EISSENBERG: We have to have an abbreviation. But it should be either ST or SLT. Because it shows up repeatedly throughout the rest of document.

DR. SAMET: So what would the group like?

DR. HATSUKAMI: ST is fine.

DR. SAMET: ST?

DR. HATSUKAMI: Yes.

DR. SAMET: So leave that. I think it's the abbreviation we're discussing --

DR. HATSUKAMI: Yes. Right.

DR. SAMET: -- which the group would like STs.

DR. EISSENBERG: That's actually letter-smithing, not wordsmithing.

[Laughter.]

DR. SAMET: All right. So we're going to take care of that.

Moving to the bottom, health risk.

DR. HATSUKAMI: Actually, I'm wondering whether we should add another bullet on cessation because in terms of the peer-reviewed literature, I think that what has been shown is that the use of DTPs may reduce cigarette consumption, but it doesn't seem to completely substitute for smoking.

I think that's demonstrated in the peer-reviewed literature, and also in your -- at the very end, you allude to it. And it would be nice to indicate that that has been found in the peer-reviewed literature.

DR. SAMET: So after abuse liability, you want a bullet that says cessation?

DR. HATSUKAMI: Right.

DR. SAMET: And now give us a sentence.

DR. HATSUKAMI: "Use of DTPs may reduce cigarette consumption, but does not completely substitute for smoking."

DR. SAMET: In smokers? In regular smokers? Regular users?

DR. HATSUKAMI: In regular smokers.

DR. SAMET: In regular cigarette smokers.

DR. LAUTERBACH: Dr. Samet, does that mean all cigarette smokers, or most, or cigarette smokers in a clinical setting?

DR. SAMET: Dorothy?

DR. HATSUKAMI: Yes. That's a good point.

DR. SAMET: And, again, this should be couched around what we've heard and the evidence. So if you want to say, "Evidence considered by TPSAC suggests that," I think that's --

DR. HATSUKAMI: That's a good point.

DR. SAMET: That's true of all of these.

Okay with this one? Then on to health risk, the next page.

DR. LAUTERBACH: Dr. Samet? Can you say that "for most regular cigarette smokers"?

DR. HATSUKAMI: Yes. That sounds good.

DR. LAUTERBACH: The last, that we have "most."

DR. HATSUKAMI: Yes. Good point.

DR. SAMET: Next, health risk.

DR. HATSUKAMI: I have a point.

DR. SAMET: Dorothy?

DR. HATSUKAMI: So I think that in the last part of that sentence, it should be, "less hazardous than either cigarettes or most conventional STs." Because we do have those snus products now that may be just as hazardous as DTPs.

DR. SAMET: All right. Other comments here on health risk?

DR. HECK: Just a comment. You can capture some of what John was saying, and additionally, something that Neal said earlier about the great diversity, what, worldwide or maybe even domestically in smokeless products.

Shouldn't we consider just dropping the mention of smokeless tobaccos here and just stick to the more clearcut cigarette versus this category, rather than getting enmeshed in the snus versus traditional moist smokeless versus offshore things?

DR. SAMET: What does the group think? So the proposal is essentially to make this a comparison to cigarette smoking.

DR. HECK: Where there's much more clearcut

and there's less -- yes, just much more clearcut. What do we gain by bringing the traditional smokeless in here?

DR. HATSUKAMI: Well, I think, in part, some of the traditional smokeless tobacco products have high levels of toxicity. And so I think DTPs have an advantage in that those toxicants are lower than some of the smokeless tobacco products that are sold here in the U.S.

DR. HECK: Certainly, in some of the older epi studies, and I guess the Winn study we're thinking of from some time ago with dry snuff, there was a significant elevated health risk. But as John points out or as was pointed out in the comments we heard this morning, the contemporary smokeless products, the studies after, let's say, 1990, there really hasn't been a significant risk of oral cancer demonstrated.

So rather than getting into that, I'm just suggesting maybe we could make the simpler point that there seems to be a stark contrast to cigarette smoking.

DR. SAMET: Neal?

DR. BENOWITZ: I would agree with that. I don't think we really have any data on health risks of current smokeless tobacco products in the U.S., the currently marketed ones.

MALE VOICE: But we do have data on TSNAs.

DR. SAMET: Yes. We certainly don't have epidemiological data, obviously, because that's still a long time to come.

DR. BENOWITZ: Right.

DR. SAMET: So the proposal is to basically say this exclusive use of DTPs should be less hazardous than that associated with regular cigarette smoking, period.

DR. BENOWITZ: Yes.

DR. HATSUKAMI: Yes. That's all right.

DR. SAMET: No, that stays. Based on TSNAs -- do you want to leave nicotine -- "and nicotine" -- "Based on the information on TSNAs and nicotine," and then get rid of the studies of cancer risk of SMTs, or STs, or whatever.

DR. HATSUKAMI: But on the other hand -- I'm

sorry to say this -- levels of nicotine in the conventional products are pretty high relative to --

DR. SAMET: Yes. So take out nicotine, too? So maybe we should say, "Based on information on TSNAs, exclusive use of DPTs" -- DTPs -- you know, this is so easy for those of us who are physicians. DPT is sort of like a natural -- "should be less hazardous than regular smoking of cigarettes."

Mirjana?

DR. DJORDJEVIC: Since we are taking about health risks, we should also have non-tobacco users as a control because risk of those who never used tobacco and start with the dissolvables can be higher.

DR. SAMET: Well, I think this is one of those issues where we can make this comparison. I'm not sure we know what to say about what you suggested based on the data that we have seen, unless we say that some TSNAs from a dissolvable product are more than one would have had otherwise. But let's see.

DR. BENOWITZ: Actually, I would like to change this. I don't think that this sentence on

hazard is really based on TSNAs. It's based on the fact that cigarette smoke generates a lot of toxins, a lot of combustion products, a lot of carcinogens, a lot of things.

So I think we can say, based on just overall exposure, these products should be less hazardous than regular smoking. We can also say that DTPs contain less TSNAs than currently marketed smokeless tobacco, but the health consequences of that are not known.

So I'd recommend something like that, or --

DR. SAMET: So we made the comment before about TSNAs. So what you really want to say is based on understanding of the delivery of toxins to smokers --

DR. BENOWITZ: Right.

DR. SAMET: -- from cigarettes.

DR. BENOWITZ: Right. So it's not TSNAs. It's just toxins from tobacco smoke.

DR. SAMET: Of the delivery of toxins to cigarette smokers.

DR. BENOWITZ: Right.

DR. SAMET: Exclusive use of DTPs should be less hazardous than regular cigarette smoke. I think that's --

DR. BENOWITZ: Than cigarette smoking. Right.

DR. SAMET: The key question, of course, is how much, but I think this is a qualitatively correct judgment.

DR. BENOWITZ: Yes. That's fine.

DR. SAMET: Yes. Ellen?

DR. BENOWITZ: And I think we should -- since we have the data, we should also say something about TSNAs, where we can say that their contents are lower than that of currently marketed commercial --

DR. SAMET: Well, we've done that. That was previously.

DR. BENOWITZ: No, no, no. But I'm saying here, we can say that it's lower than commercial smokeless tobacco, but the implications with respect to health are unknown.

So just bring it up in terms of the health risk because before, we had smokeless tobacco here.

We took that out because we don't have epidemiology. We do have data on carcinogen exposure. We can say that carcinogen exposure is less, but we don't know what the implications are in terms of health.

DR. SAMET: Let's go back up to where we talked about content.

DR. BENOWITZ: No. But I'm talking about health risk here.

DR. SAMET: No, I know. I know. But I just want to go back to what we said earlier. So that's a page or two back.

MALE VOICE: That's right there.

DR. SAMET: No. Keep going. Here. So we say, "Available data for some products show delivery to users of lower amounts of nicotine and TSNAs than are delivered by cigarettes."

DR. BENOWITZ: Right.

DR. SAMET: So we've said that.

DR. BENOWITZ: Yes. What I'm talking about here is smokeless tobacco. I'm comparing these products to the usual forms of smokeless tobacco. I'm just making the point that TSNAs in the currently

marketed dissolvables are lower than the currently marketed smokeless tobacco products, but the health implications of that are, at present, unknown.

DR. SAMET: Or should the point, if we want to make it about the comparison of TSNA content of DTPs versus other products, should that be in the earlier bullet?

DR. BENOWITZ: Well, but if we're talking about health risks, I think we should bring something on the health risk, but just say that the implications with respect to health are not presently known.

DR. SAMET: So let me see. Do you have that sentence? So here. Give Caryn the sentence one more time.

DR. BENOWITZ: "The TSNA content of DTPs is lower than that of currently marketed ST products, but the health implications of this difference are not presently known." Something like -- does that sound okay?

DR. SAMET: It sounds okay, although less is likely to be better than more. I mean, it seems a

little -- I mean, you're saying that the yield of carcinogens, tobacco-specific, a group of carcinogens is less.

DR. BENOWITZ: Right.

DR. SAMET: And then we're saying we don't know what that means. I'm actually a little troubled by that.

DR. BENOWITZ: Well, because we know that smokeless tobacco products deliver carcinogens. But many studies, like in Sweden and possibly in the U.S. in the future, have not shown a cancer risk. And so there's probably a threshold.

DR. SAMET: Okay. So, then, why don't we say, "but the public health implications of this difference are unknown," or something. Because I think that's where we get into -- yes, Mark?

DR. CLANTON: May I? I was wondering, Neal, are you making a distinction between pro-carcinogens, TSNAs, versus toxins overall? Because I'm trying to understand whether or not the original statement is comprehensive and would include TSNAs.

But if you're making a distinction between

pro-carcinogens and overall toxins, formaldehyde, et cetera, then I understand why there'd be a difference.

DR. BENOWITZ: Well, cigarette smoke is just a mixture of thousands of carcinogens.

DR. CLANTON: Absolutely.

DR. BENOWITZ: Or not thousands. Lots.

DR. CLANTON: Right.

DR. BENOWITZ: And so there it's very clear that tobacco smoke is much more hazardous. For commercial smokeless tobacco, I think it's an interesting question because these DTPs do expose people to less. We don't know if that matters or not. It might.

DR. CLANTON: We don't know.

DR. BENOWITZ: We just don't have the data. We don't have the data in the U.S. yet, the epidemiology, to say is there any increased risk of pancreatic cancer in the U.S. or other cancers? There could be a difference. There could be an impact. We just don't know.

DR. SAMET: John, did you have a comment, or

have we gone by it?

DR. LAUTERBACH: Well, I did have one comment. There's a paper that came out in Chemical Research and Toxicology within the past week -- I thought I had a copy with me; I left it back in the hotel room -- which would shed light on this question, albeit it's a theoretical paper.

DR. SAMET: Then the next time this is reviewed, they will look at that paper.

[Laughter.]

DR. SAMET: Ellen?

DR. PETERS: This goes back to a comment that Mirjana made a minute ago and that I mentioned earlier. I think we need something, some kind of judgment or evaluation, of the absolute risk of currently marketed products, whether that is unknown, which I think might be what you've suggested.

I think some comment is made on that because it's relevant to people who use the products and never would have smoked. But it's also relevant to people who are trying to step down from cigarettes and are currently only using dissolvable tobacco

products and might want to consider stepping down from there.

DR. SAMET: So let's put an Ellen placeholder there and see if this is something here or there. I mean, we really don't have information on absolute risk, and we could say that, and maybe that would be helpful. Of course we don't have information. We couldn't.

Yes, Bob?

DR. BALSTER: So this is the same thing I was basically trying to raise way early out, and that is that no tobacco-containing product is safe. Is this a place to just say that? No tobacco -- when you talk about health risks, no tobacco-containing product is safe. It simply isn't.

DR. SAMET: Again, I'm going to keep us on charge, though, which is what I said before. I think the question is that whether we want to say that at this point on health risk, that there are no data available that allow TPSAC to comment on the attributable risk, whatever we want to use, or the risk of these products as they might be used in the

population. We just simply don't have it.

So if a comment here is to say there are no epidemiological data available to assess risk of these products in actual use, period -- I mean, if that's the comment, we can put that in.

MS. COHEN: You want to put it right here?

DR. SAMET: Yes. Sure. That's the Ellen placeholder.

Dan?

DR. HECK: Just a slight change to the sentence that Neal has added here. If we could say something like, then, "some or many currently marketed," because we're really talking about the traditional moist snuffs here, I think. But some traditional products like loose leaf chew, for instance, has always been in the area of the Swedish levels.

So we just say "some" or "most" or something other than "all currently marketed," I think it would be more accurate.

DR. SAMET: Neal?

DR. BENOWITZ: I'm happy with "most."

DR. SAMET: I'm actually on strike. No microphone.

[Laughter.]

DR. SAMET: So you want to put "most" in front of "currently marketed."

DR. HECK: Something to not sweepingly include all products because somebody may raise an objection because there may be other products, like snus, for instance.

DR. SAMET: All right. Fine.

Fred?

DR. PAMPEL: As a non-expert on this, I'm puzzled by the minimization of the importance of TSNAs in these changes. In all the studies we've looked at, I thought that came up again and again as a criterion for what's harmful and what's not. This whole paragraph sort of reads like we just don't know. It's not important.

DR. SAMET: Neal?

DR. BENOWITZ: Well, they are one of many carcinogens in cigarette smoke, and there are certainly potent lung carcinogens, and probably

esophageal carcinogens and pancreatic carcinogens, in tobacco smoke. But based on the experience, say, with the Swedish snus, which does deliver TSNAs but not the other combustion products, cancer risks for most cancers is nil; there may be a pancreatic cancer risk, and even that is less than cigarette smoking.

So there's probably a factor of the combined exposure to TSNAs plus other carcinogens and also dose response. So while it's not good to have any, there could be some level that causes relatively few cancers. So that's why it's so speculative.

DR. SAMET: Is there another hand?

DR. PETERS: Just quickly. I think you have to, in that last sentence, just make it, "There are no epidemiological data available on the absolute health risks." Otherwise it's going to read very funny compared to the comparative health risks that you had above.

DR. SAMET: Okay. Turn the page. Consumer perception. There's a comment here I actually -- if somebody asked me to quote exactly which study was the one study, I would say, go look at all the

materials. But at least that was what came out of the notes.

Does anybody recall this? Dorothy?

DR. HATSUKAMI: Yes. It was the O'Hegarty study. They did a focus group, trying to see what people's perceptions were of Ariva. And I guess they had indicated that a significant number thought that they were non-tobacco products.

DR. SAMET: And John, you cite under Romito, et al. Do you remember what that shows?

DR. LAUTERBACH: Well, what I did is went into PubMed and looked at dissolvables versus the different brand names. And I couldn't find anything with Ariva and perception. But this Romito did come with -- included Camel products in their study.

DR. SAMET: Do you by chance have that with you?

DR. LAUTERBACH: Let's see. Romito is 2011.

DR. SAMET: Does this study ring a bell with anyone? Dorothy, does this --

DR. HATSUKAMI: Yes. Romito was in our packet of information.

DR. SAMET: Microphone.

So why don't we try and sort that out. So the sentence, as written, may not be inclusive of all the studies that we saw. All right.

So while you two are thinking, let's go on. "Consumer response. Consumers have not responded positively to current products."

Neal?

DR. BENOWITZ: Again, it's sort of wordsmithing. But I think we should just say, "In general, consumers have not responded," because there are some who do.

DR. SAMET: Okay.

So while this is getting sorted out, let's go to page 17. So childhood poisoning, with the move of the "to date."

[No response.]

DR. SAMET: All right. Then on to Industry Presentations and Documents. So product range, I think that's pretty straightforward.

Neal?

DR. BENOWITZ: I would just add, "and other

constituent yields," because they did look -- some studies looked at things besides nicotine and TSNAs.

DR. SAMET: And there should be contents, probably. Right?

DR. BENOWITZ: Yes. Contents.

DR. SAMET: Contents.

DR. BENOWITZ: That's right. Contents.

DR. SAMET: "With different contents of nicotine, TSNAs, and other constituents."

DR. BENOWITZ: Yes.

DR. SAMET: Nicotine, TSNAs, and other constituents. Make that "TSNAs -- no. And other constituents, period."

DR. DJORDJEVIC: What about such as benzo-a-pyrene and heavy metals? Because this is all Group 1, carcinogens by IARC.

DR. SAMET: You want to say, "and other constituents," put an S, comma, "such as"?

DR. DJORDJEVIC: BaP, heavy metals.

DR. SAMET: "Benzo-a-pyrene and heavy metals." B-e-n-z-o dash a dash p-y-r-e-n-e, and heavy metals.

Then we come to something in red here.

DR. HECK: Yes. I suggested this sentence because I thought we did hear from some of the industry manufacturer presentations that the manufacturers do manufacture against the voluntary Swedish standard, and that's really the panel of analytes that has, at the minimum, been developed for most of these products. So I thought we could consider a sentence like this.

DR. SAMET: Mirjana?

DR. DJORDJEVIC: I would like to remember the presentation by Irina Stepanov and the graph which she presented showing a very wide variation in TSNA content, especially Marlboro products, which are like having over like 3 micrograms per gram of tobacco, which is way beyond Gothia standards. So I guess if these products are going to refer to Gothia standard, then they have to keep the levels within those standards.

DR. SAMET: So should this, say, indicate that some meet the voluntary standard? Is that -- John?

DR. LAUTERBACH: Dr. Samet, I don't think the sampling reported in the articles by Stepanov was anywhere near as extensive to say anything one way or the other. I mean, people just can't go to a store, take a sample, and say it represents a whole product line, or just do a limited number of analyses.

That was my comment back and forth when we first got into this thing on constituents. We really do not have any solid data one way or the other in terms of the extent of sampling, based on what's in the peer-reviewed literature.

DR. SAMET: Then what I would actually suggest is that we delete Dan's addition on the argument that we don't really have the requisite data for the products to make this statement as they are actually in use and as one might sample them if you were going to try and do exactly what he suggested, John. So I would suggest we delete it because we might not be able to support it.

Was that okay?

DR. HECK: Yes.

DR. SAMET: All right. So that we're going

to delete.

Then, all right, cigarette use. We're on to page 18. So again, this is now essentially a summary of what we were presented with by industry. So this is the evidence presented to us.

[Pause.]

DR. SAMET: Tim. Tim and then Neal.

DR. MCAFEE: I have a real quick question just on the cigarette use, users smoke fewer cigarettes than nonusers. If there's anything we could modulate it to make it clear that we don't know that this is correlative or causal, that we don't know that they're smoking fewer cigarettes because they're using DTPs?

DR. SAMET: So what is the suggested wording change? I mean, again, just remembering that this is just a summary of what we heard. So, I mean, I think it's okay. This is --

DR. MCAFEE: Yes. Okay. I'm all right.

DR. SAMET: Your question of interpretation is different.

Let's see. Neal?

DR. BENOWITZ: I just thought we should say that among those who both smoke and use DTPs, et cetera.

DR. SAMET: Okay. Fred?

DR. PAMPEL: I was thinking just cross-sectional data show users of DTPs smoke because -- well, people might realize that cross-sectional data can prevent causality, the way longitudinal data would.

DR. SAMET: Maybe I'm remembering wrong, but didn't some of this come from studies in which people were given DTPs and use was tracked? So I don't think it was strictly cross-sectional, but my brain is strained here.

MALE VOICE: I thought cross-sectional, then, just remembering.

DR. SAMET: Yes. I actually think some of this comes from studies in which these products were provided. So I think it's okay. "Among those who both smoke cigarettes" -- I mean, maybe it's obvious, but let's just be explicit.

Down to marketing. So this is again just

descriptive of what we heard and saw.

Then cessation? And, let's see, Ellen. You've got a comment here.

DR. PETERS: I had thought that either Dr. Lauterbach or Heck had brought up some advertising exception to this. But if you guys don't remember, I must be misremembering.

DR. HECK: I can't say that I remember. But it's possible that in the pre-FDA era, some of the real early Ariva/Stonewall copy may have made that kind of reference, but certainly not since the FDA rule.

DR. SAMET: So it does have the leadoff of "Presently."

Tom?

DR. EISSENBERG: Yes. Actually, that's what primed me to write "Presently, and consistent with current regulatory standards, DTPs are not being positioned by the industry as useful for cessation."

DR. SAMET: Speak slowly.

DR. EISSENBERG: Presently, comma, and consistent with current regulatory standards, comma,

DTPs are not being positioned.

DR. SAMET: Okay. Page 19?

MALE VOICE: Did you say current?

DR. EISSENBERG: Yes. Current regulatory standards.

DR. MCAFEE: Can I make one other on this one? Is whether we should say, they are not being positioned by the industry as useful for cessation or as replacements for cigarettes.

DR. SAMET: Well, the bullet, though, is about cessation.

DR. MCAFEE: Okay.

DR. SAMET: So I think probably that --

DR. HECK: But just building on what Tim said, should we say cigarette cessation here? It wouldn't take much room and --

DR. SAMET: For cessation of cigarette smoking, as opposed to cessation of exercising.

[Laughter.]

DR. SAMET: Youth. And again, I --

DR. MCAFEE: The only thing I have a question on, though, in that wording, is that a true

statement, that current regulatory standards would not allow positioning as them being useful for cessation of cigarette smoking?

Because I know Reynolds did this around some snus campaigns, where they were encouraging people to be abstinent for a month or two months, with prizes and all this. It's not cessation in the classic sense, but it's product -- I mean, can't the tobacco industry compete one product versus another product without requiring the regulatory signoff on that?

DR. HECK: I guess they're trying to encourage trial by smokers with various promotions. But whether that would be explicit enough to be termed a smoking cessation effort, I don't know.

DR. SAMET: I think it's probably okay as it stands. I mean, I think not being as useful or -- maybe you could make it stronger and say "effective." I don't think there's any claim being made that they are effective for smoking cessation -- for cessation of -- so maybe change "useful" to "effective," and I think that's probably correct.

Are you okay, Ellen? Okay.

So open public hearing and public submissions. So this is, again, a caption of what we heard. And actually, for those who --

DR. CLANTON: To tell us what it was.

DR. SAMET: What?

DR. CLANTON: I mean, and that's accurate.

DR. SAMET: Yes. And for those who went in the public docket, there are also many submissions there as well from members of the public.

DR. BALSTER: I have a -- am I on? About product perception, I mean, would it be fair to say something like, "There is some evidence that SLTs can be perceived as non-tobacco products"?

DR. SAMET: DTPs?

DR. BALSTER: That DTPs can be perceived as non-tobacco products. Could we say that there is some evidence -- product perception. Could we say, "There is some evidence that SLTs can be perceived as non-tobacco products"? I'm thinking specifically of, for example, the Virginia study, which has -- that came in through the open public hearing.

DR. BENOWITZ: It's also mentioned in the peer-reviewed literature review.

DR. BALSTER: Yes, we mentioned it earlier, but we're thinking about taking it out there. So I'm just wondering if it's okay to put it here. We certainly obtained some evidence on it; we got more materials in our packets today. It would just simply say, "There is some evidence that SLTs can be perceived as non-tobacco products."

DR. SAMET: You mean DTPs every time you're saying --

DR. BALSTER: DTPs. I'm sorry. DTPs.

DR. SAMET: So I'm noticing, if you skip to page 25, there's a comment on youth use of DTPs. But we don't say anything there about youth perception. But I think the data you're citing, Bob, would all be in reference to youth, wouldn't they?

DR. BALSTER: Yes.

DR. SAMET: So maybe -- I mean, it's a little hard to split this out. But this, in terms of what we heard at the public hearings and I think what was in some of the comments would support making these

statements. I mean, if we want to say that, "Data presented from youth surveys suggested that these products may not be perceived as tobacco products by youth," that could go in here. That would be --

DR. BALSTER: Something like that.

DR. SAMET: I think that would be --

DR. BALSTER: That'll work.

DR. SAMET: Is that okay?

DR. BALSTER: Yes.

DR. SAMET: So the awkward -- "Data presented from youth surveys suggested that DTPs may not be recognized as tobacco products by youth."

DR. BALSTER: That's fine.

DR. SAMET: It's a little awkward, but --

DR. BALSTER: You've got "youth surveys" there. That seems -- how about, "Data presented from surveys of youth suggested"?

DR. SAMET: I think we've got a double youth here no matter what.

DR. BALSTER: Then take out the final one.

DR. SAMET: Okay. John?

DR. LAUTERBACH: Are we really that confident

in the validity of those surveys?

DR. SAMET: What is your concern?

DR. LAUTERBACH: I think that they were -- my understanding was, some of these things had almost hidden messages, like a thing of Tic-Tacs in there and, you know, whether they had been validated. I mean, certain things out of the hardware store, packages like that, were any of these things checked to see whether people could recognize something that wasn't tobacco instead of candy? I mean, it just seemed like, from what I saw of those surveys, those things are of questionable validity.

DR. SAMET: Well, I think we've described what we saw, we heard. And we said "suggested." I mean, we're not finding a conclusion here. We're just presenting the findings of the surveys.

DR. BALSTER: I mean, it's no more or less true of the previous sentence, the perception that the risks are exaggerated. But we have no hard data on that, either. That was also basically coming from public comment.

DR. SAMET: I think we have not reached a

conclusion here. We just have captured what was said.

Yes, Tom?

DR. EISSENBERG: I'm unclear. This stuff we got in preparation for this meeting from Star Scientific, I'm unclear what category it fits in because it comes with a lot of public comments, if you will, individuals writing in.

DR. SAMET: Right.

DR. EISSENBERG: And those individuals contradict the statement, "nor being used by themselves for smoking cessation." So I don't know where we want to put that.

DR. SAMET: Would you like to propose a particular -- a specific change here? There's a lot of material that was presented in here.

DR. EISSENBERG: If this counts as public comment --

DR. SAMET: It does.

DR. EISSENBERG: -- then it's not true that they are not being used by themselves for smoking cessation. There are several reports in this book of

people using Ariva by itself for smoking cessation.

DR. SAMET: Okay. So maybe the way to do this is "were neither well liked nor being widely used by themselves for smoking cessation" --

DR. EISSENBERG: I'll go with that.

DR. SAMET: -- is that all right? Okay.

DR. EISSENBERG: Being widely used.

DR. SAMET: Yes. By themselves. I mean, obviously our evidence here is so fragmentary that I think we just have to be careful.

So we're on the government actions. I think the answer was both, Ellen.

MALE VOICE: It is both.

DR. SAMET: It's both, yes. Certainly, we've probably heard more vociferously about e-cigarettes, but I think the answer is both.

DR. HECK: I think this last sentence reflects two sets of comments that were -- one of which is mind, kind of reworking the phrasing. It's a little confusing now, but --

[Pause.]

DR. SAMET: Additionally, should more

proactively educate the public on the risks associated with -- how about if we just -- I'm not sure. I mean, the comment really was about specific products and not --

DR. CLANTON: "Specific" is probably a word you want to substitute.

DR. SAMET: What if we just said, "with specific products," period, and then got rid of everything that follows, which I don't quite understand at this moment?

DR. BENOWITZ: Well, I think there are several -- Jon?

DR. SAMET: Neal?

DR. BENOWITZ: There were a number of speakers who made the point about generalizing to all tobacco products, so that there was no differentiation of risk. So that point was made by many public speakers.

DR. SAMET: Yes. That's true.

DR. HECK: Change it to "relative risk."

DR. SAMET: Associated with various products --

DR. BENOWITZ: Really, it is specific products versus tobacco products in general.

DR. SAMET: So I guess the sentence should be, "should more actively educate the public on the risks associated with specific products and not just the risks of tobacco in general," if that's okay.

DR. BENOWITZ: Yes.

DR. SAMET: Are you scratching your head, John, or is that a question?

DR. LAUTERBACH: I'm contemplating.

MALE VOICE: Wouldn't it be better read, "the public on the relative risks associated"?

DR. SAMET: I think, actually, risks is probably better, I think.

On to Swedish Experience. So my remembrance of this was that the bullet labeled "Context," if we could go to it, which is page 22 -- I will note that this gets us halfway there -- was quite -- that we were quite unanimous in feeling that there was limited generalizability of the Swedish experience.

We discussed this at some length, that there really were unique characteristics. I think the

addition of "government engagement" helps. But I think we said, "that limits generalizability." We haven't said that it excludes any generalizability, but I think we're really suggesting caution.

So I think the context bullet, as it stands, we had extensive discussion about in our January meeting. "Government engagement" is a useful addition. And I'm going to suggest that we don't need -- unless somebody wants to re-engage on this, that this was a pretty firm conclusion from us.

Now, I'm going to come back because I recognize there's some green language before that. But I want to just take a look at all this, and then we can come back and have the more generic discussion.

So, I don't know, where did the next bullet, the new red bullet -- Dan?

DR. HECK: Mr. Chairman, I just got the impression that although true enough, the first bullet, I just thought it kind of cast aside this vast literature and natural experiment, if you will, from decades of experience. I think there's some

value there to inform this. I wanted to capture this, not just "limited generalizability" and we move on. That's kind of the point I wanted to make, if the committee agrees.

DR. SAMET: So we've got sort of a one hand/other hand kind of thing here.

Comments about this? Mark?

DR. CLANTON: This almost sounds like an issue related to certainty and uncertainty. So the question is making a hard statement about limited generalizability versus another statement that says, we're uncertain, or we don't know what the generalizability might be from Sweden to the United States. So that's what I would throw out.

DR. HECK: Even the existing first bullet imposes some limits on the -- salvaged some value out of what I think is quite an informative history and literature.

DR. MCAFEE: It looks to me like we're doing that, we're implying that, because we don't stop there. That's the context. We then go on to talk about it and give specific examples of things that

we've learned from the Swedish experience. So it seems a little unnecessary.

DR. SIMONS-MORTON: It seems to me that in context, we might want to say something about the uniqueness of the Swedish experience, representing the only national population experience we have that has data, so it makes it an interesting case. However -- I mean, it is useful.

DR. SAMET: Well, I guess the question is, is it useful in any way for dissolvable tobacco products? I think that's actually the question, not substitution of snus in the United States. That's not what is at issue here. It's dissolvable tobacco products.

So does this experience help us in any way with our task of risks and benefits of DTPs? Neal?

DR. BENOWITZ: I think it does in terms of direct harm because we have a lot of data, epidemiological data, on snus and direct harm in Scandinavia. So it sort of gives us an outside boundary of what the risks might be.

In terms of social use, I think that's where

it's really limited because of the whole context of use in the U.S., and the people who start using it in the U.S. versus Scandinavia are quite different.

So I think in terms of quitting behaviors and things like that, it's not very generalizable, but in terms of direct harm, I think it is generalizable.

DR. SAMET: Let me ask if there should be a bullet before the one that says context that says -- and we did hear about the Swedish experience in some detail and saw a number of papers -- that could say exactly what you said. There could be a bullet before context that says, "The presentation of the Swedish experience with snus documented," and then we could refer to the patterns of lung cancer, for example, or whatever you feel appropriate.

Then the next bullet is context, which says we're not certain about the generalizability of this for DTPs in the United States. I think that's a very fair comment. I mean, I think that we have to say that.

So to fully describe what we heard, there would be a bullet antecedent to the one now that says

context that captures what you said.

Dorothy?

DR. HATSUKAMI: I wonder if you can put the second bullet -- that's the modified, the addition, if you can put it under health benefits. And in that way, it acknowledges the fact that the Swedish experience has contributed to our knowledge about the potential health benefits of DTPs if they're used exclusively.

DR. SAMET: So you want Neal's statement --

DR. HATSUKAMI: So it is --

DR. SAMET: -- that might come before health benefits. There's a sentence there that says, "The Swedish experience documents," and we'll fill in the blank. And then, "For health benefits to be fully realized, complete substitution of cigarettes" -- I'm not sure "was needed" -- I'm not sure I quite understand that now.

I think the context statement is the one that says, well, how important is this for us addressing our charge around DTPs? The answer, we don't know, and that we have some concerns about its

generalizability.

John?

DR. LAUTERBACH: Yes, Dr. Samet. One of the concerns I have here is that DTPs have been under attack from the word go. For example, when Star first brought out their product in 2001, there was an immediate attack on it from health organizations. There was an immediate attack on it from Glaxo. And it took quite a while to straighten those things out and get these products properly classified and recognized as smokeless tobacco products.

Then when this current round of more contemporary DTPs came out, again we had a whole anti-approach to them, including putting the statute in about this committee studying them. And I think this is -- and then we have the continual warning on these products that they're just as dangerous as cigarettes. And you may remember Dr. Rutqvist's statement when he read in his testimony what the warning was in Sweden versus the warning here in the States.

You know, we've done everything possible to

compromise the ability of these products to be treated in the same manner as snus is in Sweden.

DR. SAMET: Well, I actually think that speaks to the point. The context is quite different at the moment, as you point out. So I think the context statement is correct. I think that we are at the point of deleting the red bullet, the bullets added by Dan, but under health benefits, making a further description of what happened in Sweden, if that works for everybody.

Dorothy?

DR. HATSUKAMI: I guess my suggestion is to put Dan's comment under the health benefits and make it specific -- Dan's comment specific to how the Swedish experience can inform us about the potential health effects of DTPs. So if you --

DR. SAMET: So I think that's consistent with what we want. We want a sentence that goes, "Health benefits, colon: The Swedish experience, as presented to TPSAC and documented in the literature, shows that the pattern of heavy snus use in Sweden was associated with lower lung cancer rates," period.

Neal, does that work for you?

DR. BENOWITZ: Yes. We could also look at the epidemiology of snus use in cancer itself, so it's much lower risks of all cancers.

DR. SAMET: So let's generalize. "It was associated with lower risk of lung cancer and other smoking-caused cancers."

Got that? What?

MS. COHEN: Where do you -- put this back up, then?

DR. SAMET: You don't remember that?

MS. COHEN: No. Where do you --

DR. SAMET: Health benefits.

MS. COHEN: Health benefits, which is back up --

DR. SAMET: No. No, no, no, no, no. No. Page 22. No, no, no. We're talking about the Swedish -- next. Keep going down. Don't go backwards. All right. Kill off the red.

MS. COHEN: Kill off?

DR. SAMET: I'm sorry. Delete.

MS. COHEN: I see. I'm sorry.

DR. SAMET: And then there's a sentence, "Health benefits," and then -- no, right after health benefits. Right there. Oh, it was so beautiful when I said it.

I think what we want to say is that "presentations to TPSAC and peer-reviewed literature document a lowering of rates of lung cancer and other tobacco-caused cancers as snus use increased in Sweden."

DR. LAUTERBACH: Should we say "other smoking-related diseases"?

DR. SAMET: Neal?

DR. BENOWITZ: Jon, two points. One, you're mixing two different kinds of studies. The lung cancer study is sort of the temporal trends.

DR. SAMET: Right.

DR. BENOWITZ: The other cancers are case control studies.

DR. SAMET: Case control studies. Correct.

DR. BENOWITZ: And also, I think as John's saying, there are also data showing lower risks of cardiovascular disease.

DR. SAMET: Disease. That's right. That's true. So "peer reviewed document a lowering of rates of lung cancer and other tobacco-caused cancers as snus use increased in Sweden. Epidemiological studies showed lower relative risks for major smoking-caused diseases, comparing users of snus with regular cigarette" -- "comparing snus use" -- well, "use of snus with regular cigarette smoking."

DR. CLANTON: I thought it was relative risk.

DR. SAMET: Relative risk, yes. Relative risk. "Showed lower relative risks" -- I know this is all being captured and could be read back to us -- "for major smoking-caused diseases associated" -- "among snus users compared with regular smokers."

This is a little tricky because, of course, there are people who switched, if you look at those studies.

MS. COHEN: Cigarette smokers?

DR. SAMET: "Among regular cigarette smokers." I guess that's correct because these are people who use it either in some mixed form or -- so

it's probably okay.

Neal, are you comfortable with that?

DR. BENOWITZ: Yes. The first sentence, then, I would get rid of "other tobacco-caused cancers" because the only data I know of are for lung cancer in terms of --

DR. SAMET: Yes. Fair. That's right. So, "lowering the rates of lung cancer as snus used increased." And get of the "and other tobacco-caused cancers."

All right. And then, "For health benefits to be fully realized" -- now, let's look at the rest of this -- "complete substitution of snus for cigarettes was needed." I guess that refers to the reduction of relative risk.

Neal?

DR. BENOWITZ: I've got a problem with wording, "health benefits being fully realized," because obviously, if you cut the risk of something by 25 percent, there is a health benefit that's realized. So the wording is not quite right. I'm not sure what the right wording should be.

DR. SAMET: Do we need this? Could it go?

DR. BENOWITZ: Yes. I think so.

DR. EISSENBERG: Well, I would like to argue with that because this was a point that I pressed Dr. Rutqvist on several times because I was struck by his statement using data that he presented, that in order for the -- and I don't have the transcript in front of me, so I'm paraphrasing, but I'm pretty clear on his message -- in order for the health benefits of snus in Sweden to be seen, people had to switch completely to snus from cigarettes.

He said it several times because I asked him to say it several times, and he kept agreeing with it. And I was struck with it because, of course, this goes to the conceptual model, the dual use issue. Okay? And if we're willing to accept a large amount of dual use, given what we're hearing from Sweden, that with snus, dual use does not lead to a health benefit, then we've got a problem there.

DR. SAMET: Dan?

DR. HECK: But I think, as we heard in I guess Dr. Ogden's presentation this morning, harking

back to the '89 Surgeon General's report showing the dose responsiveness of the smoking-related risk, to the extent that any of these products displace smoking, it's hard to imagine there's not a benefit that may or may not be detectable in a given study.

We have a new study in I guess the American Journal of Epidemiology this week looking at smoking reducers in Israel, showing a modest but statistically measurable benefit.

So I don't know how many of these studies have analyzed dual users versus exclusive snus-ers or ex-smokers, but it seems to me that the "fully realized" statement or something like that, as opposed to there's absolutely no benefit unless you've completely quit smoking -- I think that's --

DR. SAMET: Well, "fully realized" gets at -- Tim?

DR. MCAFEE: I'm okay with it, but I strongly agree with Dr. Eissenberg that this is a very important point, especially because of our situation in the United States, where it may have been a more minor component of the situation in Sweden because

there were many more people that were single users of snus.

But in our situation, this is a pivotal issue around the role of whether it's dissolvables or snus. And I think this is a controversial area. And if anything, the evidence is moving more towards -- particularly the area for people that have been using tobacco products for significant periods of time, that switching to dual use may be overrated.

I think, as Dan mentioned, if the benefits are modest of introducing these products in terms of dual use, it ups the ante around the danger that can be associated around anything that would increase people's sense that they would not quit where they might have otherwise quit. And even if a small fraction -- say it cuts your risk by 10 percent. Well, if it cuts your risk -- if it decreases your probability of quitting by 10 percent, that's worse.

I mean, I think this is okay the way it is, but I think taking it out, we would lose a very important issue and concept.

DR. SAMET: Mark?

DR. CLANTON: I think the statement is important to have in there, but it's really talking about relative risk on a sliding scale. And maybe the word "maximized" or some synonym of maximization might be more precise. In other words, in order to maximize the health benefit, you have to stop smoking, and I think that might be more precise than "fully realized."

DR. SAMET: So you say, "For health benefits" -- and then this really should be -- I hate to say it -- "for health benefits of snus use to be maximized, complete substitution of snus for cigarettes is needed."

DR. CLANTON: I'm offering that up as maybe a more precise --

DR. SAMET: Tom?

DR. EISSENBERG: Well, first, to that specific language, that's not what Dr. Rutqvist said. And so if we're going, based on the data we were presented, then I'm not sure that's the message we would want to give.

DR. SAMET: So this is about what we heard,

so how do you want to --

DR. EISSENBERG: Well, again, I wish I had the transcript in front of me, and I don't. But what I thought I heard him say several times was that for there to be a health benefit, people had to quit cigarettes completely and use only snus. That's what he said.

DR. LAUTERBACH: Dr. Samet --

DR. EISSENBERG: But I wanted to respond to Dan's comment. And Dan, I'm not at all picking on you; it's just that I've heard this a lot. You said, it's hard to imagine that there wouldn't be some health benefit if people were using dissolvables and their cigarette use went down, something like that. And I've heard that from a lot of people, it's hard to imagine; it's difficult to believe. And I don't think we want to make public health statements on what's hard to imagine or what's difficult to believe. We want to make them based on data. And in this case, we were presented with clear data and somebody who seemed quite knowledgeable on the subject articulating several times this point.

So I don't actually care what's hard to imagine. I care what the data show.

DR. SAMET: John?

DR. LAUTERBACH: Well, to address Dr. Eissenberg's concern, can we have that particularly stated that that was the opinion of Dr. Rutqvist of Swedish Match?

DR. EISSENBERG: Not at all. It was not the opinion. Those were the data that he presented.

DR. LAUTERBACH: Based on the data he presented. Okay.

DR. SAMET: All right, Tom. Give us the wording you want here?

DR. EISSENBERG: I thought I had it.

DR. SAMET: So say it --

DR. EISSENBERG: "For health benefits to be obtained, complete substitution of snus for cigarettes was needed."

DR. CLANTON: No. That's not what you just agreed to here. The suggestion was that you specifically attributed to the speaker based on the data that he presented.

John, isn't that what you were saying?

DR. LAUTERBACH: That would be correct, yes.

DR. HECK: If I may, I don't think I expressed myself well in the phrase that was mentioned. But we should recall, in addition to or beyond Dr. Rutqvist's presentation, we've seen, incorporated by reference as well as in some of the other comments, additional discussion of the Swedish snus experience, showing in a good number of studies that snus dual users are much more likely to quit smoking than are exclusive cigarette smokers.

Now, I don't know how you'd capture that public health benefit quantitatively other than there are 10 or 12 studies that show that.

DR. SAMET: All right. I'm going to take a last try.

Tom, are you ready? "For maximum health benefits to be obtained, complete substitution" --

DR. EISSENBERG: Well, that implies that there's some other benefits that will be obtained if there's less than full substitution, and that's not what we heard. But I take John's point that

the -- I'm going based on the data that were presented to us. And so the sentence could start out with, "Data from the Swedish experience indicate that for health benefits of snus use to be obtained, complete substitution of snus for cigarettes was needed."

[Pause.]

DR. SAMET: Further comments?

[No response.]

DR. SAMET: All right. We're moving on. New users.

DR. HATSUKAMI: Oh, wait a second, Jon. I do have one comment.

DR. SAMET: Too late. No.

[Laughter.]

DR. HATSUKAMI: I'm wondering -- I'm sorry. I thought it was relevant to that particular sentence. I'm wondering whether in that bullet, we should say that the lowering of rates of lung cancer -- literature documents a lowering of rates of lung cancer as snus use increased and smoking decreased in Sweden.

I don't know if we should just say that --

DR. SAMET: That's fine.

DR. HATSUKAMI: Okay. Good.

DR. SAMET: "As snus use increased and cigarette smoking decreased."

DR. HATSUKAMI: Decreased. Yes.

DR. SAMET: Right after "increased, and cigarette smoking decreased."

New users.

[Pause.]

DR. SAMET: New users. Yes, Fred?

DR. PAMPEL: Is there any implication about what that means, or are we just stating the fact? And it sort of implies --

DR. SAMET: Yes. It's --

DR. BALSTER: -- or people read into it that those 50 percent would not be smokers anyway. But you could reason just the opposite, that those people starting snus might have been smokers.

DR. SAMET: Well, I think this comes back, then, to how we sort of integrate and synthesize these findings. I think it's okay, and I think our

interpretation will come.

Yes, Mark?

DR. CLANTON: I'm not trying to slow things up. But given the way we're proceeding, it may be helpful to go back to open public hearing and public submission and put a sentence in there that qualifies all of this, and makes it clear that these were the data we received from the people who participated in the hearings.

That's missing. And so we seem to keep going back to, well, let's add what the studies show and the data show. But in fact, what this section -- the spirit of this section, I think, is to simply report on what we heard. So we need to inform the reader.

DR. SAMET: Okay. So we'll put in a little sentence there.

New users. Use by sex. There's some editing here.

DR. HECK: I had a little difficulty. I tried to rephrase it here, but I'm not sure I quite captured what the original statement was. So do we really -- the statement seemed to say to me that dual

use is extremely prominent among females, kind of uniquely. And I kind of didn't get that impression from the presentations or a review of the slides and things.

DR. SAMET: I'm not uncomfortable with the wording change here in red.

Is everybody okay with that?

[No audible response.]

DR. SAMET: All right. Next page. Go quick before somebody --

[Laughter.]

DR. SAMET: We're up to labeling. Certainly no one will disagree with this. In fact, they're in Swedish in Sweden and they're English in England -- not England, the United States.

[Laughter.]

DR. BENOWITZ: Jon, I've got a question. Should we make it more reader-friendly by stating what the warning difference is?

DR. SAMET: I guess this was part of the effort to just keep this very brief, the report itself. I don't think we should go into it,

personally.

DR. BENOWITZ: I would argue that this is what most people are going to read. And if they don't know what the difference is, then this is kind of cryptic.

DR. SAMET: It is kind of cryptic. The whole summary is cryptic. I mean, what can I say? I don't have any motivation for us to make one part less cryptic than another, I guess, Neal.

DR. LAUTERBACH: Dr. Samet, I think Dr. Benowitz's comment is very appropriate here because we have this -- on one hand, we're telling people here in the United States that all these smokeless tobacco products are just the same hazard as using cigarettes, when we know they're not. And over in Sweden, they put in a different warning.

I think it's very important that we have the comparison of the warning as it was expressed in that testimony by Dr. Rutqvist.

DR. SAMET: I don't see that an analysis of wording with regard to smokeless tobacco is in any way relevant to our charge, John. I mean, it's just

not. We're talking here about the Swedish experience and its potential relevance to dissolvable tobacco products, and the point is simply that there is a difference, and this is part of the generalizability issue.

We're at Indiana and youth presentations. This is page 25. So youth use of DTPs. This is describing the various data sets we heard about, and particularly the Indiana surveys.

So comments here?

[Pause.]

DR. SAMET: Ellen?

DR. PETERS: This goes to Dr. Lauterbach's comments and also to some comments that were made by the committee after this presentation. I do think that in this one in particular, that we might need a note that says, "A number of limitations exist to the quality of this study," or something like that.

DR. SAMET: You know, I actually think that we're really reporting on the findings of this and other studies. I'm not sure -- I mean, I think the Indiana experience suggested that some youth would

try it. I mean, that's a true statement about what was found and presented to us.

There's obviously limitations of many of the sources of data we heard from. I don't think we heard from any data source that didn't have its limitations. So I'm not sure why we start it again, just in summarizing key findings start pointing out finger at one or another study. It just doesn't quite make sense to me.

Sandrine?

DR. PIRARD: Yes. I wanted to include that because I think if we start doing that, we really -- I mean, what about the public comments? I mean, it comes from individuals. What is valid about that? What about an industry-sponsored study? There are limitations to it. So we really have to be careful and just focus on what we heard.

DR. SAMET: I think probably the only question here -- I mean, if we want to say, the Indiana experience during test-marketing of one DTP, unnamed, I think that would be an appropriate modification to the text there. So "of one DTP," and

leave it unmentioned.

DR. LAUTERBACH: Dr. Samet, I'm very concerned, though. If you look at what these people have written on their website, that these people have a very strong bias against these things, and, for example, have said on their website, "Smokers who use these products may get a higher dose of nicotine than they are used to, possibly resulting in nicotine poisoning, adverse reactions such as tremors, nausea, vomiting, agitation, and in more extreme cases, seizure, coma, and death."

This is what these people have put on their website about dissolvables --

DR. SAMET: So I'm not quite sure I know the relevance of what's on their website to the data that were presented. John, that's just really off the point. If your implication is that they have some form of potential bias in their work, I don't think we can make that inference from what's on their website.

Other comments? Yes, Tim, did you have a comment?

DR. MCAFEE: Just quickly, Jon. If you're going to do that -- I mean, come on. Are you trying to say that all the various -- we should discount the research from the tobacco industry because it's explicitly -- if we go on their website, we'll see that it's in their financial interest to try to sell more of the product? If you start going there, it's not even going to be in your interest, really.

DR. LAUTERBACH: I don't work for the tobacco industry, sir. But, I mean, the point is, I think if there's observer bias, we need to point that out in any of the situations.

DR. SAMET: Okay. I'm going to just suggest that we move on from this --

DR. BALSTER: Yes. I'm going to say that as stated, this seems to be an accurate description of what we heard.

DR. SAMET: Okay. Packaging. And this comment is I think a general comment based on what we heard. We heard from a number of groups on the packaging issue.

So comments here? Sandrine?

DR. PIRARD: I would just move what we've put under perception, coming from the youth survey there, like putting a bullet, perception, just to be consistent, that that basically was coming from those hearings.

DR. SAMET: So let me see. What do you want to add? Do you want to call this perception of packaging? Or is this --

DR. PIRARD: Yes. Under -- what page was it? Like we had the description with perception, which was on page -- under public -- sorry. I will tell you where it is. It's just basically to move the section we added.

Sixteen?

MR. HAMM: Nineteen.

DR. SAMET: So 19, product perception. So that was from the open public hearing, and we've moved on to the youth.

DR. PIRARD: Yes. I think that was there, and we just added something from the youth presentation there. And I would just suggest to move it to this section, just so that we are consistent

that whatever we talk about is related to --

DR. SAMET: So I think you need to go back up. About 19. Keep going. Somewhere in here. Product perception?

DR. PIRARD: Yes. It's the last sentence of product perception on page 19. Youth, yes. That bullet.

MS. COHEN: This one?

DR. PIRARD: No, no, no. Sorry.

DR. SAMET: Keep going.

MALE VOICE: There it is.

DR. SAMET: Stop.

DR. PIRARD: Yes. Data presented from youth. So that sentence, that last sentence from the bullet, perception.

DR. SAMET: But, I mean, this bullet is about packaging and not overall perception, which is what that comment refers to.

DR. PIRARD: Yes. I was just suggesting to add a bullet, youth perception, and put that sentence there. But it's just a detail, I guess.

DR. SAMET: I think it's okay.

DR. HECK: Just a small point, Mr. Chairman. In the section heading, Indiana Experience and Youth Presentation, is youth -- was that the name of that organization, or should we use the more explicit name? This is the Virginia presentation.

DR. SAMET: Sure. Sure. That's fine.

DR. HECK: Whatever that was.

DR. SAMET: The Virginia -- so we're going to modify that to Indiana Experience and Virginia --

DR. EISSENBERG: Foundation for Healthy Youth.

DR. BALSTER: But I think we're getting confused because the main thing they talked about was what we put on page 19. So I'm just saying -- I'm not sure why we're covering it in two places. I mean, we have a section there that was on public-submitted documents and presentations. That was where that information was presented to us. I'm just saying I don't understand why we have it in two places.

DR. SAMET: Yes. And we also heard from the American Academy of Pediatrics. So maybe the heading

should be not Indiana Experience and so on. Maybe it should be Presentations and Information -- or just say information on youth.

DR. CLANTON: Make it general?

DR. SAMET: Make it general because we heard from other groups.

All right.

DR. PIRARD: One question. Sorry. Should we add the information that the Virginia people gave us in those additional studies or analyses that they did, and that we got in the package for this meeting? The fact that basically among people -- among youth who perceived those DTPs as non-tobacco product, there was a higher risk or -- I mean, they were more likely to try them. That's something that we got in the package for this meeting. I don't know if we want to talk about that or not.

DR. SAMET: Comments about this? The sentence that starts, "The Indiana experience during test marketing suggests that some youth would try DTPs, particularly those already smoking cigarettes," period. And then if we want to add a sentence that

says, "Data from Virginia suggests that youth not perceiving DTPs as tobacco-containing would be more likely to try them."

So if we go back to youth use of DTPs -- I suggested some -- so write down there, "already smoking cigarettes." Put a period. Down, down, down, down, down, down. Right -- down, down. Right there, at the end of that sentence, put a period, which should be there anyway. Keep going..

MS. COHEN: Here?

DR. SAMET: Yes. There. Put a period. And then the next sentence would be, "Data from a survey in Virginia suggested that youth not perceiving DTPs as a tobacco product would be more likely to try them." Period

Again, I just want to remind everybody, we don't have to mention every single study in this summary, because then it will turn into a non-summary.

Okay. Got it?

We are now going to go to Responses to Charge Questions -- Charge Issues, sorry.

DR. LAUTERBACH: Dr. Samet? (Inaudible – mic off.)

DR. SAMET: I can't tell you till we're done.

So Responses to Charge Issues. So we need to look carefully at this. And this really goes back to our capturing the discussion that we had at the end. So let's read through this carefully. This is page 26, and our charge was risks and benefits.

So this idea of this comparison in our figure, and scenarios with current types of DTPs, which I think is a useful addition. And in constructing comparison scenarios, TPSAC was constrained by the limited real world experience to date. Since John is out of the room, I will say that I don't think we want to replace that by "chose to be constrained." We were.

So again, are there comments or additions? We don't have any red on this. Okay. So then that would take us to what used to be page 28, the risks and benefits to the population as a whole. And again, I think just read to the paragraph that starts, "TPSAC considered."

[Pause.]

DR. SAMET: And there's an addition here. Let's see. It's a rather cumbersome sentence at the moment.

DR. CLANTON: I have a question about -- on number 4, it says, "DTPs sufficiently reduces cigarette smoking or use of other types of SMTs."

Are you talking --

DR. SAMET: I'm sorry. Where are you?

DR. CLANTON: Page 29. Well, we have numbers on the side. I'm sorry. So one, two, three, four -- four lines down. The next-to-last line up here, I guess it is. It's easier for me to read it from here. "DTPs could reduce," or "significantly reduces" -- where is it up there?

You see it on yours. Right?

DR. BALSTER: Jon, I'm the author of the "decreases the likelihood of initiation and use." That's just basically bullet 1 on the figure. You failed to include bullet 1, that locus on possible effect. That's why I added that. That was your -- that's bullet point 1.

DR. SAMET: Yes. And I think, actually -- and that was your addition to it. So the TPSAC framework, "that DTPs could reduce the disease burden caused by tobacco use, decreasing the number of smokers, if availability increases successful cessation, or decreases the likelihood of initiation and use of smoked products."

DR. CLANTON: I'm missing this. I still don't see this.

MALE VOICE: Your point is the "sufficiently" in the sentence, right?

DR. CLANTON: Yes. "If the availability of DTPs sufficiently reduces cigarette smoking." And I'm asking, are we focusing on the individual or are we looking at the population effects of fewer smokers?

DR. SAMET: These are population.

DR. CLANTON: Population. Okay.

DR. SAMET: So I'm still trying to figure out where you are, Mark, but --

MALE VOICE: He's at the second line from the bottom. "DTPs sufficiently reduces cigarette

smoking."

DR. CLANTON: There's a red line under DTPs, the second line.

MALE VOICE: There.

DR. CLANTON: Yes. And I was simply asking, we were looking at the individual level and trying to make some comment about relative risk reduction in the individual, if they smoke fewer cigarettes, or are we trying to make a comment about fewer smokers altogether in the population?

DR. SAMET: No. This is really population. I mean, the whole text begins with a discussion of burden.

Tim?

DR. BENOWITZ: Well, but I think the last part is individual. The first part was population. This is individual.

MALE VOICE: That's what I was trying to figure out.

DR. SAMET: You can't have -- so fair enough. So you can't have population without individual.

DR. CLANTON: No. The issue is whether

you're going on or off bimodal, no smoking versus smoking less. That's what I'm trying to understand.

DR. BENOWITZ: The first part says, "decreasing the" --

DR. SAMET: Which first part?

DR. BENOWITZ: After "burden caused by tobacco use, decreasing the number of smokers," that's the population effect. Then the third part of that, "sufficiently reduces cigarette smoking," that's an individual effect.

DR. SAMET: Yes. True. All right. So let's try and maybe deconstruct this a little bit. I think there's too much possibly in this sentence, which goes on forever, and I must have understood when I wrote it.

Tim?

DR. MCAFEE: Well, Jon, I'd like to raise a larger question as to where the sentence is going because the way I see this larger construction is you've got a very long, very complicated and elaborate essentially rephrasing of the entire framework about how dissolvables might end up

creating a positive population effect.

Then you have one sentence that basically says that we think that DTPs are likely to be associated with far lower disease risks. And then you have one sentence that says, well, they could also increase the disease burden by increasing the number of tobacco users or reducing cessation.

This is like the only time I'm actually going to use the "we" voice, so this is "we." I'm speaking for CDC here. We have a grave concern about how this is set up. This is the section, all this stuff, this is the one on population as a whole. And our concern is that basically, it appears -- and it's already been said twice, or three times by commentators, that TPSAC has taken the position that dissolvable tobacco products are likely to be associated with far lower disease risks than cigarettes.

I think I would include with Neal, well, do we mean at the individual level? Do we mean if things just go along the way? Because it's kind of contradictory with early statements that we're saying that they don't seem to be having much effect.

So I think that's a very dangerous statement. And I think the way we've teed it up with five or six -- or a very long paragraph about all the different ways that they could possibly improve population health, and then one short sentence that says how they might increase it with no specific benefit examples of how that might happen, is -- I don't know if that was intent or if that's just how it ends up being read.

I would propose that we should substitute something that just reiterates the fact that long-term use of dissolvable tobacco products by an individual is likely to be associated with far lower disease risk than smoking cigarettes, but not make a population-based claim.

DR. SAMET: Okay. So let's go back to the text, and let's see what we're saying now and try and understand if that's what we want to say.

DR. MCAFEE: Did you want to move it down a little bit so you get the rest of the sentence that says that, "TPSAC members concurred that," so we can see the rest of it? And there was one attempt by I

don't know who to partially address this issue.

So was your intent when you wrote that, "TPSAC members concurred that available evidence supports a conclusion that DTPs are likely to be associated with far lower disease risks than cigarettes," was that a population statement or was that an individual statement?

DR. SAMET: You know, actually, Tim, I'm not sure we had refined our discussions to make that comment one way or the other. So let's get on the table what you mean by population versus individual; population meaning the combination of penetrance or prevalence and effect on risk versus what happens in an individual who may choose to change their smoking pattern. That's I think what you mean, but let's just make sure we have a common understanding.

DR. MCAFEE: Yes. Well, I would have said that -- I thought the committee, based on prior statements in this document and conversation, that we actually had reached an agreement that was pretty broadly shared that if an individual, particularly if they exclusively were to use dissolvable tobacco

products -- if that individual does that, particularly if they do it early on in life as opposed to after smoking for 40 years -- but if they do that, that we are pretty firm that they will have --

DR. SAMET: So to bring --

DR. MCAFEE: -- that they are at a far lower disease risk.

DR. SAMET: To bring the specificity you want to the statement that says that TPSAC members concurred, you want it to say that TPSAC members concurred that available evidence supports a conclusion that exclusive use of DTPs by individuals --

DR. MCAFEE: Is likely to be associated with far lower disease risk than --

DR. SAMET: Right. Right. Is that what you want there?

DR. MCAFEE: Yes. Although again, I don't even, a hundred percent, think it belongs there because this is supposed to be something on population risk. But I think it's fine to have that

there.

DR. SAMET: And then the sentence that comes after that is the consequences of DTPs for population burden, however, depend on actual -- depend on patterns of use, and particularly on the prevalence of DTP use. That's the follow-up point.

DR. MCAFEE: Yes. The only issue is it gets back to some of the complaints we had that John had raised about the model in our original thing. It's like a consistency issue.

If we meticulously lay out every single point relating to how this could improve population health by going all the way through the model, and then we just have a sentence that only mentions two things, that it could increase the number of tobacco users, reducing cessation, it gives the appearance that the committee feels that there's this vast weight of possibilities for how it could improve things, but only two things that could disprove it.

So one way to solve it would be to go back to this beginning thing and just, again, have these neutral statements that say it could impact, as

opposed to that it could increase, the effect. So it could -- several ways that DTPs could reduce or increase the disease burden caused by tobacco use, by decreasing or increasing the number of smokers, et cetera, et cetera. I don't see --

DR. SAMET: Well, maybe the way to do this -- I'm not sure that's useful. I think if we were to construct this paragraph in a way that said, here's how it could increase disease burden, go through whatever -- or reduce disease burden and individual risk, and then come back and do the same thing on the possibilities of effects that might increase disease burden, i.e., fewer people quit; children move from dissolvable to smoking, so at the population level, there could be effects --

DR. MCAFEE: We could do that.

DR. SAMET: So I think the way to address your concern is to have one paragraph that says, here are the ways that DTPs could decrease the burden, and here's the way -- burden and risk for individuals, and here's how burden and risk could be increased, and then follows a lot of stuff on uncertainty.

I think, if for some reason --

DR. MCAFEE: Yes. That's all fine.

DR. SAMET: -- somebody chose to use dissolvable tobacco products for 50 years, they probably would have lower risk for tobacco-caused diseases than had they chosen to smoke for 50 years. But I think what you're saying is that things are sort of mixed up and muddled in this text, and we should probably speak to whoever wrote it.

[Laughter.]

DR. MCAFEE: What you're proposing would work fine.

DR. SAMET: Yes. John?

DR. LAUTERBACH: Dr. Samet, on population effects, if we had a major portion of the cigarette smokers switch to dissolvables or smokeless tobacco in general, then we have all the disease related to sidestream, and third-hand smoke would go down also.

DR. SAMET: Sure. I think that -- and perhaps we may or may not want to make that comment. But I think right now let's focus on trying to straighten out the text. So let's go back to the

start of this section. Okay. You're there.

So this was introductory text, and so, actually, what I would suggest is go back to Figure 1 and do a paragraph there. Yes. And we're going to have two paragraphs. One is going to say, ways that disease burden could be reduced, and risk; and the other will say how it might be increased.

So let's start with this. And, Tim, then we're going to come back with the other piece of this. So it indicates several ways that DTPs can reduce disease burden caused by tobacco use. Decreasing the number of smokers -- so why don't we do 1, just a 1 right there, so we can just sort of separate this out.

DR. BENOWITZ: Jon, can I make a suggestion? I think you said this before. It might be worthwhile having a transition sentence after Figure 1 saying that the impact needs to be considered both on an individual and a population basis. And then you could say in the next paragraph, for someone who's a sole user of DTPs, the risk is likely to be much less than cigarette smoking.

DR. SAMET: So we start off with --

DR. BENOWITZ: And everything else is population.

DR. SAMET: So here, the charge is the risks and benefits to the population as a whole, including users and nonusers. So we could say that, and then why don't we say -- the next sentence after Figure 1, just say, "Additionally" --

MS. COHEN: That's a new paragraph?

DR. SAMET: No. "Additionally, TPSAC considered how DTPs might affect the risk for individuals," which I think is your comment, Neal.

DR. BENOWITZ: Yes.

DR. SAMET: Then we're going to have this paragraph. "The TPSAC framework indicates several ways that DTPs could reduce disease burden: 1) decreasing the number of smokers." And then go down, 2), where it says, the other decreasing. No. Keep going down. Down, then down. Last sentence. Right there, after "and." No, leave "and." "And 2) decreasing" --

DR. BENOWITZ: Jon, again, wouldn't it be

clearer if the first statement just said, on an individual basis, if someone were an exclusive user of DTPs, their risk would be less than cigarette smoking?

DR. SAMET: Well, but let's have --

DR. BENOWITZ: And then you get all the individual risk --

DR. SAMET: Let's have that after this discussion about the framework because I think this is the population burden piece, and then we'll have the individual piece.

DR. BENOWITZ: I just thought it would be simpler to get it out of the way because then everything else is population. When you make that statement clear, then everything else you're dealing with is population.

DR. SAMET: Well, okay. So if you want to have a first sentence, before, "The TPSAC framework" -- it's right there -- and just say, "With regard to benefit, comma, TPSAC concludes that exclusive use of DTPs would greatly reduce risk for tobacco-caused disease compared with regular

smoking."

Is that your --

DR. BENOWITZ: Yes.

DR. MCAFEE: Can you put the word "individual" in there?

DR. SAMET: "Exclusive use of DTPs by" --

DR. MCAFEE: "By an individual."

DR. LAUTERBACH: Dr. Samet, aren't we talking smoking-related disease in that sentence, not tobacco-related disease?

DR. SAMET: (Inaudible – mic off.)

DR. BENOWITZ: I think "smoking" is reasonable.

DR. SAMET: Okay. So "smoking-caused disease, compared with regular use of cigarettes," just to get --

All right. So now we're into the population level and the TPSAC framework. So we indicate several ways that DTPs could reduce the disease burden caused by tobacco use.

DR. BENOWITZ: Jon, would you want to say "population disease burden" here, just to make it

really clear?

DR. SAMET: That's fine. So "population" up there. Right.

Decrease in the number of smokers. Are we going to accept the red, whoever -- that's Bob's or somebody's. Yes, that was Bob's. Okay. We're going to accept -- sure. We like Bob.

[Laughter.]

Sometimes. DR. BALSTER: (Inaudible - mic off.)

DR. SAMET: Sometimes.

And, "decreasing the risk of tobacco-caused disease if" -- why don't we say, "if availability of DTPs sufficiently reduces cigarette smoking," period. I think that's probably safer. Yes. Now, this would now come out because we said that up front.

DR. BENOWITZ: Right.

DR. SAMET: So we actually concurred on somebody, that that goes, all the way down to "exist."

All right. Now -- all right. So then, that's the new paragraph that starts with, "The

framework also shows how availability of DTPs could increase the disease burden by either increasing the number of tobacco users or reducing cessation."

All right. For those who -- does anybody want to add to this? Tim?

DR. MCAFEE: Well, I think the easiest thing to do would just be to actually literally -- if you transpose the wording that you used in the first section and then flip "decreasing" to "increasing." So it would read, "increasing the number of smokers if availability of DTPs decreases successful cessation or increases the likelihood of initiation and use of smoked products." So you're just flipping around the core directional --

DR. SAMET: So, actually, go back and give us a specific sentence.

MALE VOICE: He wants you to copy and paste and then change the word.

DR. MCAFEE: So copy the -- it would be, "The TPSAC framework indicates several ways that DTPs could increase the population disease burden caused" --

DR. SAMET: Oh, you want to have -- okay. So you want to copy that sentence.

DR. MCAFEE: You just take that sentence, starting there. That one. That one, right.

DR. SAMET: The whole thing.

DR. MCAFEE: Take it all the way down.

DR. SAMET: But we're not going to propose that exclusive use of DTPs might increase disease risk. So that we're not going to say.

DR. MCAFEE: Yes. When we get there, we'll have to alter that.

DR. SAMET: Don't move it. Copy it. All right. Now go -- so go up. I think you want to insert where it says -- right?

DR. MCAFEE: Yes. Insert that whole -- the framework would just be replaced.

DR. SAMET: And then he wants to change "reduce" to "increase."

DR. MCAFEE: Change increase -- "reduce" goes to "increase" in the second line.

DR. SAMET: "Increase of population" --

DR. MCAFEE: Now, the other way -- again,

Jon, the other way you could do this would be by having the first phrase be neutral. But this is the -- and by increasing the of smokers, if the DTPs decreases --

DR. SAMET: So it then would be, "If availability of DTPs reduces rates of successful cessation."

DR. MCAFEE: Right. "Or increases the likelihood of initiation."

Now, I don't think you need to take away number 2.

DR. SAMET: I think the rest goes.

DR. MCAFEE: You just say, "and increasing the risk of tobacco-caused disease if it sufficiently increases cigarette smoking."

DR. SAMET: But that's actually -- that's already covered in the first bit. I don't think we need a 2.

DR. MCAFEE: Well, then, we don't need it in the one above, either, do we?

DR. BENOWITZ: Well, I think this gets back to the issue of prevalence versus how many cigarettes

you smoke per day. Certainly these things might increase the prevalence if there was less quitting. But there's no evidence that these products would increase how many cigarettes you smoke per day.

DR. SAMET: Yes. I think, sticking to our framework, we're not going to propose -- and I think Neal just captured it. I mean, the way that DTPs could increase the population disease burden, our current understanding is by increasing the number of smokers.

DR. HECK: And just a comment. With respect to Tim's concerns here or a need for some kind of symmetry between the pro and the con, the fact is that the literature we have from the very similar snus products is very asymmetrical. And it does speak strongly to the health benefits, and the negatives are rather speculative, I think. I think that's a fair statement.

DR. MCAFEE: I don't think that's a fair statement. And I think there have been several studies -- there's the Shu-Hong Zhu study that looked at this around what's actually happening in the

United States. I think taking what happened in Sweden and then assuming it would happen in the United States is speculative.

This is the area where this whole -- and again, I'm not even opposed to the idea of saying something that we're a little optimistic that we'd be able to get around this. But I don't think it is speculative or sort of the opposite of pie-in-the-sky to be worried about this. And I think these things could happen, and I think there's actually some evidence that if you --

DR. SAMET: But Tim, just to be clear, in terms of the framework and the way we've laid this out, the way this sentence reads now, "The TPSAC framework indicates several ways that DTPs could increase the population disease burden caused by tobacco use, increasing the number of smokers by decreasing cessation or increasing the likelihood of initiation in use of smoked products," that is what our concern is. And I think that's there and clearly laid out.

I mean, is there something --

DR. MCAFEE: Yes. I'm okay with that. You mean, in other words, if we leave off the number 2? Is that the --

DR. SAMET: Yes. The number 2, I think, is something that we don't think is the case. The number 2, we don't think that DTPs are going to increase the risk of disease caused by cigarette smoking. I think we've set that aside.

So I think that this next thing is a repetition of the sentence that says, "The framework also shows," that should go away.

DR. MCAFEE: Yes.

DR. SAMET: And the only question is whether we want another sentence that expands on what we have said here. But I think that's a straightforward statement that is parallel to the one we made earlier about the possibility of a gain within the framework.

So let's keep going. And now we get into all our uncertainty. And so this is, I think, statements of interpretation now and how strong we feel our comments can be.

Actually, at least as I recall the statement,

so I think the "apparent" is fine. If that's okay with everybody, we'll accept that. And then the statement, "Furthermore, TPSAC concluded that the context set by industry marketing will be critical in determining the impact of DTPs," I thought that was something that we all quite agreed on. Perhaps John doesn't, but I actually -- certainly there was no vote in closed session. But again, I was simply capturing what I thought was actually something that we all felt fairly strongly about here.

Ellen?

DR. PETERS: I wonder if I could just add one suggestion, that we define the term "marketing." I was going to suggest this later, but it might be appropriate here. A lot of times, when people see the word "marketing," they think it means advertising, and marketing goes beyond advertising. It's about product design; promotion, which includes advertising; also, pricing strategies, and I'm probably missing one of them.

DR. SAMET: Would it be fair to say, then, how about something, "In the context set by all

aspects of industry marketing"? Would that be okay?

DR. PETERS: Sure, as long people can understand marketing to mean more than advertising.

DR. SAMET: Why don't we say -- yes, fine. Why don't we say, "all aspects of industry marketing." I agree. When we had that discussion about packaging and so on, if you -- set by all -- it will be critical.

Then this other comment -- keep going down -- was also I think something that we felt strongly about, that availability of DTPs might affect public perception of all tobacco products. I think that was, again, another conclusion that we reached.

John?

DR. LAUTERBACH: I'm a little bit lost because one of the things here is essentially the whole impact of the federal government's view on smokeless tobacco and dissolvable tobaccos. If we had a different warning system, and we didn't have statements from the government saying they're as dangerous as cigarettes, that could make a bigger

perception on the market for DTPs than anything any company could do.

DR. SAMET: That may be true. I mean, again, I'm just going to say that we were not considering, yes, what FDA might do and what they're doing now. I think this statement as is written -- I mean, I understand the caveats you're raising and the alternative scenarios for the future around labeling. We can only deal with what we have in hand now.

DR. BENOWITZ: Jon, you could say, "set by industry marketing and regulatory actions," or regulatory somethings. It gets put in a better context.

DR. SAMET: You could say that. I'm not sure we actually either discussed or heard anything about regulatory actions.

DR. BENOWITZ: Except industry marketing is limited by the regulatory environment.

DR. SAMET: Right.

DR. BENOWITZ: So I think the context really involves both.

DR. EISSENBERG: Well, and we heard from

Dr. Rutqvist in Sweden about a difference in regulatory action with regard to the labeling that they use in Sweden and the labels that we use here.

DR. SAMET: So what is the wording change that you would like to make?

DR. EISSENBERG: Neal, I liked what you said. "Furthermore, TPSAC concluded that the context set by industry marketing and regulatory action will be critical in determining the impact of DTPs." Or "regulatory oversight" or something -- "regulation."

DR. SAMET: Okay. Now let's go to this little paragraph that says, "Given."

John?

DR. LAUTERBACH: I just have this concern here. I know it's reflected in the article by Zhu in Tobacco Control 2009. Is this really something we definitely feel, that if -- (inaudible – mic off.)

DR. SAMET: Well, I think we've appropriately given the caveats here. We say the committee was concerned. Might affect, I mean, I think this is a concern to be noted. That's all that is.

So to the paragraphs starting with "Given."

DR. HATSUKAMI: Jon, can we add "on public health" at the end of the sentence? "The risks and benefits of DTPs on public health"?

DR. SAMET: Sure. That's at the bottom of the last sentence. Right there, yes.

So this is sort of a no-call here. All right.

So now -- my microphone's tired -- we're speaking to the increased or decreased likelihood that existing users of tobacco products will stop using such products. So let's look at this.

[Pause.]

DR. SAMET: And again, this paragraph -- so keep going. "Beyond some anecdotal reports with no information would increase the likelihood of cessation of cigarette use." And I don't know whether we want to have that "or of smokeless tobacco" or delete that.

Comments?

DR. BENOWITZ: I think you should drop the smokeless tobacco because we're really not trying to deal with the public health consequences of smokeless

tobacco.

DR. SAMET: John, I'm not sure about your comment because this is not about the harm. So is there any -- can we just delete that? I don't --

DR. LAUTERBACH: Yes. I think Neal just solved the problem. I think Dr. Benowitz's comment removing SMTs solved the problem.

DR. SAMET: Okay. And then we're going back to -- so let's look at this in considering scenarios now.

[Pause.]

DR. SAMET: I think we have some additions. So these are sort of stating that we don't quite know what the future will be, and that there are different possibilities that could be important. So comments here?

So why don't you go on -- see if you can get a little more of that in. Just try and move on down to that paragraph.

Again, we have some additions. We have a sentence added by something that seems like a reasonable addition. Unknown person. "Will adopters

use the product as a cessation tool or to maintain their habit"?

DR. BENOWITZ: I would change habit.

DR. SAMET: To "addiction"?

MALE VOICE: Or "sustained regular use."

DR. SAMET: Or to maintain -- probably addiction is probably the right word. "Their addiction to nicotine."

So going back, if you're okay with the "will current marketing" and then the addition of "end product development approaches," if you continue, that seems okay?

DR. MCAFEE: In terms of the "facilitating cessation," I mean, since they can't be marketed to facilitate cessation because of the regulatory constraints around that --

DR. SAMET: That's fair. So do you want to take that out, Tim?

DR. MCAFEE: It seems to me, unless somebody has an alternate in terms of what we're getting at with that.

DR. EISSENBERG: I was going to make that

comment, too. But in fact, they can market them as for facilitating cessation if they're willing to present the data that allows them to do so. So the possibility exists. It's up to the company who wants to make that marketing claim to demonstrate that they can make that marketing claim.

DR. SAMET: So you would want to say, "Will DTPs" --

DR. MCAFEE: Well, it's a separate process --

DR. SAMET: -- "Will DTPs be marketed as" -- really, it's a cessation product -- "if appropriate testing is done."

DR. MCAFEE: Well, can I -- I guess I'd say there's an alternate framework, which I actually think is much more important, which would be -- because, again, I think classically, when we use the word "cessation," 99 percent of the time what we're referring to is people quitting all tobacco products. And the probably more potential possibility that's got more public health oomph would be, will they be marketed as facilitating a switch to

non-combustible or something? Which again, I think we weren't clear -- I'm still a little fuzzy as to whether that would require -- they couldn't perhaps do that within the regulatory framework because it's just competition between tobacco products.

DR. SAMET: I think the best thing to do is to delete the sentence.

DR. HATSUKAMI: Actually, you could say, "facilitating" or "marketed as a complete substitution for cigarettes" --

DR. MCAFEE: As a substitution product. Complete substitution product. Right.

DR. HATSUKAMI: Substitution, "complete substitution for cigarettes," because that's what they're doing for some of the snus products right now.

DR. SAMET: Right.

DR. HECK: And you could say, instead of marketing, which might have some regulatory implications, just say, "perceived as." They could be perceived that way by consumers. That perception could be facilitated by a public health authority or

by the company.

DR. SAMET: But I think this goes back to the whole context thing, which is sort of what starts this. So I think, actually, I'm going to suggest leave "marketing," but, Dorothy, "as a complete substitution," I think let's leave it at that.

MS. COHEN: Substitution of --

DR. SAMET: No. I think it's okay as you've got it. Yes.

Then let's go to the paragraph that starts, "TPSAC concluded." Oh, well, the nicotine yield in forthcoming products, I think that would be a useful addition.

So let me take the pulse of the group, which still seems to be barely beating.

[Laughter.]

DR. SAMET: Would a brief break be useful? Votes for a break?

DR. MCAFEE: If we say yes to that and we come back energized, does that mean that we'll finish by 6:00, and you'll excuse us? Is that the goal? We need a goal.

DR. SAMET: I think the goal is to be finished by 7:00.

DR. MCAFEE: 7:00?

DR. SAMET: You can stay up that late. I think we need -- I think it's going to take that long, at least, to finish this off. I don't want to give it short shift.

All right. Five-minute break. None of this five minutes turned into 15 or 20. Real five-minute break. Go.

(Whereupon, a brief recess was taken.)

DR. SAMET: I want to just have a quick procedural discussion here. At this point, I wanted to remind everybody that we do have to vote. I want us to take a quick lookback when we get to the end; I put in the paragraph that Neal wanted, and a few other things.

So procedurally, I think there's two possibilities, and we need to make a decision. We keep going now and get to the end and vote, and I think that's going to take us -- we're at page 34; hopefully the rest is easy. It's about research

recommendations and so on. But we do have to vote. So we get to the end and vote tonight.

The other option is we get to the end. Everybody gets a little email for bedtime reading that has the report in it, and we come back tomorrow, have any further discussion, vote, and go home.

So in a rare display of democracy, let me ask Mark.

DR. CLANTON: I have an 8:00 a.m. flight home tomorrow, so that might pose some problems.

DR. SAMET: Well, we can meet at 5:00 --

DR. CLANTON: That would be fine.

DR. SAMET: -- and then we'd have a chance for you to -- so that's a vote for getting it done. Is that sort of a consensus? The consensus is, get it done?

[Heads nodding affirmatively.]

DR. SAMET: Okay. Back to work.

We are at -- here. This is where we are, I guess. "TPSAC concluded." So let's go through this. And this again goes back to the net consequences of what will happen around quitting. And if you keep

going down, so we're saying that this uncertainty provides a strong rationale for close surveillance of cessation and any impact of DTPs.

John, I think your comment here seems to have slipped into a wrong spot, wherever you meant it to go.

DR. HECK: And quickly, on the opening sentence, should we say "smoking tobacco products" when we're talking about cessation?

DR. SAMET: You mean at the very start of the paragraph, Dan?

DR. HECK: Yes. This paragraph. "Use of smoking tobacco products." Isn't that what we mean?

DR. SAMET: "The likelihood, cessation of smoking of tobacco products." Right there. No, up. Next sentence. "Cessation of" -- not use, but "smoking of tobacco products."

DR. HECK: Or use of smoking tobacco products.

DR. SAMET: Of smoking tobacco products?

DR. HECK: Or combustible tobacco products.

DR. SAMET: Of smoking?

DR. HECK: Well, yes.

DR. SAMET: Smoking. I think in this context it's clear it's tobacco products and not other smoke products.

[Laughter.]

DR. SAMET: All right. So let's continue to our next charge element. The increased or decreased likelihood that those who do not use tobacco products will start using such products.

Okay. So here we have a sort of conclusory comment. For this component of the charge, the TPSAC concluded the available evidence, while limited, leads to a qualitative judgment that availability of DTPs could increase the number of users of tobacco products. And this refers to the possibility of increased initiation.

So then we follow that with, "This judgment was based on experience with other smokeless tobacco products, the data presented from the state of Indiana, and the survey data on youth perceptions, and the potential for youth to be drawn to a novel product."

So this is a qualitative judgment only on the possibility that the number of youth smoking might be increased by the availability of this product, the comparison being world without DTPs to world with DTPs. And then we say, "The TPSAC could find no basis for the contrary finding that availability of DTPs would decrease product initiation." I think that's probably fair, and somebody's made a useful edit here.

DR. HECK: I was a little unclear on what "product initiation" meant there. Should we --

DR. BALSTER: Should it say "tobacco product initiation"?

DR. SAMET: Tobacco product initiation. And then we say that, "With the very limited information available, however, the TPSAC could not estimate the magnitude of any potential increase in numbers of tobacco product users because of sales of DTPs." And again, leading to a recommendation for surveillance.

So we're saying we're concerned. We don't think that having DTPs on the market would decrease use of tobacco products and could possibly increase,

but we don't know by how much. That's the message here.

DR. BALSTER: Initiation.

DR. SAMET: Initiation. Yes.

DR. MCAFEE: Jon, I had one question which was --

DR. SAMET: Tim?

DR. MCAFEE: It's essentially for a possibility of an addition that I thought might fit right here, or it could fit within the recommendations. But essentially, it's not information-gathering or surveillance or research. It was essentially that we make a suggestion that, "Marketing and product design should avoid characteristics that make DTPs more attractive to youth or encourage long-term dual use."

I put "long-term dual use" as opposed to simply "dual use" since there seemed to be -- I think there's a case that's being made that it may be possible that a brief period of dual use will actually facilitate cessation.

But I would assume that we all agree that we

would not like to see situations where people are actually being encouraged to permanently reside in dual use, and certainly that we wouldn't want to see situations that DTPs are actually attractive to youth.

DR. SAMET: I'm trying to sort this out with the charge and what we're trying to address here. And I want us to try and avoid what I will call a policy recommendation, which is kind of in part where you're heading.

I think if we were to look at this comment, we could not estimate, based on the sales of DTPs, if there were going to be another -- based on this finding, I'm sort of coming in this -- we said, "The TPSAC offers strong recommendations as to the need for informative surveillance related to DTPs and youth."

I think a way to get at what you're saying, Tim, might be to say, such surveillance should extend to marketing approaches or something that might make products more attractive to youth or something. But I think you have, maybe in what you said, moved a

step beyond where this report should be.

DR. MCAFEE: Okay.

DR. SAMET: If you see what I'm getting at.

So if we wanted to, based on this finding, offer strong recommendations of the need for informative surveillance related to DTPs and youth, including marketing approaches, is that okay?

Ellen, would that fit?

Yes. Fred?

DR. PAMPEL: On the statement that TPSAC could find no basis for the contrary finding that availability of DTPs would decrease product initiation, where would the evidence from Sweden fit in, that is the rising -- well, I guess that's the issue, that in Sweden the evidence is on snus, not on DTPs, so it wouldn't be included?

DR. SAMET: Yes.

DR. PAMPEL: Thank you.

DR. SAMET: So let me see. Any other comments? The section we've just been through is answering our charge, as given in the Act. So we're going to make a very -- this is not the last time

you're going to see this. About 9:00, we're going to make a last run through this.

All right. Recommendations for Further Information Gathering, Surveillance, and Research. I want to go through these. I see you have a sweeping comment here, John. Don't speak to it yet. We're going to look at what we said.

DR. BENOWITZ: Jon, I've got a comment.

DR. SAMET: So first, Additional Product Testing.

DR. BENOWITZ: And I've got a comment to go before that. And I wrote, basically, "To guide regulatory activities and to facilitate accumulation of data on various DTPs, a standard product definition is needed." That's my first recommendation.

DR. SAMET: So say it again.

DR. BENOWITZ: "To guide regulatory activities and to facilitate accumulation of data on various DTPs, a standard product definition is needed."

MALE VOICE: I think it goes above --

DR. BENOWITZ: Oh, yes. That goes above --

MALE VOICE: Above this preamble. Yes.

DR. BENOWITZ: That's like a preamble. It goes above that.

DR. SAMET: And TPSAC should not write it. We sort of in the beginning say DTPs are what -- there must be an Alice in Wonderland quote for this. But I think, ultimately, that may be a useful recommendation, particularly as products proliferate and begin to morph into one or another form. So everybody's comfortable with that as a general recommendation? Okay.

So Additional Product Testing. And again, the world "yield" is not correct. Content and delivery.

DR. DJORDJEVIC: Jon?

DR. SAMET: Yes, Mirjana?

DR. DJORDJEVIC: Well, this is the place that we should go back to recommendations or that list which was developed by the SAP committee of TPSAC on harmful and potentially harmful constituents. And I calculated the other day there are 36 or 37 on the

list which pertain to smokeless tobacco products.

So just again, limited to nicotine and TSNAs is not enough. It would be good for reporting to have the whole profile of constituents which are harmful or potentially harmful, and especially that several of them are classified again by IARC as carcinogens, Group 1. And in addition to that, pH and unproteinated nicotine need to be reported.

DR. SAMET: So the question is whether that's covered sufficiently by other health-relevant components, or you want to say, and other health-relevant components as set out in the list of harmful -- I'm not sure, what's the exact name for that?

DR. ASHLEY: Harmful and potentially harmful constituents.

DR. SAMET: And other health -- as set out in --

DR. ASHLEY: The list of harmful and potentially harmful constituents.

DR. SAMET: And pH would not be there, would it?

DR. DJORDJEVIC: I don't think pH was on that list. So that is why that needs to be spelled out. So pH and --

DR. SAMET: So maybe as just a separate -- since pH was -- and what else did you say?

DR. DJORDJEVIC: pH, which in a way enables to calculate free nicotine.

DR. SAMET: Right. So why don't we just say pH should also be measured.

DR. DJORDJEVIC: Yes.

DR. SAMET: John?

DR. LAUTERBACH: Dr. Samet, it appears that we're trying to create business for those in chemistry. That's where I came from before getting to regulatory. But it seems to me we're just going through quite a lot of information which is not relevant, particularly at the levels that could be found in here.

Remember, there -- and I call everybody's attention to a paper that just came out in Chemical Research in Toxicology by Hausmann, which he covers

this particular situation as, what's necessary to measure the toxicity of smokeless tobacco? The latest issue of Chemical Research in Toxicology; the article is just in press.

DR. SAMET: But what's your point, John? Is this a listing that is somehow different from what is proposed here, or you're concerned about the fact that concentrations might be low and are not to be measured, or --

DR. LAUTERBACH: We're just basically generating numbers that have no usable purpose. I mean, if we're concerned about levels, we say we adopt the GothiaTek standard and work from there. If we're concerned -- if people could show the health -- some of these ultra-trace levels of these things, then that's different.

DR. SAMET: So I think it's not our mandate here to recommend a product standard. I do think that we heard, I think, a rather incomplete list of components, and I think that was why we had this suggestion, and that also there was variation within products, so that this was something that should be

better understood.

I don't think this is -- we don't say how much further characterization. But I think, from what we heard and judged was that within-product variation, that was not sufficiently characterized.

Neal?

DR. BENOWITZ: Just to go back to the top of the sentence. This focuses on within-product variation. Shouldn't we be talking about across and within-product variation insofar as it may be new product?

DR. SAMET: Yes. I actually think, when we said this, we were thinking about the products we had heard about based on the information provided. So let me ask if -- again, I'm sort of the reporter here, so I'm not going to speak one way or the other to how important we think this is.

Bob, do you have comments here?

DR. BALSTER: Well, I was just trying and get at that same thing with the very last bullet that I introduced under this section because, as Neal just said, this section didn't talk about getting

information on comparing products. So I don't know if that's the right way to word it, but I'm concerned about the same thing. This is on product, you know, and the other one is comparing within-product variation. This is more on new products and different products.

DR. SAMET: So again, I think, pushing my memory here, that when we proposed that this might be needed, it was because there was substantial within-product variation, based on preliminary information we heard, and that some additional characterization of that might be useful.

So that was what this was about. And again, it shouldn't be surprising that there's some variability, I guess.

So do we want to leave this as is? I guess I'm -- if you characterize it as within-product variation and you have the data, then you have the opportunity to compare across products.

DR. BENOWITZ: I would just say, if you're prioritizing these, I would make the first priority to characterize new products as they get developed,

and the second one would be to look at within-product variation.

DR. SAMET: Yes. Actually, and maybe we should make this statement, I don't think we've given any priority to these, one versus another. I suggest that we not do that, in fact, because I'm not sure I would know how to do it.

But I guess a point is, Neal, whether a last bullet here is -- or somewhere where we get -- is to get to this point. Well, there actually is a new bullet added that speaks to this. So let's hang on.

Are we sticking with our first, within-product variation? Okay. Then product composition variation at point of sale across the country?

DR. BENOWITZ: Let me just go back. Delivery is really subsumed under the biomarker bullet.

DR. SAMET: So you would just leave this one at content?

DR. BENOWITZ: Right.

DR. SAMET: Tom?

DR. EISSENBERG: I'm just wondering, above

all the bullets, where it says "Additional Product Testing," do we want to make clear that we're talking about -- I think we're talking about additional product testing for current and future products.

DR. SAMET: Okay. So that's the heading Tom wants to go back up to.

So you're deleting that, yes. And then you're going to go back up and --

DR. EISSENBERG: Yes.

DR. SAMET: -- of current and future products.

DR. EISSENBERG: Yes.

DR. SAMET: Of current and future products -- or "testing of current" -- "additional testing of current and future products." And then take out the other "product." Right.

All right. So, let's see, going down the bullets, point of sale. Change in product composition with time since manufacturing. Influences of heat and moisture exposure on composition.

Composition or content?

DR. EISSENBERG: The same.

DR. SAMET: Composition? Okay. Then the biomarker recommendation. Topography.

Tom?

DR. EISSENBERG: So obviously, Bob and I (inaudible – mic cuts off). Rather than make a new bullet, I added to this one, and Bob won't be surprised to hear that I like mine better. So let's hear it.

So that bullet, for each product, "For each product, detailed information is needed on topography of actual use as well as effects produced by the products, including but not limited to subjective effect profile, abuse liability, and behavioral effects such as influence on concurrent or subsequent cigarette smoking."

I was trying to get the wealth of everything that we would want to know there.

DR. SAMET: Comments? For each product, everything should be known. Dorothy?

DR. HATSUKAMI: Why don't you just say, as needed on abuse liability and topography and actual

use, because topography would include other tobacco products as well. Is that right? Abuse liability would include subjective responses.

DR. EISSENBERG: Well, abuse liability involves -- I mean, there are other things that you might ask about other than would be in a standard abuse liability battery.

DR. HATSUKAMI: Well, I'm just saying that -- you said subjective responses, abuse liability, and how it affects other tobacco use behavior. Abuse liability includes subjective responses.

DR. EISSENBERG: Yes. Okay.

DR. HATSUKAMI: So just saying abuse liability and topography of actual use might include everything that you had indicated.

DR. BENOWITZ: And Jon, I'm not sure how much detail you want here, but we might want to consider the Iowa equivalence analogy for drugs. So if you have two products that basically have exactly the same composition and pharmacokinetics, we may not want to -- well, we may not need to do abuse

liability, say, for every single product. I'm not sure we want to get into that much subtlety here or not.

DR. SAMET: I don't think so. I think it's too much.

So Tom, Dorothy, Neal, everybody's happy with "for each product detail"?

DR. EISSENBERG: No. I really think that influence on concurrent or subsequent cigarette smoking is at the heart of the matter and should be explicitly addressed because that's what we're interested again.

DR. SAMET: Say that again, Tom?

DR. EISSENBERG: Influence on concurrent cigarette smoking.

DR. BALSTER: Tom, that comes under another bullet. That's not a characteristic of the product.

DR. SAMET: Yes. That's almost a surveillance issue, I think. I don't --

DR. EISSENBERG: Where does it come under? If it's somewhere else, I'm happy.

DR. SAMET: All right. Hang onto it, and

then let's -- because I agree with Bob. I don't think it goes here.

Dan?

DR. HECK: And I just want to remind everyone. You know, we may not need to get so tied up in every detail and not leave anything out because with the new product application, as these products come under FDA oversight, a lot of these things are touched on in the new product guidance, including the abuse liability and the composition. So a lot of this information will be available to FDA.

DR. SAMET: So can we leave -- go to the one that says, "To facilitate accumulation." Keep going.

DR. BALSTER: That should go because we put that up front as a preamble to the whole thing.

DR. SAMET: Standard product. So that one can go. It's part of the definition.

DR. BALSTER: This bullet is just intended to compliment the one about within-product variation. This is basically saying the same thing is needed on --

DR. SAMET: Do we need --

DR. BALSTER: So I guess you're arguing that this would be included; in collecting within-product variation --

DR. SAMET: Right.

DR. BALSTER: -- we would know this. If that's --

DR. SAMET: I think we actually got this with Tom's change to the section. So I think we could delete it.

Okay. Surveillance.

DR. EISSENBERG: So there was one thing I thought was really important and another that I suspect people aren't going to want to include. On the second bullet point, "Surveillance instrument will need to be developed for tracking DTP use," I wanted to add, "and a mechanism developed for adding these instruments rapidly to national surveys." Because there's a big problem. People develop an instrument on how to assess something, and then it never gets put in anywhere, and we don't collect the data that we need.

DR. SAMET: I know that Tim is going to make

sure that he's got rapidly into -- are you coming here, Tim?

DR. MCAFEE: Well, yes. I think it's a very important point. And actually, one concern would be that we don't make it more complicated than it has to be. And it may not be -- if you call it instruments, it may be question batteries or something because --

DR. SAMET: Okay. So people --

DR. MCAFEE: -- unless somebody thinks we literally need a new instrument or a new survey method, the main issue is getting the right questions --

DR. SAMET: So how about "appropriate surveillance questions"? Would that be okay? "Appropriate survey questions"?

DR. MCAFEE: Yes.

DR. SAMET: Instead of "surveillance instruments."

Ellen?

DR. PETERS: It's also relevant to assessing perceptions of DTPs. And so I wonder -- I'm not quite sure how to do the restructuring, but maybe

just repeat the same sentence again under the perceptions of DTPs.

DR. SAMET: Okay. And then, Tom, you had -- let's make sure we've got your mechanisms to get them in. "Appropriate survey questions will need to be developed for tracking DTP use."

DR. EISSENBERG: "And a mechanism developed for adding" --

DR. SAMET: "And a mechanism developed" --

DR. EISSENBERG: For rapid integration?

DR. SAMET: -- "for their rapid integration into ongoing surveys," or something.

DR. EISSENBERG: Something like that is fine.

Then there was something I was going to add that I think you'll tell me is beyond the scope of our report.

DR. SAMET: Okay.

[Laughter.]

DR. EISSENBERG: Which is, in the first bullet after it says DTP use, "sensitivity to track patterns of DTP use," I was suggesting, in parentheses, "and all novel tobacco products." There

are numerous products coming down the pike, and we miss every one of them in our national surveys.

DR. SAMET: Tim?

DR. MCAFEE: Well, I had a suggestion which I was going to hold off, but I'll make it now, which we might want to have a sentence at the beginning of this entire section that says something like, "Many of these" -- let's see. I'd actually -- "Many of these recommendations may also be relevant to other smokeless and novel products," something, because -- we could put that in a lot of these.

DR. SAMET: So you want to put something to start -- I suppose there's no harm in doing so -- Surveillance, and then actually not a bullet, but just under Surveillance, just put a comment that would essentially say, "TPSAC notes that the following recommendations with regard to DTPs extend more generally to novel tobacco products."

Is that okay, the spirit of what you want, Tim?

DR. MCAFEE: Yes. I think it may also apply to some of the conversation that we had about product

testing as well. So you could put it at the top. Your discretion.

DR. SAMET: Yes. Well, I think I feel more comfortable making the comment here. I mean, it's getting hard to take a history of tobacco use. That's true. Yes, I think, actually, under the Surveillance, "and in vulnerable populations," is probably an addition everybody welcomes.

So keep going. Keep going.

DR. EISSENBERG: Oh, there was something right at the very top of the page, that bullet. "Research/ surveillance will be needed to assess perceptions of DTPs and how availability," blah blah blah, "of DTPs affects perception of other tobacco products."

Are we referring -- do we mean cigarettes there of traditional tobacco products?

DR. SAMET: Well, this was our concern generally. I think this was other tobacco products, I think, as written. And then we had voiced this concern earlier.

DR. EISSENBERG: Oh, sorry. Okay.

DR. SAMET: Yes, Ellen?

DR. PETERS: "How availability and marketing," blah blah blah, "of DTPs affects perceptions of them and other tobacco products." "Perceptions of them and other tobacco products."

DR. SAMET: Okay. "Denominators reflecting" -- so who's the denominator person? Bob?

DR. BALSTER: So again, we had a discussion, a fairly lengthy discussion, about this problem with presenting raw data when you don't know what the denominator is for each particular product penetration. So we were mainly told that the denominators are expensive, but we weren't told they weren't needed.

I think they really are needed. It's just basically some way of getting at relative risk. And if you want to know what the -- you have to have a denominator for what each product's market penetration is; if you're measuring something related to it, you have to know -- I mean, obviously the products that are out there the more are going to have the biggest numbers.

DR. SAMET: But doesn't this -- I mean, isn't this answered by having the surveys that provide us with prevalence of use? That is the denominator.

DR. BALSTER: This is a huge problem in prescription drugs, where there's a bunch of numbers out there about the incidence of the use, adolescent use, for example, of these products. But there's no way to connect them or it's difficult to connect them to how much those products are out there for them to use. So it's basically -- it's a denominator for individual product comparisons.

DR. SAMET: Let's see. Our other denominator person, Fred. Does this make -- I'm not sure I get it. It seems like you get what you need from having good survey data.

DR. BALSTER: Not if the surveys just simply count the number over observations of something without knowing the observations per opportunity for that event to occur. So if you have a particular product that has a massive market penetration, and you're going to have a lot more counts of, let's just say, adverse effects for that product, but it's not

going to necessarily reflect relative risk; it's going to reflect market penetration. I'll give it up. This is a huge problem in assessing the problems associated with the abuse of prescription drugs.

DR. SAMET: Yes. No, I've got you there, that if you only have the numerator, you don't have the denominator. But I'm not sure. We're talking about population-level surveillance here, which is going to give us a picture of the users.

DR. BALSTER: It's simply not going to tell you -- what you need to know is how much product is out there for them to gain access to. So I'll give up on it, but, I mean --

DR. SAMET: Ellen?

DR. PETERS: Just a question. Do you mean that by better understanding what that denominator is, you can gain a better understanding of why an increase in abuse liability might be occurring, whether it's due to just market penetration or whether it's due to some other aspect of the product or the product design or whatever?

DR. BALSTER: Yes.

DR. SAMET: I actually -- I think we should delete it because I don't think we understand it. And if this group doesn't quite get it, I don't think the rest will, if that's okay.

DR. BALSTER: Okay.

DR. SAMET: And then information needed on how underage users obtain DTPs. Yes. So that one goes, but not the next one we haven't discussed.

Ellen?

DR. PETERS: Not on this one. So someone else said something.

DR. SAMET: Comments on this to include on the list? Silence is yes?

DR. HECK: Unless you say "if and how" because I don't know that we've seen --

DR. SAMET: We don't know. Okay. So if and how.

All right. Okay. So is there something else on this before we go to quote "Research"?

DR. PETERS: Just the point that I mentioned before, the point about -- I don't know how it's worded now; it was up like three points, and it was

originally worded, "Surveillance instruments will need to be developed for tracking DTPs." We should have something like that underneath the perception point as well.

Yes. "Appropriate survey questions will need to be developed." If you could copy that and then paste it, or I would suggest that we -- the whole point. And there'll be a minor adjustment needed if people agree with us.

Then underneath research -- the other way. Okay, stop. Right above that "underage users" point, I think. Go up just a tiny bit more. So right before the last bullet point before Research, "Information is needed." Underneath that point. Yes.

Then it says, "Appropriate survey questions will need to be developed for tracking," take out "DTP use" and put in "for tracking perceptions of DTP use." Or "for tracking perceptions" is enough. Then just -- no, take out "DTP use" and leave the rest of it. There's a lot that goes into perceptions. We're using a single word there, and it can be expanded out

in any of number of ways.

DR. SAMET: To Research. This is actually page 42, the last one.

DR. EISSENBERG: So I'm wondering if the same statement we made underneath the heading of Surveillance should also go underneath the heading of Research, in that these research suggestions also apply to other novel tobacco products.

[Pause.]

DR. SAMET: Okay. So these -- "Short-term bioassay systems are needed and may prove useful." I would actually say, "useful/valid."

DR. BENOWITZ: I've got a problem. I've got a problem with this because we don't have anything to validate it against. So I'm not -- if I were to ask somebody to do research, they'd say, I'm not sure what I would ask them to do.

DR. SAMET: I guess my one comment to that is there's so much push now for so short-term product toxicity testing of chemicals, mixtures, and so on, that this would mirror that.

So I guess your -- I guess actually I would

almost, in a way, ask FDA to respond to this as well because I think this is probably a general question about product testing and the development of short-term bioassays and where that is going.

So you're concerned about the general issue of these types of systems?

DR. BENOWITZ: Yes. Again, If I was trying to think about what kind of research would I do that would be meaningful, you basically have to have something to validate this against. And talking about DTPs, we have to first find some harm that comes from it.

DR. SAMET: Yes. So let me ask the general question. It doesn't say -- it says they're needed. So if somebody more clever than us came along and developed them, they could be useful.

I don't know. I wonder, David, do you want to comment on this? You may not want to. Could you comment on this?

DR. ASHLEY: I mean, I will comment on it in a general term. I don't know that it applies to DTPs, particularly compared to anything else. I

think there is a lot of interest out there in developing short-term markers of long-term disease, if those are available. Some things have been proposed; whether those are completely valid or not is still definitely up in the air.

So I think there's a need for this. I don't know that there's a need for this specifically related to dissolvable tobacco products.

DR. SAMET: Yes. I think that goes back. I think there's a general, broad need for these kinds of systems for many purposes, and we all hope we're going to have them one day. Right? I mean, there's report after report on saying just this.

To say they're needed I don't think commits us to too much. Dan?

DR. HECK: Yes, Mr. Chairman. I'm going to suggest that we just -- on all these three last bullets here, we maybe just make it kind of a broad brush statement about, as for other products, we always need better biomarkers. We need better, informative tests. Because it seems like the intensity of research needed for products is kind of

proportional to both the complexity and the harm of the product. And these seem like relatively simple and relatively less harmful products in terms of their dosimetry and composition.

So we need all these things for all tobacco products, but do we really need that much for this particular category if indeed it is here to stay?

DR. SAMET: So would an alternative to bullets be to say, "For DTPs" -- and this goes back to Tom's general -- "as for other novel tobacco products, there are a variety of research needs," and list out some of these things, and quit.

That is to say, are we bringing -- there's no specificity to anything we're going to say here that is, as far as we know, for DTPs as opposed to any other product, which I think is your general point.

DR. HECK: Because it seems like we would just be testing extracts of these products, which would look a lot like the smokeless tobacco tests. And for better addiction models, well, we could all use those. But other than testing, essentially, a nicotine extract, it's kind of hard to imagine how

you could do much. Now, the behavioral and the perception, yes. Those may be unique to this category.

DR. SAMET: So actually, for DTPs, as for other tobacco products, there is a need for assay systems to -- I mean, we could list out some things generically and quit, or another possibility -- and we could just make that general comment and quit. We can not have a section that's called "Research." Or we can just leave it as a couple of general sentences that start with, "For DTPs, as for other tobacco products, there is a need for" -- I would actually say, "for research methodology and applied research that will be informative as to potential toxicity and abuse liability."

We could either list some of those or quit. I don't think we're saying anything profound here or that's particularly applicable to DTPs, that's specific to DTPs.

Neal?

DR. BENOWITZ: Well, the fourth bullet is, and the fourth one, I think, is important.

DR. SAMET: And this fits within a broader need for population models. But I think -- so we could -- "There's a need for research methodology and applied research," let's say, "that will be informative with regard to risks, individual risks and public health consequences." That's pretty generic, and I don't think anybody's going to disagree with that. And then we could follow with -- say, "Additionally, population models are needed for assessing consequences of DTP availability," period, and quit.

Is that okay with everybody?

DR. BALSTER: Then we'll take out the first?

DR. SAMET: Yes. Then we'll take out the first. Yes. Assessing the consequences, consequences of DTP availability. And then the rest of this goes.

[Pause.]

DR. SAMET: So we're at the end, so now we're going to go back up and we're going to just scroll through this quickly. We're going to save it because we don't want to lose this beautiful piece of work.

Let me actually -- if we're going to finish, let's say in the next 20, 30 minutes, we probably should think about getting some transportation arranged back to the hotel.

So who needs to go back to a hotel?

[Show of hands.]

DR. SAMET: Ten of us, Caryn, would have to get back.

So let's go through, and I want us to eyeball each page. And somewhere here -- let's see, go down through it -- I did add a couple sentences for Neal's comment earlier. Committee approach. Where's my -- okay. So where's my new -- no. Back up. Yes. It should be up towards the front.

Oh, here it is. So that should be, "TPSAC addressed the charge as stated." So this is added, and that should be a separate paragraph.

MS. COHEN: This?

DR. SAMET: Yes, make it a separate paragraph.

So this was in response to Neal's opening comment.

DR. ASHLEY: Mr. Chairman?

DR. SAMET: Yes?

DR. ASHLEY: While we're here, if you'd go back up and change March 2nd, hopefully, to March 1st.

DR. SAMET: Well, that was in case we went after midnight.

Sarah, did you have -- no?

[Pause.]

DR. SAMET: So I added this in. So I think this is what Neal said he wanted to add. I'm trying to say what we did and did not do. And then this issue of what dissolvable products are.

So is that the spirit of what you wanted?

DR. BENOWITZ: Looks good.

DR. SAMET: Is everybody okay? Okay.

So then the Committee Framework. So we spent a lot of time doing framework-smithing. And let's just, again, take a look at the text here and how it reads now. And I think, just to check with Caryn or David or Sarah, that as we see editorial glitches, even after we vote, presumably we can get all that

fixed without --

DR. ASHLEY: Caryn, I believe that is correct. If we find missing commas or spaces or things like that, we can make those changes.

DR. SAMET: Okay. So Committee Framework. And we added that sentence about how we have a simplified diagram; we did not show everything possible. I'm not sure -- yes. "For simplicity, the framework presents only three potential patterns of product use." So we added that. And then, if you'll remember, I think particularly Tom had substantial input in changing the descriptions of the numbers.

Let's keep going down. Let's see. And we changed the boxes, if you'll remember, in several ways. So we made comments. We did the regular use/addiction, and then we have risk for tobacco-caused disease in the new and improved framework.

Then some green goes. Okay. Let's see. And then -- yes, that's added. Yes.

MALE VOICE: Can't we do the green releases later?

DR. SAMET: We probably can.

Okay. Key Findings from the Evidence Review. I don't think we made any changes here. This is all -- okay. Keep going.

All right. Peer-Reviewed Literature.

Actually, Constituent, go back up. We have the wrong name there. Constituent Yield is now Constituent Content, Contents.

MALE VOICE: Or just Constituent.

MALE VOICE: Constituents, "S."

DR. SAMET: Constituents. Yes. You know what I mean. Yes, it usually goes at the end.

Okay. So we played with this about delivery and got the contents straight. Abuse liability. Oops, we're going too fast. Okay. Cessation. Health risks, we edited this. So this says, "Exclusive use of DTPs should be less hazardous." Okay.

Continue. All right. Then we had this TSNA comment, that we said that they're lower, but public health implications aren't certain. We had the extensive discussion with Neal about this point. No

epidemiological data.

Okay. Now, consumer perception, actually, I'm not sure we -- this is something that I think, between Dorothy and John, you were trying to figure out if this is one study or there are other studies.

DR. HATSUKAMI: I think it's just one study. It doesn't seem like the Romito study did much in terms of perception.

DR. SAMET: Ellen?

DR. PETERS: I wonder if the most important point under consumer perception is that, "Little data exists."

DR. SAMET: Fair enough. So you want to have, as the first sentence, "Little data are available"?

DR. PETERS: Yes.

DR. SAMET: There's -- okay. That's good.

Oops, you're going too fast. Consumer response. Childhood poisonings. And then we're on to the Industry Presentations and Documents. Variety of products with different contents. Next. Oops, cigarette use. Marketing. Cessation. Youth.

Open Public Hearing. Is commenters e-r or o-r? It's o-r-s? Still doesn't like it. Commentators. That's it.

MS. COHEN: Commenters is e-r.

DR. SAMET: E-r? It's probably not a preferred use. I don't know. We'll sort this out later.

MALE VOICE: Those who comment.

DR. SAMET: Yes, those who comment. Some people. All right. "Data presented from youth surveys suggested that DTPs may not be recognized as tobacco products." Okay.

Government actions. Oops. Back, back, back. Some suggest -- recommend that it should more proactively educate the public. Okay. All right.

Then to Sweden. Context. Health benefits. And there's that last complete substitution business, so just make sure you've got it. Okay.

Onward. New users. Use by sex. You know, this could have been a short report if people hadn't written all this green stuff.

[Laughter.]

DR. SAMET: Labeling. Okay. Information on Youth. Youth use. We added that bit here about the Virginia data.

DR. HECK: The last statement, that youth perceiving them not as a product, would be more -- that is factual? I didn't go back and check.

Do people remember that?

DR. BALSTER: It was in a packet that we got.

DR. SAMET: Okay. I wonder, appeal to youth is likely to depend on packaging. The newer packaging may have greater youth appeal.

Do we actually have reason to say that, or should we delete that?

MALE VOICE: I don't recall that.

DR. SAMET: What?

MALE VOICE: I don't recall.

DR. SAMET: Yes. Ellen?

DR. PETERS: I think we -- well, I think we -- I would probably delete it, too. I think we talked about it a little bit, but there's no data on it.

DR. SAMET: So I think we should probably

just take that out. Okay.

Now here -- so now we're, the Responses to Charge Issues. So this is where we -- so what happened? Something got lost here. Go back up. I think I had given responses -- I thought I had listed each of the charge issues originally and -- or else it's in the wrong spot. Let's see.

[Pause.]

DR. SAMET: Okay. So this is the charge. So I think, actually, the -- so actually I think this text -- I think we need the -- if you go down a little bit to the italics where I have the charge listed, I think that needs to come up at the start of this.

Keep going. Right there. So that bit in italics is what this is about. I think that needs to come up to the top. So that should come -- yes. Yes. So it should come right before -- right. So insert it there. Yes. Okay. Then this makes sense.

You know, actually, with this -- TPSAC constrained by the real world -- so keep going down. I wonder if there is some text that we shouldn't

go -- "Consequently, the TPSAC posed scenarios that would be most useful to addressing its charge" -- "gave way to a scenario of widespread availability as" -- I'm not sure we really did that. It sounds really good, but maybe that should be deleted.

We really talked qualitatively about directionality and such, but we didn't say what would really happen if. So I think we should take that out. Yes. So I think that should go.

MS. COHEN: All of this?

DR. SAMET: All of that. Okay. And then keep going. So now this does actually set the stage for thinking about individual risk and population risk.

DR. HECK: Have we lost entirely that sentence about the Ariva and Stonewall really having no net impact to date?

DR. SAMET: No. I think that's still up there.

DR. PETERS: If you go backwards to (inaudible – mic off).

DR. SAMET: So go back -- put it back in, then, and see which --

DR. PETERS: One more. The last sentence. I think that's what you're talking about?

DR. HECK: Yes. It seemed like a fairly important point. But do we want to lose it? I don't -- whatever the committee thinks, the current situation sentence, at the end.

DR. SAMET: So leave the last sentence, I think, is the proposal. Is that right? So that would go. Is that --

DR. BALSTER: That doesn't make sense now. That sentence just sort of sits there kind of curiously.

DR. SAMET: Yes. I think it should go.

Now, let's see. Go back. Did you undo the deletion that we had already done, or is that -- no? Okay.

DR. ASHLEY: While we're here, just so we catch it, on the last line, right about "page 26 of 40," it says, "cause diseased." It should be "cause disease." Well, now it's gone.

[Pause.]

DR. SAMET: Okay. Continue on down. So this was our benefit side, so dealt with the individual tobacco user and our theoretical lifelong DTP user versus cigarette smoking. And then we go on down, and then sort of the other side, how could things be made worse by DTPs. And that's where we -- having to do with the numbers of smokers going up. Okay.

Then we say there's a lot of uncertainty. Limited impact of the products from Star Scientific. Keep going. Context will be important. And our comment, our general comment, about sort of the idea that tobacco products in general are safer because DTPs are portrayed as -- are viewed as lower risk.

Then, our bottom-line conclusion on this element of our charge, risks versus benefits, no conclusion because the data are not there. Okay.

Then the next element of the charge, increased or decreased likelihood that existing users of tobacco products will stop using such products. And some discussion here about the way that DTPs are being used and how they're perceived.

Then we say how they've been positioned. Continue on down. We talk about the context issue. And then, bottom line, keep going. And again, we say that things could go either way around the likelihood of cessation, that there's reasons to think they could facilitate cessation of tobacco products.

So should this be -- let me go back to our charge. It's tobacco products. Okay. I think we're really -- well, the charge is tobacco products. I think we really mean smoking more than -- well. We make clear that we're talking about smoking in our answer, if you keep reading. I think it's okay.

Okay. So our bottom line here is, again, not sure. And then on to initiation. And so here again we offer up, first, our qualitative judgment that availability of DTPs could increase the number of users of tobacco products, and we cite some reasons why. And we find no reason for the contrary finding that the availability of DTPs would decrease product initiation, which I think is fair. And again, we say that we're not sure what the quantitative increment might be if DTPs were widely available and marketed.

So then we say we need surveillance, which takes us now to our recommendations.

DR. BALSTER: Do we need -- just going back up, since we're talking in this section about initiation, do we want to say about new users and we could not make a conclusion about -- while DTPs could increase the number of new users -- I mean, that's what we're talking about in this section.

DR. SAMET: Well, so if you want to make that -- so if you go right to the very end, I think I can make Bob happy.

DR. BALSTER: Okay.

DR. SAMET: Keep going. Stop. "TPSAC could not estimate the magnitude of any potential increase in numbers of new tobacco product users." Okay?

DR. BALSTER: Okay.

DR. SAMET: So do you see where I want that?

Okay. All right. Recommendations. We have our Additional Product Testing. Should we call that additional product testing or product testing? Oh, Additional Testing of Current and Future Products.

Should we call this testing? I'm not sure

what the "additional" means. Just testing.

Okay. So within-product variation. Keep going.

DR. BALSTER: Jon, I think we talked about this before. Is this the TOREG (ph) list that Mirjana was talking about?

DR. SAMET: It was the -- I think this is the FDA, the list that we looked at. Right?

MS. COHEN: Yes.

DR. SAMET: Yes.

DR. BALSTER: Oh, it was the FDA list?

DR. SAMET: Yes.

DR. BENOWITZ: Well, should we specify that so people know what list?

DR. SAMET: "As set out in the FDA list." Is that the right name for it?

DR. ASHLEY: You could put "FDA list of harmful" -- yes. That would work.

DR. SAMET: Okay.

All right. Then point-of-sale characterization. Understanding of the change in composition with time since manufacture and so on.

Heat and moisture. Let's see. Then we have our biomarkers. Abuse liability and topography and actual use. Okay. Then keep going -- and don't forget our recommendation for a standard definition was up front. We added that.

All right. Then Surveillance. Do it, was sort of our recommended.

[Laughter.]

DR. SAMET: And then existing surveillance products. Surveillance systems. So they should be reviewed for their sensitivity to track patterns in the various use. Do we want to say that, "and reviewed for the sensitivity and suitable systems used to track," or something?

Are we missing something in there?

DR. PETERS: How about, "should be reviewed and selected for their sensitivity"?

DR. HECK: "Suitability and sensitivity."

DR. SAMET: "For their suitability and" -- So "reviewed and" --

DR. HECK: Adequacy and sensitivity.

DR. SAMET: "Should be reviewed and selected

based on their suitability and sensitivity." Yes.

Okay. Survey questions developed and used.

Next. Surveillance recommendation. Perceptions. Role of marketing survey questions on perceptions. Okay. Underage users.

What about overage users? No, I'm just -- all right. Sorry.

And then our last, Research. Put that up so we can see it. That's the end? Okay.

Want to do it again?

DR. HECK: Just one quick thing. I think I saw in passing that detailed information on the products, including abuse liability, should be required, and then we call for research to develop that.

Is that kind of a chicken-and-egg thing?

DR. SAMET: Not sure I got it, Dan. Try again.

DR. HECK: Farther up, there should be detailed information provided for the products on abuse liability and some other features. And then we call at the end for the research to develop those

measures.

Is there any inconsistency there?

DR. SAMET: I think we're okay.

DR. HECK: I can't remember exactly where it was now.

DR. EISSENBERG: I think we took that out.

[Pause.]

Can you go up a little? Keep going. Up, up. There. Stop. So I think what Dan is saying is here it says for each product we need information on abuse liability. And down below, it seems perhaps to be implying that we need to develop the methods for assessing abuse liability.

Is that what you're saying?

DR. HECK: I think so, because short of -- I don't know what exactly a test for abuse liability would be in this case for this particular class of product, other than something looking at nicotine -- would there be special tests for this particular category of product?

DR. EISSENBERG: No, there wouldn't be special tests, but it would be nice to validate the

current methods we have with these products. But I don't think there's anything inconsistent with this. It's saying that we need the information on abuse liability, and down below we're saying that the models need to be refined for testing it. So I think it's okay.

DR. SAMET: Okay. Ready to vote? Does everybody know who votes and who doesn't?

Do you have the voting members?

MS. COHEN: Yes. I gave you.

DR. SAMET: Oh, good. No, you did.

Okay. Voting. Who votes? Dorothy, Neal, Bob, Fred, Mark, Tom, and me. And Sherry, if she's on -- no, Sherry's nonvoting. Okay. That's right.

Sherry, are you still there? If so, you get a Mark Clanton medal for hanging in.

[Laughter.]

DR. EISSENBERG: I heard her click off.

DR. SAMET: Did you? Oh, okay. You may retire the Mark Clanton award.

DR. CLANTON: I was just going to say that I could just keep it.

Okay. So these were our original questions, if you remember. What changes should be made to any part of the document? We've made changes. Second, disagreements or concerns. I hope we've had a full discussion of all of those and made changes. Recommendations for further information-gathering, surveillance, and research. We've certainly made changes in those. So this is about the material that we then provided, which actually is quite voluminous.

Next. And here is the voting question. All right, now I have a voting script.

We will be using an electronic voting system for this meeting. Those of you who are here in the meeting room have voting buttons on your microphone. There are actually three, "Yes," "No," and "Abstain." Once we begin the vote, please press the button that corresponds to your vote. That's a good idea. After everyone has completed their vote, the local votes will be locked in.

The final result will then be displayed on the screen. I will read the vote from the screen into the record. Next, we will go around the table,

and each individual who voted will state their name and vote into the record, as well as the reason why they voted as they did.

Okay. So the voting question is, do you agree with the report, which consists of a summary from the committee as well as background materials, transcripts, presentations, and minutes from all TPSAC meetings on dissolvable products?

So we will now begin the --

DR. EISSENBERG: Wait. Can I ask a question? I'm confused about how we can vote. I actually want to vote, but I'm really confused on how we can vote on it when I haven't seen the transcript from the last meeting.

Oh, it's on the Web somewhere? In that case, I withdraw my question because I've seen it.

[Laughter.]

DR. SAMET: There's really interesting stuff on the Web.

[Laughter.]

DR. SAMET: All right. So are we back to voting process? Okay.

We will now begin the voting process for question number 3. Please press the button your microphone that corresponds to your vote.

[Vote taken.]

DR. SAMET: Wow, okay. Everyone has now voted, and the vote is now complete and locked in. So the vote is 7 yeses, zero abstain, and zero noes.

So now we're going to go around the table, and everyone who voted will state your name, your vote, and the reason why you voted as you did into the record.

So Dorothy, you can go first. And just in case, Dorothy Hatsukami, that's her name.

DR. HATSUKAMI: Yes. My name is Dorothy Hatsukami, and I did agree with the report. And the reason why I agreed is because I thought the process of compiling the report and reviewing the report was adequate.

DR. SAMET: Neal Benowitz?

DR. BENOWITZ: Neal. I voted yes because I think the report fairly summarizes the process and our current state of understanding of dissolvable

tobacco products.

DR. SAMET: Okay. Bob?

DR. BALSTER: My name is Bob Balster. I voted yes, and I agree with the report as written.

DR. SAMET: Fred?

DR. PAMPEL: I'm Fred Pampel, and I voted yes. I agree with the report as written. I thought it was fair-minded and recognized the difficulties of trying to reach a decision, given the limited kind of data we have.

DR. SAMET: Okay. Mark?

DR. CLANTON: My name is Mark Clanton, and I agree with the report as written.

DR. SAMET: Tom?

DR. EISSENBERG: My name is Tom Eissenberg. I voted yes because I agree with the report as written.

DR. SAMET: I'm Jonathan Samet. I voted yes, also agreeing that the reports reflects the materials that we heard and addresses the charge that we were given.

So I think that completes our job with regard

to this report.

David?

DR. ASHLEY: I just have a final statement before everybody gets up. So do you have more that you need to say before I --

DR. SAMET: No. I think, actually, the only thing I was going to say was that I appreciate everybody's effort in looking at this and really, I think, putting a lot of thought into the responses.

John, I even appreciate all your comments and keeping us sharp about what we are saying. It's helpful to have people looking very closely and critically at our work.

I really appreciate everybody's efforts. I think the dissolvable report was probably, fortunately, not quite so memorable an experience as the menthol report. And we'll look with interest to what our next work entails.

David?

DR. ASHLEY: Mr. Chairman and the committee, we appreciate the work that has been done and how the committee has approached this task. By discussing

and finalizing your report and recommendations, the committee has now completed your second charge under the Tobacco Control Act, providing a report and recommendation on the issue and the nature and impact of the use of dissolvable tobacco products on the public health, including such use among children. We have reached another important milestone today.

As described in the Tobacco Control Act, you are submitting your report to FDA by March 23, 2012. The TPSAC final report is very important advice given to FDA, but it does not set FDA policy or actions. FDA's receipt of the final report will not have a direct and immediate effect on the market availability of dissolvable tobacco products.

FDA will consider the report and recommendations and other sources of scientific information as we assess how these issues apply to the regulatory authorities given in the Tobacco Control Act.

The Tobacco Control Act does not set a required deadline or timeline for the FDA to act on the recommendations provided by the committee in this

report. We do recognize the strong interest in this issue and will communicate, as appropriate, steps FDA is taking as we determine what, if any, future regulatory actions are warranted.

Ultimately, FDA's decision about what actions to take, if any, with respect to dissolvable tobacco products will be driven by our commitment to reduce the total of disease, disability, and death caused by tobacco in the U.S., and the requirements of the Tobacco Control Act.

So on behalf of Commissioner Hamburg and all of us here at the Center for Tobacco Products, I want to thank each member of TPSAC for all the time, the expertise, and the effort that you have put into this important process over the last year. I also want to thank members of the public who have attended these meetings and who have offered their helpful comments. But now it is up to us to do our job, and I want to thank you for doing yours.

Adjournment

DR. SAMET: Great. Okay. Thank you, and thanks to everybody, and we'll be seeing some of you

in the future.

Thanks for your efforts, and let's quit. We're adjourned.

(Whereupon, at 6:58 p.m., the committee was adjourned.)