FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS (CTP)

TOBACCO PRODUCTS SCIENTIFIC ADIVSORY COMMITTEE

(TPSAC)

THURSDAY, JULY 15, 2010

8:30 a.m. to 5:30 p.m.

Gaithersburg Marriott Washingtonian Center

9751 Washingtonian Boulevard

Rockville, Maryland

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P R O C E E D I N G S

(8:30 a.m.)

DR. SAMET: Good morning. I think I'll take advantage of this hushed silence to get us started. It's 8:30 a.m., time to start. I'm Jon Samet, the chair of the Tobacco Products Scientific Advisory Committee.

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

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members

take care that their conversations about the topic at hand take place in 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 topic during breaks or lunch. Thank you.

So we'll begin now, and if we can just go around the table. Dan, I'm going to start with you and ask the committee members to introduce themselves. So we'll start with Dr. Heck.

DR. HECK: I'm Dan Heck, a principal scientist at the Lorillard Tobacco Company, and I'm here representing the tobacco manufacturers.

DR. LAUTERBACH: Good morning, I'm John Lauterbach, owner of Lauterbach and Associates, consultants in chemistry and toxicology of tobacco and tobacco products. And I'm here representing the interests of the small business tobacco

manufacturers.

MR. HAMM: I'm Arnold Hamm. I'm the representative for the United States Tobacco Growers.

DR. KAROL: Good morning, I'm Susan Karol. I'm the chief medical officer for the Indian Health Service.

DR. BAUER: Good morning, I'm Ursula Bauer, director of the National Center for Chronic Disease Prevention and Health Promotion at the Centers for Disease Control and Prevention.

DR. BACKINGER: Good morning, I'm Cathy Backinger. I'm the chief of the Tobacco Control Research branch at the National Cancer Institute, representing the National Institutes of Health.

DR. CLANTON: I'm Mark Clanton, and I'm chief medical officer of the High Plains division of the American Cancer Society.

MS. DELEEUW: Good morning, Karen DeLeeuw, I'm with the Colorado Department of Public Health and Environment, and I'm representing government.

MS. STARK: Christi Stark, acting designated federal official.

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

DR. WAKEFIELD: Melanie Wakefield, I'm director of the Center for Behavioral Research in Cancer at the Cancer Council Victoria in Australia.

DR. HATSUKAMI: I'm Dorothy Hatsukami from the University of Minnesota, department of psychiatry.

DR. HENNINGFIELD: Good morning, I'm Jack Henningfield, professor of behavioral biology at Johns Hopkins University School of Medicine and vice president for research and health policy, Pinney Associates. And my specialty is addiction.

DR. NEZ HENDERSON: Good morning, my name is Patricia Nez Henderson. I'm the vice president for the Black Hills Center for American Indian Health.

DR. CONNOLLY: Good morning, my name is

Gregory Connolly, and I am professor at the Harvard School of Public Health.

DR. HUSTEN: Hello, I'm Corinne Husten, senior medical advisor at the Center for Tobacco Products, FDA.

DR. ASHLEY: I'm David Ashley. I'm director of the office of science, Center for Tobacco Products at FDA.

DR. DEYTON: Good morning, I'm Lawrence Deyton, director of the Center for Tobacco Products, FDA.

DR. SAMET: Okay. Thank you. I'll turn to Christi Stark.

MS. STARK: Good morning. I'm going to now read the meeting statement. 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, temporary voting members, temporary nonvoting members and the guest speakers are special government

1 employees, SGEs, or regular federal employees from
2 other agencies and are subject to federal conflict
3 of interest laws and regulations.
4 The following information on the status
5 of this committee's compliance with federal ethics
6 and conflict of interest laws covered by but not
7 limited to those found at 18 U.S.C. Section 208
8 and Section 712 of the Federal Food, Drug and
9 Cosmetic Act, FD&C Act, is being provided to
10 participants in today's meeting and to the public.
11 FDA has determined that members and temporary
12 voting members of these committees are in
13 compliance with federal ethics and conflict of
14 interest laws.
15 Under 18 U.S.C. Section 208, Congress has
16 authorized FDA to grant waivers to special
17 government employees and regular federal employees
18 who have potential financial conflicts when it's
19 determined that the agency's need for particular
20 individual services outweigh his or her potential
21 financial conflict of interest. Under Section 712
22 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 of today's meeting, members and temporary voting members of this committee have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their spouses or minor children and for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves, one, receiving updates on upcoming committee business related to menthol, including agency requests for information from industry on menthol cigarettes in order to prepare for the Tobacco Products Scientific Advisory Committee's required report to the Secretary of Health and Human Services regarding

the impact of use of menthol in cigarettes on the public health; and two, receiving and discussing industry presentations on menthol and cigarettes as they relate to five topics -- characterization of menthol, clinical effects of menthol, biomarkers of disease risk, marketing data, and population effects.

These discussions are preliminary to the preparation of the Tobacco Products Scientific Advisory Committee's required report to the Secretary of Health and Human Services regarding the impact of use of menthol in cigarettes on the public's health. 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 and temporary voting members, no conflict of interest waivers have been issued in connection with this meeting. To ensure transparency, we encourage all standing committee members and temporary voting members to disclose

1 any public statements that they have made
2 concerning the issues before the committee.
3 With respect to FDA's invited industry
4 representatives, we would like to disclose that
5 Drs. Daniel Heck and John Lauterbach and Mr.
6 Arnold Hamm are participating in this meeting as
7 nonvoting industry representatives acting on
8 behalf of the interests of the tobacco
9 manufacturing industry, the small business tobacco
10 manufacturing industry and tobacco growers,
11 respectively. Their role at this meeting is to
12 represent these industries in general and not any
13 particular company. Dr. Heck is employed by
14 Lorillard Tobacco Company, Dr. Lauterbach is
15 employed by Lauterbach and Associates, LLC, and
16 Mr. Hamm is retired.
17 FDA encourages all other participants to
18 advise the committee of any financial
19 relationships that they may have with any firms at
20 issue. Thank you.
21 Now, I'd like to remind everyone present
22 to please silence your cell phones if you've not

already done so. I'd also like to identify the FDA press contact. Tesfa Alexander, if you're here present, please stand. Thank you.

DR. SAMET: Okay. I think our next agenda item will be the FDA update on upcoming items and other committee requests for information on menthol cigarettes.

Corinne?

DR. HUSTEN: Good morning. So as you recall from the last meeting, immediately upon establishment of this advisory committee, the statute says that the Secretary shall refer to the committee for report and recommendation, the issue of the impact of the use of menthol in cigarettes on the public health, including its use among children, African Americans, Hispanics, and other racial and ethnic minorities. The report is due no later than one year after the establishment of the committee, so it's due March 23rd of 2011.

Just a review from the last meeting, the committee heard presentations of the published literature on the use of menthol cigarettes by

demographic groups, menthol cigarettes and smoking initiation, the marketing of menthol cigarettes and consumer perceptions, menthol cigarette sensory qualities and topography, menthol's effect on nicotine dependence, menthol cigarettes and cigarette smoking behavior, and the health effects of mentholated cigarettes.

At this meeting, the committee will hear presentations from the industry on five topics; the characterization of menthol in cigarettes, the clinical effects of menthol cigarettes, biomarkers of disease risk for menthol cigarette smokers, marketing data on the menthol cigarettes, and the population effects of menthol cigarettes.

At the last meeting, some areas of interest identified by the committee around the characterization of menthol were the trends and quantities of menthol present in the cigarette rod and smoke over time for various brands and sub-brands of menthol and non- menthol products. As determined by the Cambridge filter ISO test method, using standard parameters as well as the

intense smoking conditions set forth in Canadian regulations, information regarding the manufacturing of menthol cigarettes including the source and type of menthol used, the presence or use of any menthol analogs, the types of manufacturing processes through which menthol is introduced into the tobacco products, as well as considerations in selecting a particular method.

Other areas of interest identified around the characterization of menthol were the threshold at which a product is identified and marketed as a menthol cigarette, the rationale for adding menthol to cigarettes not marketed as menthol cigarettes and the criteria for determining the quantity of menthol to be added and information about international brands of menthol cigarettes, the quantities of menthol in both menthol and non-menthol cigarettes sold internationally, and the factors considered in determining the quantities of menthol to be added.

As far as the clinical effects of menthol, the areas of interest identified by the

committees were studies of the dose response relationships for the physiologic effects of mentholated tobacco smoke, mechanistic studies of menthol's effects, including chemosensory effects of menthol compounds in tobacco smoke, including effects at thermal and trigeminal receptors, the effect of menthol on the neural biology of tobacco dependence, the effect of menthol on clinical and behavioral measures.

Also, studies addressing the dosing relationship and metabolic interactions between nicotine and menthol, including resulting perceptions of nicotine strength and the interaction between menthol delivery and nicotine tar levels for both low-menthol and high-menthol products, and information on correlations between menthol content and consumer perceptions regarding taste, nicotine strength, and product harm.

Areas of interest identified by the committee around biomarkers were analyses of laboratory and population studies using biomarkers to assess the effect of menthol content on disease

risk for cigarette smokers based on cigarette consumption, including data related to menthol among population subgroups.

Areas of identified by the committee as far as marketing data were data on consumer preferences for menthol cigarettes, consumer perception studies of the advertising and packaging of menthol cigarettes, marketing strategies for various brands and sub-brands of menthol cigarettes, including strategies directed at particular demographic groups, marketing strategies for various brands and sub-brands of menthol cigarettes sold internationally.

Areas of interest identified by the committee around population effects were among cigarette smokers, the rates of switching from menthol to non-menthol cigarettes and vice versa, comparative rates of initiation by youth and young adults for menthol and non-menthol cigarettes, and comparative rates of cessation for users of menthol and non-menthol cigarettes.

I wanted to give the committee an update

on other information that had been requested at the last meeting. The request for industry documents was sent on May 26th, and the mandatory and voluntary submissions are due to FDA August 26th. We are in the progress of doing the analysis of the publicly-available internal tobacco industry documents and completing the white paper on the studies presented at the first meeting, as well as updating with references that were provided by industry representatives and others.

We expect a contract to be awarded shortly to fund the secondary data analyses of the existing research studies on initiation, cessation, addiction, and health effects of cigarette use in order to assess the impact of menthol cigarettes on these measures, the analysis of menthol cigarettes sales data, and developing a statistical model of menthol cigarettes' effects on initiation and cessation.

We also are planning to start the writing of the menthol report by establishing a menthol

report subcommittee so that the report can then be presented back to the full committee for review and approval.

Any clarifying questions?

[No response.]

DR. SAMET: Thank you, Corinne.

Dr. Clark, I wonder, we had gone around and made committee introductions, and now you've joined. Perhaps you could just say a word of introduction. Thank you.

DR. CLARK: I'm West Clark. I'm the director of the Center for Substance Abuse Treatment at the Substance Abuse Mental Health Services Administration.

DR. SAMET: Okay. Thank you.

We are ahead of time, and I think with this then, we will turn to the industry presentations on characterization of menthol. And I want to thank you in advance for a lot of work and a lot of reading material for the plane flight from Los Angeles. Probably only Melanie, coming from Australia, had a chance to get through it

all.

So I understand that Mr. Dillard will provide the introductions. Thank you.

MR. DILLARD: Yes, sir. Thank you, Dr. Samet. I appreciate it.

Good morning, members of the advisory panel. My name is Jim Dillard, and I'm the senior vice president for regulatory affairs at Altria Client Services. And I'm here today, as well as my staff is here today, on behalf of Philip Morris, USA.

To begin with, though, I have been the designee to introduce the couple of days and what you're going to hear. So I'd like to frame that out for you a little bit before we begin. Number one, we do have representation, as was mentioned earlier, on behalf of three of the industry representatives, Altria Client Services on behalf of Philip Morris USA, Lorillard Tobacco Company, and R.J. Reynolds Tobacco Company.

At the request of the agency, we have worked as diligently as possible, and as

requested, to pull together integrated presentations where it was possible. And I think you'll see that with the magnitude of information that's presented to you, obviously, within three and more submissions, it was quite a task.

What we've tried to do is assemble our information and answer the five topical areas and as many of the 17 questions as possible. However, of note, what you'll see today and tomorrow is that these three companies are predominantly domestic U.S. tobacco companies today. So we have very little international information as we look forward and as you look at the data.

Some topics also necessarily, based on competitive considerations, necessitate individual presentations. So I think you'll see in the marketing section, particularly, each company has to come at marketing and give you a perspective of each company's marketing, and how we approach the market today.

The manufacturing representatives will come up in each section. They'll clearly identify

1 themselves by both title and their company, and
2 then the group will be available for questions
3 from the Tobacco Products Scientific Advisory
4 Committee on each topic.
5 What Philip Morris USA, Lorillard, and
6 Reynolds have done in their submissions and as, I
7 think Dr. Samet, you just mentioned, lengthy
8 submissions, we have tried to be thoughtful.
9 We've tried to be considerate. And we've tried to
10 come at this with the best science and evidence
11 base that we can. That includes the published
12 information, and it also includes unpublished
13 information that each of the three companies has
14 as well. And we'll be willing to speak to those.
15 We think, if you look at the data, both
16 the published and the unpublished scientific
17 information, taken as a whole, there are some key
18 findings. Menthol has a long history of use in a
19 wide range of consumer products, including
20 cigarettes. Menthol is a well-established flavor
21 preference that a significant percentage of adult
22 smokers have used for decades, and that millions

of adult smokers continue to use today.

Menthol added to cigarettes does not increase the inherent health risk of cigarette smoking. Menthol cigarettes do not play a unique role in smoking initiation, dependence or cessation. And we believe there is no science or evidence-based reason that would support a Tobacco Products Scientific Advisory Committee recommendation to ban menthol cigarettes or otherwise impose additional restrictions.

So with that brief introduction, I'd like to bring up our first speaker, Dr. Jane Lewis from Altria Client Services on behalf of Philip Morris USA.

DR. LEWIS: Good morning. I'm Jane Lewis. I am senior vice president of health and analytical sciences at Altria Client Services. With that role, I have responsibility for areas such as our toxicology evaluations and our clinical studies. Additionally, I have responsibility for the analytical sciences department, the statistics and modeling group.

Thank you for the opportunity today to speak on issues of menthol for your consideration. I will start with characterization of menthol and talk about design, development, manufacturing, and testing of menthol cigarettes.

Cigarettes are harmful and addictive, and there is no safe cigarette. These statements appear on Philip Morris USA's website and in other communications for consumers. These statements apply equally to menthol and non-menthol cigarettes.

Philip Morris USA has provided a comprehensive written submission to the advisory committee for consideration. The presentations that you will see today are excerpts from that submission. And just from the restriction of time, we can only cover so much information, so I encourage you to refer to that submission for complete information.

Before we get to cigarettes, menthol itself has a long history of use. It enjoys a GRAS status, generally recognized as safe for

1 direct addition to foods. It's been approved by
2 these other committees you see, the Joint Food and
3 Agricultural Association, the World Health
4 Organization Expert Committee on Food Additives.
5 It also enjoys a FEMA GRAS status, the Flavor and
6 Extract Manufacturers Association. It's also been
7 approved by the FDA as an inactive ingredient in
8 nicotine replacement therapy products, such as a
9 nicotine inhalation system.
10 In cigarettes, menthol is used as a
11 flavor. It addresses taste preferences of adult
12 smokers. Philip Morris USA only adds menthol to
13 the flavor recipes of cigarettes labeled as
14 menthol cigarettes. There may be trace levels in
15 non-menthol cigarettes. For example, we make
16 menthol and non-menthol cigarettes in the same
17 manufacturing facility, but those levels are below
18 the limit of quantification of 10 parts per
19 million.
20 L-menthol is the isomer of menthol that's
21 associated with the minty flavor of menthol.
22 Typically, it may be sourced from natural sources

as well as synthetic sources. From natural sources, it comes from the mentha arvensis plant, primarily from China and India. Shipments coming into Philip Morris USA of menthol are inspected for quality. We look at quality such as color, odor, appearance. We do purity verifications on the materials. And typically, the materials will be 97, 98, 99 percent pure. What makes up the remainder of the material will be naturally occurring isomers of l-menthol such as neomenthol, isomenthol, and neoisomenthol.

In manufacturing, menthol can be applied to tobacco, to filter, and to packaging materials. Menthol is a volatile material, so no matter where it’s applied in manufacturing, it will equilibrate throughout the cigarette packaging.

When we develop cigarettes, menthol or non menthol, there are a number of design parameters that our developers use to control the amount of tar as tested by the Cambridge filter method, or menthol in smoke. These design parameters that they use are common, and both

affect tar and menthol in smoke. So there are tobaccos that we use. There are blends of burley, bright, and Oriental. There are reconstituted tobacco materials. There are expanded tobacco materials. So the use of these expanded materials and reconstituted tobacco materials can be used to come up with different blends. There are different tobacco weights involved. There are different levels of menthol applied.

The tobacco's wrapped with cigarette paper. That paper can have more or less porosity, which will influence how much tar is received or menthol in smoke. The filter is made of a plug material known as cellulose acetate tow, typically. It's firmed up with a plasticizer known as triacetin. That filter can be more or less dense. It can be longer or shorter. It may be made of other materials, but typically, it's cellulose acetate tow. And again, those types of parameters will control the amount of tar and menthol in smoke.

The plug then is wrapped with something

1 called plug wrap. Then the plug and the tobacco
2 column are joined with the use of an overwrap
3 called tipping paper, and that tipping paper has
4 ventilation holes in it, typically 12 to 13
5 millimeters from the mouth end. And the amount of
6 ventilation also controls the amount of tar and
7 menthol in smoke. And the point of the
8 ventilation is that air flows through the
9 ventilation holes upon puffing, as opposed to
10 through the burning coal of the cigarette.
11 Typically, up to 20 percent of menthol in
12 the tobacco transfers into smoke. And menthol
13 transfer is essentially intact at a level of about
14 99 percent. We did some C-14 labeling studies
15 that showed that menthol essentially does not
16 pyrolyze, but transfers intact.
17 We design cigarettes to meet adult
18 cigarette smoker taste preferences. There’s a
19 balance of menthol and smoke and tar and other
20 types of characteristics, that make up the overall
21 taste character of smoke that consumers, adult
22 consumers, describe to us as strength of taste.

1 As we increase tar, consumers tell us there's more
2 strength of taste. And as we increase menthol,
3 they tell us there's more strength of taste. And
4 with the same panel of adult smokers in a product
5 with similar tar levels, with and without menthol,
6 consumers tell us when menthol is added, there's
7 more strength of taste.
8 This chart shows the range of menthol in
9 smoke and menthol in cigarette levels in Philip
10 Morris USA's products on the market. This was a
11 market survey done in 2008 and 2009. And you can
12 see that the menthol in cigarette levels range
13 from about 2 and a half milligrams per cigarette
14 up to about 6 and a half milligrams per cigarette.
15 And in smoke, the products range from .35
16 milligrams per cigarette up to about .75
17 milligrams per cigarette. When we think
18 about how much menthol to add to cigarettes, we
19 use really two things. One is adult cigarette
20 consumer taste preferences, and the second is a
21 toxicological review of the material itself. What
22 is the safety of the material itself as added to

cigarettes?

So we have a comprehensive process, evaluation process, that we use to look at our products. We start off with a comprehensive literature review. We look at what's known, what's been published. If there's a lot of information, we clearly rely on that. If there's missing information, we'll generate that information through our own studies, chemistry studies, smoke chemistry studies, in vitro and in vivo tests.

We use this process to evaluate pieces and parts of the products, plus the manufacturing processes and the integrated product at the end, integrated technologies, the final product at the end. Menthol cigarettes have been through this toxicological evaluation process, and menthol has been approved for use as an ingredient in Philip Morris USA's cigarettes.

There's a lot known about menthol cigarettes. There's a lot of information in the literature. It's not a new topic. It's been

covered extensively. There are two review articles listed here, one by Werley in 2004, one by Heck in 2009 that is an extensive literature review of what's known about menthol. These reviews cover areas of smoke chemistry, cytotoxicity, mutagenicity, rodent inhalation, mouse skin painting studies.

There are many, many peer-reviewed publications on menthol. And the weight of the scientific evidence from this evaluation process shows that the addition of menthol to cigarettes does not increase the inherent risk of cigarette smoking.

In addition, there are epidemiological studies which really in the end are the most important studies to rely on because they look at the effect of something like menthol cigarettes smoking on an actual disease risk. There's a lot of studies that have been done over the course of time.

There are 13 studies here that suggest no effect of the addition of menthol into cigarette

1 smoke, lung disease risk. There was one study
2 done that showed, in men, there was an effect. In
3 a later study by those same authors, looking at
4 different cancers, they realized that this study
5 was inconsistent. The findings were inconsistent
6 with other studies. They did not see the effect
7 in women, and so they cited in their article that
8 this may have been a chance finding. And there's
9 been a number of studies done since then that
10 showed no effect of menthol.
11 So in summary then, menthol is a flavor
12 used in cigarettes. It's used to address consumer
13 preferences for taste. Philip Morris USA only
14 adds menthol to cigarettes labeled as menthol.
15 Menthol increases the strength of taste of
16 cigarettes compared to non-menthol cigarettes.
17 And the addition of menthol does not increase the
18 inherent risk of cigarette smoking. Thank you.
19 DR. OGDEN: Good morning, ladies and
20 gentlemen. My name is Mike Ogden. I'm senior
21 director of regulatory oversight with the R.J.
22 Reynolds Tobacco Company in Winston-Salem, North

Carolina. And I thank you for the opportunity to address the committee this morning on the characterization of menthol in cigarettes.

My presentation will focus on the history and the design of menthol cigarettes. By way of an agenda, I will talk about that history. I will also cover cigarette design from an R.J. Reynolds perspective and will talk about general factors and also specific menthol considerations for the design of cigarettes. I will also focus on several of the major R.J. Reynolds brand families that use menthol, that being Kool, Salem, and Camel. And we'll show you inclusion levels with share of market for those brand families, and then we'll draw some conclusions.

By way of history, the first menthol cigarette, based on historical documents, was actually discovered by accident. In the early 1920s, a man by the name of Spud Hughes, accidentally as far as we know, stored his smoking tobacco in a box with menthol crystals. The next day, when he smoked his tobacco, he noticed that

the menthol had imparted a taste to the smoke. He liked the combination. He made cigarettes for his friends, and through a process over the next few years, there was increasing demand for those cigarettes and he actually began manufacturing operations. The first cigarette commercially introduced was the Spud cigarette in 1926.

Other nonfiltered menthol cigarettes brands became introduced in the 1930s, many brands that no longer exist, Penguin, Menthorets, Snowball, et cetera. And also, Kool was introduced by the Brown and Williamson Tobacco Company in 1933.

During the period from the 1920s from its discovery to the mid 1950s, the entire U.S. cigarette market was nonfiltered, and menthol was primarily an occasional use product. Moving from the mid ‘50s forward, we saw the introduction of the filter-tipped cigarette. Salem was introduced by R.J. Reynolds in 1956 as the first filtered menthol cigarette. And since that time, there have been hundreds of menthol cigarettes styles

introduced. Most of those were mentholated versions of non-menthol brands. That is, in the early days, there were not specific designs around menthol. Menthol was simply applied to the non-menthol brands.

The preference for menthol cigarettes among U.S. smokers really grew in prominence starting in the 1960s through the ‘70s and on to today. There’s been a fairly consistent trend over certainly recent decades or so of about 27 percent of the total US smoking population that show a preference for menthol.

I’ll first talk about some of the design characteristics of cigarettes in general. These are true of both menthol and non-menthol cigarettes. Of course, the definition of a cigarette is a tobacco wrapped in paper. The focus on the cigarette design, really, is the fundamental properties of smoke generation, and transfer to smokers.

There are many factors that affect those fundamental properties of generation and transfer.

1 Some of those you've heard about already this
2 morning. You'll hear about some more in a few
3 moments. But these affect the draw, which is the
4 ability to draw the smoke through the cigarette;
5 certainly the perceived taste of the smoke, the
6 yield, which is the amount of smoke that transfers
7 to the smoker, and various oral sensations that
8 can be characterized any number of ways. And
9 we'll talk about those more in a subsequent
10 presentation.
11 There are two basic types of menthol.
12 One is natural, which is crystallized from the
13 steam-distilled oil of the corn mint plant.
14 Another is synthetic, which can be chemically
15 produced, synthesized by chemists from a variety
16 of feedstocks. Both of those types of menthol are
17 available. They're over 99.5 percent pure. R.J.
18 Reynolds uses only natural menthol in its
19 mentholated cigarettes.
20 There are a variety of ways to apply
21 menthol to a cigarette. There are seven common
22 methods that are used and really an eighth, which

is a variety of combinations of some of the other seven. The decision a manufacturer would make, as to which application method or combination of methods to apply, really is driven by several factors. One is primarily historical, which is the manufacturing capability that they've generated over time. It also is driven by the type of equipment that the manufacturer possesses in terms of making cigarettes. It's also driven in many cases by the volume of cigarettes. Some of these methods are more applicable to large volume productions. Others are more applicable to small volume.

But those methods include spraying a solution of menthol directly on the tobacco before blending. It can be applied to the pack foil in its pure state. A small amount of menthol can be applied to that foil, and then that foil is used to wrap the cigarettes on a packing machine. Menthol can also be injected into the tobacco stream on a cigarette maker. That is done in sort of real time, if you will. It's injected as the

tobacco moves through the maker and forms the cigarette. It can also be applied to the cigarette paper, also on the cigarette maker. It can be injected into the filter on a filter maker, which is a component of the cigarette-making machine. So as the filter is formed, a solution of menthol can be applied there. Some more recent technology and innovation -- points of differentiation include the insertion of a crushable capsule in the filter that contains menthol that can then be crushed by the consumer. There’s also menthol thread or a flavor thread, one of which of the flavors could be menthol, can be applied in the filter. And as I’ve said, combinations of these application methods are possible and are, in fact, used.

Let’s look at menthol levels in current U.S. cigarettes. And the first bullet gives you a definition of a term that Reynolds uses. I’m sure others in the industry do as well. We call it pack menthol, which basically is a calculation that derives from the total amount of menthol in

1 the pack really. And, as you heard earlier,
2 regardless of the application method, menthol is
3 very volatile. It equilibrates, so all of those
4 application methods essentially give you the same
5 result after a few weeks of aging.
6 So you take the total amount of menthol
7 that’s in the pack, divide it by the tobacco
8 weight, multiply that by a hundred, which gives
9 you a percentage. That becomes pack menthol. And
10 it’s important to include the menthol if you’re
11 going to measure it particularly or if you’re
12 going to calculate it that’s applied totally to
13 the cigarette, whether it be the tobacco, the
14 filter, or the paper.
15 The menthol level that’s chosen for a
16 particular type of cigarette is strongly
17 influenced by the tar yield of the cigarette. And
18 it does increase as tar decreases because there is
19 a decreasing transfer efficiency as you go down in
20 tar. And you can see in the table by looking at
21 various tar categories -- these as measured by the
22 Cambridge filter method -- from the higher tar, 13

plus, down to a lower tar, 1-milligram products, you see an increased percentage of pack menthol. And that’s done because the transfer efficiency is different.

Transfer efficiency, as measured by Reynolds for a 13 plus milligram product, is about 20 percent. As you go down to a 1-milligram product, it’s about 4 percent. So the menthol is increased in the cigarette to give a more or less consistent yield of menthol in the smoke.

An important design element is really the smoker’s perception -- in fact, I would say the most important design element. There are two elements of menthol perception. One is menthol’s taste. A second is menthol cooling. The level of menthol taste and cooling is a function of both the source of menthol and the level or the amount of menthol that’s added to the cigarette.

There are a number of factors that affect the menthol taste and cooling. Obviously, the menthol content; that is, the amount; the delivery; the type and source of menthol; the

tobacco blend is an important consideration; the use of other flavors; and also, the filter plasticizer can play a role as well. And I will go through these and give a little bit more detail on each of those.

Leaf blending is a very component of the design of all cigarettes and certainly, menthol cigarettes as well. In R.J. Reynolds' terminology, we would say that menthol blends tend to be flue-skewed, which means skewed toward the inclusion of flue-cured tobacco. And that means simply more flue-cured than burley tobacco. And that's done to complement the menthol taste. Flue-cured, or often called bright tobacco, enhances the freshness of menthol taste. Burley tobacco has a heavier note and tends to interfere with the menthol freshness. However, there are many successful menthol brand styles that are burley-skewed, and also that are balanced, in terms of a nearly equal proportion.

Both menthol and non-menthol products contain Oriental tobacco, or sometimes called

Turkish tobacco. Menthol products that do contain Oriental tend to include a smaller amount of Oriental than a non-menthol counterpart because of the very unique aromatic character of the Oriental tobacco. But ultimately, the final blend composition is determined by the consumer. It's the consumer's taste preference that drives the design of all cigarettes, and certainly, also for menthol cigarettes.

Looking at some of the construction variables; that is, the cigarette design or construction variables that are employed in the cigarette, again, these are common for both and menthol and non-menthol cigarettes. They include the filter tip ventilation, the filter pressure drop or the density of the packing of the fibers in the filter -- that affects the sense of ability to draw smoke through the filter and also changes the filtration efficiency -- choice of cigarette paper, tobacco blend, and also, the tobacco weight.

The effect of these construction

variables on menthol delivery parallel their effects on tar delivery. You saw that in an earlier graph. Generally, as smoke increases, the menthol will increase as well, although the transfer efficiency is inversely related to that.

The filter plasticizer, that’s used for cellulose acetate filters -- the most common one is triacetin. That is used to bind the fibers in the filter together. It also happens to be a good menthol solvent. And over time, menthol becomes fixed in the filter matrix. And once it’s fixed, menthol is less able to transfer to the smoke stream. This generally occurs many months after manufacture, typically, on the order of a year. So what you often find with menthol cigarettes is, as their shelf life approaches a year, the perception of menthol reduces. And for some smokers, particularly as you get beyond a year, they will tend to report those cigarettes as stale. But the menthol is still there, but it becomes fixed in the filter. So if you analyze it, you can still find it. But it doesn’t

transfer as efficiently to smoke, so the perception of menthol can go down as menthol cigarettes age, typically beyond a year.

Other flavor additives generally do not affect menthol delivery, although the choice of flavors to use with menthol has considerations much like the tobacco. The lighter tasting flavors tend to complement menthol taste, while heavier tasting flavors tend to mute the menthol taste. And again, the only way to understand the effect of one flavor on another or a combination of flavors is to evaluate the combination on a cigarette among adult cigarette smokers.

Looking at smoke delivery, and how it’s impacted by design characteristics, smoke deliveries are a function of the blend components and also, the construction variables, as I’ve already explained. Those smoke deliveries also drive menthol delivery. It is while menthol level is held constant, menthol delivery will proportionally shift as tar increases or decreases. That’s the same relationship that

holds true for nicotine.

RJR studies indicate that menthol delivery is significantly correlated with the tobacco menthol level. It is the primary factor in the amount of smoke menthol that’s delivered in the smoke-per-unit tar. Menthol is also significantly correlated with filter pressure drop in ventilation. Deliveries decrease as the filter pressure drop and ventilation levels increase.

So delivery at a given tar level depends on the combination of filter pressure drop and ventilation. And as I said earlier, menthol transfer efficiencies, in our experience, range from about 4 to 20 percent. There is published literature on that. And that certainly depends on the design and tar level, again, with the lower transfer efficiencies for the more highly ventilated cigarettes out of the lower tar cigarettes, and the higher transfer efficiencies for the higher tar cigarettes.

One of the specific questions the committee asked for information on was taste

threshold. So we'll give some information on that from a Reynolds' perspective. The threshold to detect menthol -- this is the smoker's ability to detect menthol -- varies inversely by tar level. So in other words, the ability to detect it at higher tar is actually a little bit lower than it is at lower tar, because of the balance of menthol and the strength of taste.

The range is typically on the order of 75 to 100 parts per million, or if you prefer to think of that in percents, less than .01 percent is used at Reynolds, as sort of the taste threshold. From our experience, that is above that level, smokers can certainly detect a flavor, but it's not until you get to a much higher level that smokers typically can detect it as menthol.

The detection certainly depends on the sensory acuity of the consumers, just like it would be for other foods; tolerance for spicy foods, et cetera. There is a range of taste preferences. Thus, that's why you see a range of menthol levels in the market, trying to cater to

specific tastes of specific adult smokers.

R.J. Reynolds uses a definition of trace menthol as 50 parts per million or less. So that's .005 percent or less, and that's used for process purposes in terms of manufacturing, and also, in terms of analytical capability. We have a trace menthol method, and we have a regular menthol method. Menthol levels, from Reynolds' experience, to actually define a menthol cigarette, that is, to generally impart a characterizing menthol flavor, is usually .3 percent or higher.

Menthol can be found in non-menthol cigarettes for one of several reasons. First of all, it can be found at trace levels as a result of various tobacco processes, as you heard earlier. One example is reconstituted tobacco sheet, where quality tobacco from other products that, for example, may have been damaged on the packaging line or reclaimed and processed into sheet. So they typically can be very small amounts or trace levels that could carry over. As

was said earlier, menthol and non-menthol cigarettes are made in the same factory. Menthol is volatile, so there can be some carryover at trace levels.

Menthol can be an element of a commercial flavor. This would be a flavor that, perhaps, we would buy from an external flavor company. It can also be directly added to non-menthol cigarettes. And the reason that it’s used is to provide a fresh taste or, in our terminology, to brighten the flavor, while without imparting a menthol taste. And it’s also used to smooth or balance the taste of the blend.

I’ll finish with three charts that show you the relationship between pack menthol and share of market for the three major R.J. Reynolds brand families. The first one is Kool. To orient you to the chart, on your left-hand axis is pack menthol in percent. On the right-hand axis is the share of menthol market, also as a percent. The pack menthol is the solid blue line. The hatched line is for the share of menthol, and these are

dated over the last 11 years from 1999 to 2009. This is a weighted average of the entire Kool family, so that it’s a weighted average of the amount of pack menthol against its share of market.

So if you look at the entire Kool family as a whole, menthol inclusion levels have stayed very constant over the last 11 years, and you can see the wandering of the share of market curve dropping a bit around 2000, increasing a bit in the early 2000s, and then beginning to decline again since 2008.

Using the same analysis, we look at the Salem family. Just like Kool, all styles of Salem, as was the case for Kool, are menthol styles. So it’s very easy to look at the entire family. And again, the solid line is the pack menthol weighted across all the styles within the Salem family. The hatched line is the share of market.

You can see in terms of pack menthol, it’s reasonably consistent, between .6 and .65

percent. There have been some changes through time. There are intentional changes made to the pack menthol for a variety of reasons. Particularly within Reynolds, we consolidate blends. We have a large number of brand styles. We consolidate those over time. There are process changes that come into play with new equipment, with new materials, et cetera. We'll talk more about that in a subsequent presentation. But it's reasonably constant, and you can see the share of market has not been reasonably constant. It has dropped from about 12 percent in the last 1990s to a position of about 6 percent today. So share of menthol market for Salem has dropped by half, while the menthol has been reasonably constant, although it has increased nominally a few times through that period of 11 years.

If we know look at the Camel family, Camel, of course, is principally a non-menthol family, although there are menthol styles. This chart just looks at the menthol styles in the Camel family, and you can see the pack menthol as

a solid line on the top ranging from between .5 and .6 percent. There is one noticeable increase around 2005. That was when we redesigned and improved the entire Camel family, so there was an entire blend change of the Camel menthol product. So all of the tobaccos, everything was re-blended to entirely change the Camel menthol. And there was a concomitant increase, a slight increase of .05 or so percent in pack menthol.

The share of market for Camel, you can see on the lower chart. Camel did not have much share of market in menthol styles in the late 1990s, ticked up a little bit in the early 2000, and then, has shown some growth through the mid to late 2000s, but still, only about 3 percent of share. It still is not our major menthol family. Kool is.

So in conclusion, menthol cigarettes were introduced and discovered by accident really and introduced in the 1920s, and they really didn’t become popular in the United States until the 1960s and beyond. Cigarette design is similar for

menthol and non-menthol cigarette styles. Menthol levels typically vary inversely with tar level, due to low menthol transfer at lower tar. That's the 4-percent number. And RJR major menthol families have shown no consistent relationship between menthol levels and market share. Thank you.

DR. TRUE: Good morning. My name is Bill True, and I'm the senior vice president of research and development for the Lorillard Tobacco Company. And I thank the committee for the opportunity for Lorillard to be able to share their information and data with respect to the characterization of menthol.

As most of you know, Newport is the largest selling menthol brand in the United States. A little bit of history. Lorillard was manufactured for five decades since 1957. It was reformulated in 1972 to address relatively poor sales and declining market share. But with that reformulation in 1972, it actually wasn't until 1993 before Newport became the best selling brand

in the U.S. After the reformulation, the amount of menthol in our premium packing, the Newport Full Flavor king box, did not change substantially for 35 years between 1972 and 2009.

We are advocates of a data-driven process and scientific methodology, so as a result, we're very happy to share with you a lot of data. This graph here represents over 23,000 individual data points collected for pack menthol, that was described in the previous presentation, on our Newport Full Flavor 80-millimeter product. And as you can see from the period of 1993 to 2009, that remained absolutely flat, and a change took place in 2009 that I will come back to in just a moment.

Considering other Lorillard menthol brands, we also have menthol packings for Kent, Old Gold, Maverick, and True. Over the years, Lorillard has had as many as 65 menthol brands. So as another example of a Lorillard brand for pack menthol, I'd show you the data for our Newport Lights 80-millimeter product. Again, you see a slightly higher pack menthol, based on some

of the design considerations that were described earlier. But again, you see from 2000 to 2009, an absolutely flat trend because there have been no changes made to the level of menthol in these products.

When considering the level of menthol on particular products, it is important to keep some of these cigarette design variables in mind. First of all, this increased filter efficiency decreases the menthol in smoke. So it’s not dissimilar to see that the level of pack menthol in a Newport Light product would be higher than a regular full flavor product. Menthol is transferred at a similar rate as tar, and as a result, they are higher. For our transfer efficiencies that have been measured over time, 20 percent of the menthol in the Newport Full Flavor product is transferred to the smoke, whereas only 12 percent in the menthol in Newport Lights is transferred to the smoke.

As you can see in this particular graph, we’re looking at the menthol level on the

1 cigarette on the left for Newport Full Flavor and
2 Newport Lights, and then on the right, Newport
3 Full Flavor 100s and Newport Lights 100s,
4 comparing the menthol level on the cigarette and
5 delivered in smoke. Smoke menthol has not been a
6 routinely-used method for us. We typically do
7 this for academic purposes, and understanding a
8 bit about what kind of transfer rates we have.
9 But our products, as with the other
10 companies, are designed with consumer preference
11 in mind, and they make the ultimate decisions on
12 the amounts of menthol that we have. But as you
13 can see, despite the increasing levels of menthol
14 that might be added to the cigarette, as you go
15 and consider these other cigarette design
16 features, the amount of menthol delivered in the
17 mainstream smoke remains about constant.
18 Coming back to our increase in menthol
19 levels beginning in 2009, starting in 2004,
20 compliance with fire-safe standards became a
21 requirement of the industry. And this promulgated
22 state by state over a period of a number of years.

For Lorillard products, the new cigarette paper caused a slightly higher tar for most of our packings. So in 2009, we initiated an effort on a brand-by-brand basis to reduce the tar levels to pre-fire-standard compliant levels. In each case, it was required for us to either increase the filter efficiency and/or filter ventilation to lower the tar, and this required more menthol to be added to maintain a consistent taste.

Despite the changes in pack menthol, however, the smoke menthol in Newport did not change. If you look at this chart on the left, you take a look at the pack menthol of Newport 80-millimeter before and after the conversion. And you can see the increase that was noted from .36 to .42. And on the right-hand side, you can see the menthol delivery in mainstream smoke, pre- and post-conversion, which are essentially the same.

Now this data, in fact, was collected after the conversion took place because we used, again, our expert taste panel and our consumer panels to determine what the amount of increase of

menthol would be. But you can see, by having this data available to us, the validity of using consumers to help us direct that information.

A little bit about the specifics of how Lorillard applies menthol to tobacco. As mentioned in previous presentations, there are seven or eight different methodologies that may be commonly used. And we only use one. And I apologize that maybe the slide is not easy to read. The graphics didn’t blow up as well I’d like to. But on the right, we make up a menthol spray solution, which is simply a mixture of ethyl alcohol and menthol, that’s sprayed onto tobacco in a cylinder. And it’s then removed into what we call tub storage for anywhere from 24 to 36 hours to allow this equilibration to take place and to have the menthol be consistent throughout. And from there, the menthol is simply sent to the cigarette makers.

On the topic of synthetic menthol, Lorillard uses a mixture of both natural and synthetic menthol in most of its cigarettes.

Synthetic menthol has different taste characteristics than natural menthol, and that's one of the key reasons why we use it. In fact, the complexity and the specific special taste that we gain from the combination of synthetic and natural menthol also has to do with the sources of both the synthetic and natural menthol.

In terms of deciding levels, Lorillard does not use a specific method of menthol to classify cigarettes as menthol or non menthol. The menthol level in all of our mentholated products, that are declared as mentholated products, are very readily discernible by consumers. We do identify the optimal level of menthol to complement the tobacco taste. And the ultimate determination of menthol is based on consumer preference.

In terms of these detection levels, there was a study published in 1989 on pure menthol, not necessarily menthol in cigarettes, which indicated that individuals have very different thresholds and very different sensitivities in their ability

to taste, smell, and sense the cooling properties of menthol, as much as three orders of magnitude. So it’s very difficult to pinpoint a precise level from that basis.

Only recently in one particular study, Lorillard did some research that would indicate that menthol is generally detectable by consumers at a level of .12 percent. We say generally available because there are expert smokers with very sensitive palates, and there presumably are some consumers that can detect this at lower levels. But generally, it’s .12 percent. And the amount of menthol used a characterizing flavor in all of Lorillard products is at least three times over that detection level, and in some cases more.

Menthol at very low levels is sometimes used in non-menthol brands, along with very low levels of other flavors, as a component of proprietary top flavors to slightly augment the key signature of Lorillard products. The success of Lorillard products has always been predicated on a unique and special tobacco taste signature,

and we find that all of these proprietary top flavors have the ability to augment and allow that specific tobacco taste signature to be enjoyed by consumers.

The levels that we have in our products were established decades ago, and they've been consistently maintained. And this use is analogous to flavor practices employed in other consumer products. In addition, just to note, that all the levels for menthol and every other ingredient, is now routinely provided to the FDA on a regular basis.

In 2008, there was a publication by Kreslake that concluded that Lorillard decreased menthol concentration by 16 percent in Newport between 2000 and 2007, presumably to target younger smokers. And this is a table that's been extracted from that publication showing that. So we're kind of interested, based on some of the data I've shown you previously, as to what underlying data might be contained in that publication.

What we found is that this study's conclusion regarding Newport is based on a single 2007 analysis that was performed by the authors, based on a market pickup from a convenience store of one sample, and referring back again to a single baseline value that was found in a 2000 Lorillard internal document. Two data points are never sufficient to analyze a trend. Therefore, two analytical data points are entirely inadequate to support a conclusion with respect to Newport.

In fact, the actual trend line for menthol in Newport between 2000 and 2007 can only be described as unequivocally flat. This can be shown in the following graph. If you look at the period between 2000 and 2007 and you take the two data points that have been asserted by the authors, you end up with a line that looks like this. Once again, we're advocates of data, real data. The real data, again, of tens of thousands of data points over this period of time show that there's absolutely no change to the level of menthol in Newport products.

The two values that were used in the publication represent analysis that were conducted by different laboratories, used different methods, were presented with no statistical analysis. And these two data points, as you saw, are within routine production and analytical method variation. The design and conclusions of the study failed to consider the characteristics of cigarette manufacturing, statistical process control, and analytical method variability.

In order to conduct a valid scientific trend analysis, the following things are critically important, especially as it relates to a study on menthol. It’s important to have the documentation of a sample identity age and handling. Due to the volatility of menthol, shelf life, storage conditions are critically important to have an understanding of how fresh a product is. And if you want to do an adequate trend analysis, the age of the products should be matched. Use of standardized validated methods of analysis -- it’s important to understand that

existing menthol analysis methods produce widely variable results. Even the best analytical methods show inherent variability. In most cases, that's 8 to 10 percent.

Without a standard validated method, data generated by different laboratories should not be compared. It's also important to do multiple replicants, as an analysis of a single sample can never support a valid conclusion. And it's also important to do valid statistical analysis of numerous data points because, as we all know, statistical confidence increases with the increasing number of data points. I'll let you decide two data points, 30,000 data points. Where do you think the stronger statistical validity is?

So in summary, despite the inaccurate conclusion and deficient scientific methodology from this publication, for some reason, it still continues to be widely cited in some of the FDA proceedings as evidence that Lorillard and the industry strategically lowered menthol levels in Newport. Tens of thousands of data points over a

10-year period demonstrate that, that is absolutely false and the levels of menthol in Newport have remained consistent.

The perpetuation of scientifically invalid studies to draw conclusion does an injustice to the scientific process. And in conclusion, it’s absolutely critical that all the decisions we make going forward are data driven, founded on a rigorous review of all available data, and based on sound scientific methodology. Thank you very much.

DR. SAMET: So, Mr. Dillard, I guess this is the end of this set of presentations, correct?

MR. DILLARD: Yes, it is.

DR. SAMET: Okay. Thank you for your presentations.

Everyone will notice that we are roughly a half hour ahead of schedule. That does not mean we have a 45-minute break. And what we’re going to do is go on into the clarifying questions, and we have a half hour. And then we will go to break. I’d just like to remind the committee that

these are, in fact, clarifying questions as stated, so that these questions should address the materials that we have just been presented with or the related written materials that we heard.

Let me just get a sense of how many have clarifying questions you would like to ask, so lots of you. We'll get to everyone then, and I have a number myself.

Just for Dr. True, just before we leave, you actually didn't tell us what your data points were in those graphs. Were the dots individual packs, batches, or what were we looking at, just before I forget this point?

DR. TRUE: Those data points were individual pack menthol data points.

DR. SAMET: So you've analyzed 20 cigarettes within the pack, and you're presenting a mean value for that pack or median? Or what are we looking at?

DR. TRUE: Basically, you're seeing individual data points for the method, okay, which extracts the menthol from all of the cigarette

components in our method, the filter, the paper, and the tobacco. And what you're seeing in most of those, you're seeing a stack plot of anywhere from 5 to 9 to 10 data points per day, which is representative of statistical sampling of our production throughout the day.

DR. SAMET: Okay. Let me make sure I've got it, because I'm not sure you exactly told me. So you can see individual dots as you look at your stack plots. And an individual dot corresponds to analysis of the contents of one selected pack that's been picked by random sampling from your processing stream?

DR. TRUE: Yes.

DR. SAMET: Is that correct?

DR. TRUE: That's correct.

DR. SAMET: And so this is analysis of the fresh product as it is --

DR. TRUE: Yes, it is.

DR. SAMET: -- as it is produced and it's all menthol within that pack, then?

DR. TRUE: Yes, that's correct.

DR. SAMET: And you're presenting this as a average per cigarette? Got it. Okay.

DR. TRUE: Yes.

DR. SAMET: Okay. Good. Thank you.

Why don't we -- I think we'll start left and go around, I think. So the first -- Greg or you?

DR. CONNOLLY: Jane, I think the last time I saw you was when the snowstorm was in Boston and you got stuck. You won't get stuck today. I'll tell you right now.

DR. LEWIS: That's correct.

DR. CONNOLLY: Thank you very much for your presentation, and I found it very insightful.

A couple of questions. One is you reference consumer taste preferences. And the other company represented taste and cooling effect. Do you think taste is the primary motivator for smoking menthol cigarettes?

DR. LEWIS: Consumers that smoke menthol cigarettes have a number of reasons for doing that, and I think that there are taste preferences

for those products.

DR. CONNOLLY: More so than a sensory effect, than a smoothing effect or a cooling effect?

DR. LEWIS: I don’t know if consumers really differentiate -- consumers tell us that they’re cooling. They tell us there’s a taste preference, and they tell us that they’re cooling. And that all sort of kind of folds together, I think, into what they prefer with those cigarettes.

DR. CONNOLLY: So that the opinion of Philip Morris is there’s both a taste, as well as a cooling effect?

DR. LEWIS: Sure, and I’ll talk a little bit more about the cooling effect in my next presentation. But yes, sure. Consumers tell us that there’s a cooling effect.

DR. CONNOLLY: Just for clarification, in the introduction, you say Philip Morris agrees with the overwhelming medical science. Can I assume that to be Philip Morris believes the

overwhelming medical and scientific evidence that cigarette smoking causes lung cancer, heart disease, emphysema, that Philip Morris as a company believes this and just not agrees?

DR. LEWIS: I'm not sure I really --

DR. CONNOLLY: Well, your statement here, you say Philip Morris USA agrees with the overwhelming medical and scientific evidence. But as a company, do you believe the overwhelming medical and scientific evidence that cigarette smoking causes lung cancer?

DR. LEWIS: Sure. I mean, I think that --

DR. CONNOLLY: So the company believes that smoking causes lung cancer?

DR. LEWIS: I think the information that's out there on cigarettes for many years shows that cigarettes are harmful and addictive and that's where that statement --

DR. CONNOLLY: So the position of the company is that cigarette smoking causes lung cancer?

In your presentation that you gave us, you dealt quite a bit with the issue of mechanistic links. Do we know of a mechanistic link to lung cancer, what causes lung cancer mechanistically?

DR. SAMET: Greg, this is probably a little bit off the --

DR. CONNOLLY: Okay. Well, I think mechanistic links are an important component of the presentation. I'll try to be brief on this.

You've presented data on levels of menthol. We asked for both the ISO and the Canadian data, and I don't see the Canadian data here.

Could Philip Morris run these numbers and produce the Canadian data for the menthol levels?

DR. LEWIS: We don't routinely test our products using the Canadian method. We routinely test it using the ISO method. That's data that can be generated, but we don't have it, so we didn't produce it.

DR. CONNOLLY: Okay. I think the

committee asked for that.

This chart that you have, and you presented in your slides, could you explain that chart to me again for me?

DR. LEWIS: I can’t see that chart.

DR. CONNOLLY: This is in your slide presentation. You talked about menthol and smoke.

DR. SAMET: Greg, why don’t you refer to which number this is?

DR. CONNOLLY: Okay. I have figure -- from your main submission, Figure No. 1.5. I think you have a version just of only the Philip Morris brands, but there was a previous slide that included all brands. Well, we can go to the Philip Morris slide.

DR. OGDEN: Slide number, please?

DR. CONNOLLY: Slide number 10. Now, I’ve heard a lot this morning about transfer efficiency. And it appears you’re loading lighter cigarettes with menthol, trying to compensate for ventilation, transfer efficiency, retention by triacetate. With the inference -- and maybe

please correct me -- that that could almost look like a linear relationship there, between menthol in the cigarette, and menthol and the smoke.

Am I interpreting you correctly?

DR. LEWIS: Yes. I didn’t cover that in my presentation. But what we do is -- adult cigarette smokers tell us that they like a fairly consistent level of menthol. And as we use different design parameters to lower tar, that also affects the amount of menthol delivered in smoke. So we will add more menthol to lower tar cigarettes to maintain that consistent level of menthol that adult cigarette smokers prefer.

DR. CONNOLLY: All right. So there’s no linear relationship between what’s in the lower level and what appears in the higher level? There’s going to be no correlation on that chart?

DR. LEWIS: I’m not clear on your question.

DR. CONNOLLY: I’m just hearing that you’re loading lower lighter cigarettes with menthol in the rod to compensate for ventilation,

retention by triacetate and others. And it would appear that even though there's higher amounts of cigarette, of menthol, in the rod, that when we come to the smoke, that that's actually been reduced.

DR. LEWIS: That's right. There is somewhat of a relationship, as you can see here. We do add more menthol in the cigarette to lower tar level products, and that menthol in smoke does drop a little bit. But we strive to maintain that at a fairly consistent level. Again, based on --

DR. CONNOLLY: Okay. I think the point is, there's linear relationship between menthol in the rod and menthol in the smoke. It looks like it's pretty even across the board.

DR. SAMET: Okay. I think we better move on, Greg. We have --

DR. CONNOLLY: Okay. I just have one question, Jon, and then I'm done.

The committee also asked for menthol analogs. And Lorillard was kind enough to present data on a compound called, I believe, WS-23,

Wilkinson Sword 23. It's my understanding that Philip Morris has a menthol analog called Wilkinson Sword No. 12 and Wilkinson Sword No. 14. I don't see it in these materials.

DR. LEWIS: We have used that product in the past. We don't use it currently. We haven't used it for many years.

DR. CONNOLLY: Okay. And can I ask why did you --

DR. SAMET: I think, Greg --

DR. CONNOLLY: Okay. Fine, all right.

DR. SAMET: -- we've just got to move on.

Actually, just while you're there, perhaps you or perhaps Dr. Ogden, one, I think, further clarification. When you talk about smoke, can you tell us where the menthol is? And that is, I guess in terms of the distribution between the gas and particulate matter in the smoke, and particularly, I guess, with regard to deposition within the respiratory tract.

Do you have information?

DR. LEWIS: It's primarily in the

1 particulate phase, I believe. I think it's
2 primarily in the particulate phase. In terms of
3 deposition in the respiratory tract, it transfers
4 with smoke. And I don't know any particulars
5 about that.
6 DR. SAMET: Dr. Ogden, do you have any
7 information on this?
8 DR. OGDEN: Not today, no.
9 DR. SAMET: Patricia?
10 DR. NEZ HENDERSON: My question is for
11 Dr. Lewis and for Dr. True.
12 Dr. Lewis, let me quote you here. You
13 said that the strength of tastes of menthol
14 cigarettes increases with the strength of menthol
15 in smoke. Does this mean that if you like
16 something, you'll keep trying it, you'll keep
17 using it all the time? Because you like it so
18 much, you'll continue to use it.
19 DR. LEWIS: I think there are a number of
20 reasons why smokers continue to smoke and menthol
21 smokers continue to smoke. I think what we're
22 looking at here is brand choice. And those

menthol smokers tell us that they prefer that taste of menthol.

DR. NEZ HENDERSON: So if it’s more of a taste component and if we were to take it away, would that -- how would your company feel about that?

DR. SAMET: I think that’s probably too much off the track of a clarifying question.

DR. NEZ HENDERSON: Okay. Just because if it’s a taste component to it -- and I’m just wondering what it does to the product, other than making it so that the consumer uses it more.

DR. LEWIS: I mean, consumers have a number of products to choose, and that is one we -- the feedback is that that’s a taste that they prefer.

DR. NEZ HENDERSON: Okay.

DR. LEWIS: And we design to meet adult cigarette smoker taste preferences.

DR. NEZ HENDERSON: Okay. And the next question is for Dr. True. You presented data about the changes of menthol from 1993 to 2010.

Is there any data prior to 1993? Because there was a -- menthol became more popular --

DR. TRUE: Sure.

DR. NEZ HENDERSON: -- from 1960 to 1970. So I'm just wondering about that period between 1960 and 1990.

DR. TRUE: The period I have in the graph is actually a convenient sample because of the IT, the laboratory information system that we have. It's very convenient to get all the data from one place, and not have to paste things together. All the data we have from 1972, which is when we made that major brand formulation change for Newport, the median or mean average menthol level for Newport has remained between .36 and .37. So any change in the '70s or '80s was only a matter of one-hundredth of a percent, and again, well within that variation that we were showing there. Okay?

DR. NEZ HENDERSON: Okay.

DR. TRUE: And to the point, I think, of your previous question, I think in terms of using the product more, I think there's a number of

information that we discussed at the last meeting, as well as probably some more you'll hear this week, with respect to the fact that menthol smokers typically smoke fewer cigarettes than non-menthol smokers. So they actually smoke it less.

DR. NEZ HENDERSON: Okay. And this was a question that I had from the previous meeting that was not addressed is, is menthol used to cover the harshness of cigarettes?

DR. TRUE: Absolutely not. I've got something in the following presentation on that. But in terms of harshness, the most significant items that impact the harsh taste of a cigarette are the tobacco blend, the moisture level of the blend, and the filter ventilation. Our product developers do not use menthol in any way, shape, or form to try to cover up, mask, or minimize that harsh taste.

DR. NEZ HENDERSON: Okay. Thank you.

DR. SAMET: Jack?

DR. HENNINGFIELD: My question is really for all three or any combination. We've heard, I

1 think, from all of you, that menthol levels are
2 set by consumer preference and the word “taste”
3 over and over. And some of it just doesn’t make
4 sense.
5 So I’m trying to separate out what seems
6 to be using taste as a metaphor or a euphemism for
7 all the other things that you’re measuring. And
8 we see bits and pieces of that in the document.
9 Lorillard mentions overall satisfaction as a
10 measure. We’ve learned that with trace menthol,
11 people can’t taste it, but yet, you’re using some
12 way to set those levels of trace menthol.
13 So my question is really pretty simple.
14 What is the full battery of measures that you
15 actually use to set menthol? Because consumers
16 don’t set it; you set it. And what are the
17 scientific data that you rely on? What are all
18 the scales? We’re seeing just enough that I don’t
19 think it’s just a simple taste scale. That
20 wouldn’t make sense.
21 Is it taste, cooling, overall
22 satisfaction? If overall satisfaction is an

actual scale, what does it look like? Is it from zero to 100? Is it a visual-line analog scale? Do you have liking scales? Do you have pleasure scales? What are all the scales that you use to assess it, what you're calling taste?

DR. SAMET: I think that was one question with many parts. Why don't you speak to it overall?

DR. OGDEN: I mean, you use the word taste. To me, as a nonsensory scientist, I would perhaps better characterize that as the overall sensory experience. In a subsequent presentation that I'll make under the clinical effects and behavioral effects, I'll talk more about our sensory evaluation research.

But I think the point that I would want to make is that menthol cigarettes, as I showed earlier, were really discovered by accident, that they happened at a certain level. So it really was an art, long before science got involved, back in the 1920s. So we don't design a level of menthol in a scientific way, I think in the way

perhaps that you're asking.

There are sensory evaluations that are conducted. We have historically used at Reynolds for 25 years, I know for sure, a technique called quantitative descriptive analysis, which is we have smoker panels, both internal trained panels. We have external consumer acceptance tests. And there are a number of attributes that are scored on those ballots, and I'll give you some examples in a subsequent presentation.

But the terms that are used there -- some of the examples of terms are, cooling sensation is a term. Minty flavor is a term. Medicinal flavor is a term. But using the QDA sensory technique, all those terms are established by the panelists. They're not established by R.J. Reynolds. So they decide what the terminology should be. They decide what the meaning is, so that they own it. I mean, that's the way the QDA technique works.

So we have those descriptive terms, and the way that we develop cigarettes, again as I'll show you more, is an iterative process. I mean,

we have established cigarettes. We test them against competition. And if we find that there are deficiencies, we make prototypes that we hope will address those deficiencies. We go back to those sensory panels and see if we've made progress. And through that iterative process, again defined by consumer taste preference, we make a decision whether to implement that change or not.

DR. HENNINGFIELD: I guess you didn't answer the simplest part of my question, which is what are the measures? How do you do it? Do all the companies do the same thing? Is it really true that none of you have rating scales for taste preference? None of you ask if people like one cigarette more than another cigarette? I mean, you're saying you assess preference. How do you assess preference?

DR. OGDEN: Right. It's an open-line scale. In the QDA technique, you don't assign good or bad. It's basically none to a lot, so I don't know the exact scale. It may have changed.

It’s probably a zero to 7. So it’s a line scale.

DR. HENNINGFIELD: Okay. So there is a scale that you give people?

DR. OGDEN: Absolutely. They rank it and then those are scored.

DR. HENNINGFIELD: And you make up the scales. You give them to the panelists, and the panelists then, you’re saying --

DR. OGDEN: Well, as I said, the panelists, in the early days of defining a panel, they decide the descriptors and the definitions. We actually construct the ballot, the paper ballots.

DR. HENNINGFIELD: Yes.

DR. OGDEN: In the old days, it was paper with pencils, and later days, it is perhaps electronic. But yes, we construct those. And those are given as instruments to participants who score them. And then they’re returned and analyzed.

DR. HENNINGFIELD: Okay. So you have rating scales. And I guess I really would like to

1 see from the different companies what is on those
2 rating scales, what the specific questions are, I
3 mean what the data are that you use, not just for
4 menthol cigarettes, but for the trace menthol,
5 because I assume you're not just making up what
6 level you put in there. You're asking the people
7 something, because you keep telling us that it's
8 consumer preference.
9 So can you give us the measures and the
10 scales so that we can look at them? A lot of us
11 work on scales, and we have an idea of how to
12 interpret them.
13 DR. OGDEN: Well, I don't have those with
14 me. I've got some of the attributes in the
15 subsequent presentation. I don't have images of
16 the exact scales, but as you heard from Dr. Husten
17 this morning, there's a document production
18 request. All of those documents will come to FDA
19 in due course. We've referred to a number of them
20 perhaps in our submission, but yes, we can
21 certainly make those available.
22 DR. SAMET: Okay. Do any of the other

presenters want to comment on this point?

DR. TRUE: I apologize if I don’t capture all of these in kind of a little bit of order based on my memory. But to address, I think, one of your last points about the products that contain low levels of menthol, I think there seems to be a difference in perspective from how you’re viewing it and how we’ve actually dealt with the situation, and that we don’t think of menthol as an individual item; that we think about what level to put in low levels within a product.

Over the years, there have been complex -- I think Mike mentioned in his presentation. We have these compounded flavors that we get from people in the flavor suppliers, and menthol can be a component of some of those. People that were expert at the time -- in our case, we’re going back decades when those levels were determined. There were no detailed quantitative measures that went into that. It was a matter of analogy, of going to a master chef, trying to put a recipe together.

In the case of Lorillard products, we're always trying to optimize that premium tobacco taste. We go through great lengths to select the highest grades of tobacco that we can find, that represent our tobacco taste signature. And those very, very low levels of top flavors, menthol not being unique amongst the list of top flavors that we use, are all there intended to augment that tobacco taste; not a cooling taste, not a minty taste, not anything other than to augment that tobacco taste. So in terms of the low level menthol products, that's been the way that Lorillard has designed those.

DR. SAMET: Okay. Thank you. I think we need to move on from this.

Cathy, did you have a specific clarification here?

DR. BACKINGER: Well, I did. And it was following on to Jack's, so that's why I raised my hand. I know we jumped out of line. So my question is -- Jack brought up about looking at consumer taste preference for the optimal level of

menthol. And I think everybody mentioned that these taste preferences were done with adult smokers. But I'm wondering, getting more information to clarify who are these adult smokers. How long have they smoked? How much do they smoke? Do you look at age categories? Do you look at race, ethnicity, other kind of socio-demographics? And do you do any other kind of research on any other people, other than adult smokers, looking at nonsmokers, for example, to look at initiation? So that was my clarifying question.

DR. LEWIS: We do our cigarette tasting testing with adult cigarette smokers, and those are smokers 21 years of age or older and only with adult cigarette smokers. You're going to hear some more about how we do some of that in presentations going forward, but that's what we do our testing with.

DR. SAMET: Okay. Thank you.

Dorothy? I'm sorry.

DR. TRUE: As well, I think, Lorillard

has information on the specifics of what make up our panels. But typically, we have two types of consumer panels only, and they are addressed as adult existing smokers. Two panels we typically have would be to understand the Newport franchise, and how well they continue to like the Newport product compared to competitive products. So that is -- basically, we go out and we recruit that panel to match the known, as much as we know, about the demographic age distribution of the existing Newport franchise.

If we're looking at trying to develop a product or if we're looking at trying to compare our product to a competitive product, then we would do the best we can to try to understand and recruit a panel of adult smokers that are specifically designed towards what we believe the existing demographic makeup of that franchise is. So it's very, very simple in those bounds.

DR. SAMET: Thank you.

I think just to the panel, if we continue at the rate we're going, the clarifying questions

will be the next hour. So what I'm going to ask you to do is sort of limit your questioning to your top clarifying question as we go around, and we can see what we'll cover as we go through. And if we need to go a little long, we will.

Dorothy?

DR. HATSUKAMI: Okay. This is a question that's addressed to Dr. Lewis but can be addressed by any of the presenters. I was really struck by the lack of abuse liability testing in your toxicological studies. And when I talk about abuse liability testing, I'm talking about a combination of menthol plus nicotine versus nicotine alone in terms of the acquisition of self-administration extinction and relapse.

I was wondering if any of the companies had that type of data and if not, why not.

DR. LEWIS: You'll hear more about that in upcoming presentations, so I would encourage you to hold that question until you hear other topics.

DR. SAMET: Melanie?

DR. WAKEFIELD: I have two questions. The first is for the Philip Morris and R.J. Reynolds presenters. Both of you mentioned that consumers vary in their taste preferences for menthol. And I wondered if there are kind of underlying systematic differences in the types of consumers that prefer a lighter menthol taste versus a more obvious menthol taste. For example, younger consumers preferring a lighter taste and older consumers preferring a more advanced sort of obvious taste, for example.

DR. LEWIS: There are differences, and again, you'll see some of that in upcoming presentations. But there are differences in consumers. People are all different. There are differences in terms of age as to who prefers menthol cigarettes, differences in terms of race, differences in terms of gender as to who prefers menthol cigarettes. So there are differences in folks. And as I think one of our speakers said, there is a variety of things that consumers look for in terms of taste and menthol is one factor,

but there is a lot of just overall tobacco character and blending to appeal to those taste preferences.

DR. SAMET: I think we will stick with one, and then we'll come back.

DR. WAKEFIELD: Can I just have one more?

DR. SAMET: No.

Neal, go ahead. Sorry.

DR. BENOWITZ: On one side that Dr. Lewis presented, you made the comment that both tar and menthol contribute to the strength of the taste. And in my research, and most of the research that I've ever seen, if you look at menthol cigarettes in general, they tend to have higher tar and higher nicotine deliveries than non-menthol cigarettes. So if menthol and tar both contribute to taste, why would it be that menthol cigarettes in general have higher tar deliveries than non-menthol cigarettes? It would seem to me that you'd be able to reduce the tar with menthol.

Can you explain first? Am I correct that, on average, menthol cigarettes have higher

tar deliveries? And if so, why is that the case, given the tradeoff on menthol versus tar?

DR. LEWIS: I'm not sure that that's true for us. I think what you'll see is a variety of tar levels. So we have mentholated cigarettes in the full flavor category, at the 15-tar level category, and we have menthol cigarettes all the way down to the low, low tar cigarette category. So we have menthol cigarettes across those categories, and consumers choose what they choose. But we don't just have menthol in the higher tar categories.

DR. BENOWITZ: Certainly, if you look at what people choose -- and my studies have been on people with the cigarettes that they choose to smoke -- the most widely consumed brands on average are menthol cigarettes of higher yields than non-menthol cigarettes. And our samples are just a few hundred. There's not thousands, but that's what we find. And most papers that I've seen show the same thing. On average, menthol cigarette smokers, as they are sampled in general

populations, those cigarettes have higher yields.

Can anyone else respond to that?

DR. LEWIS: Dr. True, do you want to respond to that?

DR. TRUE: I don’t know if I have a very thorough explanation to answer your question, but I would point out that Newport is full flavor, one of the higher tar cigarettes in the category and has relatively low level of menthol compared to most of the products on the market. So I’m not sure that that’s always the case.

I think that when you look at the specific taste characteristic, that your other design elements introduce into the product, most primarily coming from the tobacco blend, but then some of the adjustments on the construction parameters we talked about, that I think each company is looking to identify that menthol level that provides the balance that their consumers are looking for, going back to some of the ballots that we were talking about previously. Our ballots continue to highlight, is the balance

between tobacco taste and menthol to your liking? Is it optimized? And that's what they're driving, but it's strictly their subjective analysis. It's not anything quantitative.

DR. BENOWITZ: I just --

DR. SAMET: I think we'd really better -- I just want to make sure we get everybody in. So we'll come back for further discussion, depending on time.

DR. BENOWITZ: Okay. Well, I just want to respond to that specific comment.

DR. SAMET: Okay. Karen?

DR. CLANTON: Thank you. My question has to do with this interesting idea that menthol perception actually diminishes over time. I think it was stated the menthol gets trapped or fixed in the filter matrix, and at about one year, you've got quite a bit in there. So clearly, smoker preference is driving the engineering of the signature, menthol signature.

So is there any data or is there any mathematical relationship between when a cigarette

is sold after manufacture and the smoking perception, and whether or not people will throw that cigarette away, return it or make a complaint that their satisfaction preferences haven't been met?

So does that happen at six months, does it happen at a year, does it happen at two years? Is there a point after manufacture and sale of the cigarette, where a person says, "This isn't meeting my taste preference and I don't want this cigarette," or, "You need to fix it for me"?

DR. OGDEN: I believe the simple answer to your complex question is yes, and I haven't done a quantitative analysis of those kinds of information. But my understanding is that there is an equilibration period on the front end, as soon as they're freshly manufactured. And that may be days to a couple of weeks until it's fully equilibrated in the pack. And that would, of course, be dictated by how the menthol is applied.

Then I was the one who said on the back end -- and this is what I've been told by

cigarette developers. My understanding is that that does occur. I don't know the frequency. But as it goes towards a year -- and again, that may be how it's packaged and made, but there are some complaints that it tastes stale; it doesn't taste fresh. And that is driven by the fixation of menthol in the plasticizer. If you analyze it, it's still there, but it's not quite as much in the smoke. So there is a period of time, and I would say it's on the order of a year, where some consumers may start to notice a different perception.

DR. SAMET: I just want to go down the other --

DR. TRUE: Just briefly to add to that, I think one thing to clarify is that over that period of time, it's not that the menthol gets taken up by the filter. Over that period of the first couple of weeks after manufacture, everything inside that pack equilibrates as far as it's going to go. The question is the quality or the integrity of the cellophane pack seal, and

that's not perfect. And over time, things do change.

So what we've done from time to time, from a product quality point of view, not necessarily from a research point of view, is to understand at what point in time. So we do have some standards through our sales department for how long we want product to be on the shelf, and that can range anywhere from probably 9 to 15 months.

DR. SAMET: Questions?

Yes, Dr. Karol?

DR. KAROL: Just very quick, I guess maybe Jane, can you tell us what is the most popular mentholated tobacco product? And then subsequent to that, what's the menthol content in that cigarette?

DR. TRUE: Newport is the most popular mentholated cigarette, and as I showed you on those slides earlier, the current pack menthol level is .43 percent.

DR. CONNOLLY: Could you break that down

by age?

DR. TRUE: No, I can't.

DR. CONNOLLY: Could I break it down by age for you?

DR. SAMET: Thank you.

Let's see. Other questions? Dr. Clark?

DR. CLARK: I just have a statement. I like Dr. Wakefield's comment, and I'm looking forward to --

DR. SAMET: Do you have a clarifying question?

DR. CLARK: The clarifying question is the demographic variables associated with the characterization. So we saw, basically, a sterilized statistical characterization. And I'd like to make it clear that we need to see some of the epidemiologic, particularly by race, for the adult consumption. So I'm looking forward to those.

DR. SAMET: Okay. Other questions going around?

Let me ask one last question myself, and

then I think we'll take a break. And then we'll see if there are other questions.

I think this is to Dr. Lewis. You described a process at Philip Morris around product integrity, and said that menthol had passed through that process with regard to safety. And could you describe for us the criteria that you use to characterize something as safe?

DR. LEWIS: What we look at? Obviously, cigarettes are harmful. And so what we're looking at is to ensure that materials that we add do not increase the inherent risk associated with cigarettes. So they're no more harmful than what's currently in the marketplace.

DR. SAMET: So just to clarify, I'm now looking at the slides that you have on page 6, and just as you went through, you described a literature review process and an evaluation process that apparently ends in an overall determination. At least as you described menthol, you said it had been through this process and was approved. So if those were your words as you made

the presentation, then what I would like to know is, then, that implies to me that there are embedded criteria for determination of safety as menthol or any other ingredient moves through this process.

So if you could describe for us, perhaps in a little more detail, the nature of the process and then, what criteria you might use at the end to decide the safety.

DR. LEWIS: Sure. The product integrity process involves looking at the material itself. So when the material comes in, first of all, we look at what’s known in the literature. Does it have a generally recognized as safe status? What are the uses in other types of materials in foods? We’ll look at chemical analysis of that material. So we will look at head space analysis. If we heat it, what comes off? We will look at pyrolysis studies. If we pyrolyze it, does it convert into something else and what is that? And then we will add the material to cigarettes. And I’m just describing kind of the general process

here.

Once we add the material to cigarettes, then we'll do some smoke chemistry work, and we'll look at some of the potentially harmful constituents in cigarette smoke and see is there a change in those because of these ingredients that we have added. We'll do some in vitro work such as Ames mutagenicity assay, the cytotoxicity assay, and others to see is there any change in those responses or those measures. And then depending on the levels that we add, we may do in vivo tests, rat inhalation studies, to see if there's any differences, again with and without the ingredients.

But again, we rely extensively on the literature as well, and epidemiological studies, because that sort of trumps everything.

DR. SAMET: Sure. And then, so I understand from your presentation, that menthol has been through that process at Philip Morris?

DR. LEWIS: We've reviewed it extensively, yes, and it's been approved for use.

DR. SAMET: Okay. Good. Thank you.

I think we will stick with our 15-minute break. Committee members, remember that you should not be discussing the meeting topic during the breaks amongst yourself or with members of the audience. So 15 minutes will be 10:35. Thank you.

(Whereupon, a recess was taken.)

DR. SAMET: We have additional time for further clarifying questions. I wanted to make sure, before break, that we had given everybody a chance to ask their questions.

I think, Melanie, you still have a question lurking, and I suspect other committee members do as well.

So do you want to proceed with your question?

DR. WAKEFIELD: This is a question for Mr. True. I was interested in your chart of menthol levels of cigarettes over time and the recent increase, which is in response to reduced ignition propensity cigarettes. And I just wanted

to put a kind of an alternate potential interpretation to that and give you the opportunity to respond to it.

There’s been a suggestion, I think, from a number of industry documents I’ve seen, that perceived draw effort is reduced in menthol cigarettes compared with non-menthol cigarettes. And an alternative explanation for this -- the fact that you’ve increased menthol in cigarettes recently is to reduce the noticeability by smokers perhaps that the cigarettes are harder to draw on with the new reduced ignition propensity cigarettes.

Would you like to respond to that?

DR. TRUE: I’m not aware of any information that would link menthol levels to draw. That’s not something that I’m familiar with. It’s not something that we would do to design. I think if you simply understand the fact that there are changes in the burning properties of cigarette paper when we had to make a change to the fire-safe compliance cigarette paper, those

burning characteristics allowed there to be an increase in tar on some of the Lorillard brands when that took place. We wanted to maintain the tar levels. We didn't want them to increase. And so we needed to make changes to filter efficiency and/or ventilation.

In the case of Newport, by the way, a point that wasn't made earlier is Newport is one of the very few products that still has no filter ventilation. So we made changes to filter efficiency. The changes to filter efficiency may affect draw and likely would affect draw. And we need to design those and pick the right configuration of our filter tow to ensure that we can get the efficiency we're looking for and still get the right draw properties. But we don't adjust back for any draw characteristics by manipulating the menthol level.

DR. WAKEFIELD: I also wondered if the other companies had done this, too.

DR. OGDEN: A generic answer to your question is in the sensory attribute ratings that

we measure -- we talked a little bit earlier, result of another question -- draw characteristics is one of our attributes that we measure. But we measure that for both menthol and non menthol, and as I stand here today, I don’t know of any adjustment that’s made based on that.

I think you’ll also see in the coming presentation about the perception of nasal patency that has been published in the literature, and we’ll show you some data that exists. Menthol has the possibility of giving the perception of an increased openness of the airways, but in fact, there is no real increase. So there could be some perception of about the ability to draw. But I don’t have any specific data on that point.

DR. WAKEFIELD: Okay.

DR. LEWIS: I don’t really have anything to add there. I know that as far as draw with the ventilation, the level of ventilation is used to draw to manage draw so that cigarettes hit a level that is acceptable to consumers. There’s really no difference between menthol and non-menthol

cigarettes on that.

DR. SAMET: Karen?

MS. DELEEUW: This is a question for Dr. Ogden. In your presentation, you provided us information about the market share of menthol markets of your brands. But could you provide us information about the market share of menthol against non menthol over that same period?

DR. OGDEN: So your question is, could we simply break across that 11-year period total share of market of all RJR non menthol versus all RJR menthol?

MS. DELEEUW: Yes.

DR. OGDEN: Sure. I can’t give it to you today, but we can provide that. Sure.

DR. SAMET: Neal?

DR. BENOWITZ: I’ve got a quality control question. I know that tobacco varies from year to year and you’re trying to standardize it. And I’ve heard that, in the manufacturing process, nicotine in cigarettes is actually measured to make sure that it’s consistent. Do you do the

same quality control with menthol? Do you measure menthol levels? Do you adjust your process to make sure that every Camel or Kool or Newport or Salem has got exactly the same amount of menthol from year to year? Is this a quality control measurement that's done in manufacturing the cigarettes?

DR. OGDEN: Since you mentioned Camel and Kool as your first examples, I figured I'd start. I'm not aware that we do that. We have a design process. We have specifications for all the design parameters and ingredients, and that information certainly has been given to FDA in the other context. So we target a design specification. That does change sometimes with years. You saw some of that wandering of the graphs I showed you earlier, but I'm not aware of any routine measurement that goes on from a QA perspective.

From an R&D perspective, we use pack menthol. We have made some measurements of smoke menthol, but we generally don't rely on it because

they're highly correlated. So we don't have a wealth of data on manufacturing quality control points.

DR. TRUE: With respect to Newport and Lorillard brands, we exclusively spray menthol onto our tobacco with a solution that I described earlier. As far as quality control, we're monitoring the spray application rate, and it's necessary to allow the equilibration time. So there is no in-process check until we get to the pack menthol, which is after it's fully packed.

DR. BENOWITZ: So are you measuring menthol in the pack, and then using that to adjust the manufacturing process?

DR. TRUE: If over time we're finding that the levels -- but we haven't really had the need to do that. But that is what we do. We spray it on. We allow it to equilibrate. The cigarettes are made. They're packed. Pack menthols are measured.

With respect to your nicotine monitoring, I would like to just point out that, at least for

1 Lorillard, we do have some monitoring in our
2 primary process, the front-end process for the
3 nicotine level, just for informational purposes so
4 we can ensure that the blending that we're doing
5 at the specific grades that take place as one crop
6 year runs out and we have to transition to the
7 next one, that we're maintaining as consistent as
8 possible a nicotine level as we can.
9 DR. SAMET: Jack?
10 DR. HENNINGFIELD: I'd like to just go
11 back to my request for understanding the different
12 tests and measures because when I asked this, the
13 answers that I got really weren't just the simple
14 thing I was looking for. What are the tests?
15 What are the questions? Are they the same across
16 companies? One representative mentioned that
17 harshness seems to have nothing to do with
18 menthol. In the Lorillard document, it talks
19 about evaluating harshness as a function of
20 menthol level.
21 So I'd like to know what are all the
22 things you use to base your decisions as to how

much menthol you put in the cigarettes. You've shown us data over time, sometimes by brand. So that shows that you're making decisions as to how much menthol you're putting in, whether they're trace menthol cigarettes or characterized menthol cigarettes. And I think it's really important to know what the basis for that decision making is. And taste just seems to be a euphemism. Consumer preference seems to be a euphemism. It looks like it has to do with harshness, attractiveness, cooling, and who knows what else.

Is that something you can give us today or that you have to come back another time?

DR. LEWIS: I have two comments. One, I just want to reiterate that Philip Morris USA does not add menthol to its non-menthol cigarettes. So we don't have the trace levels. The lowest levels I believe we have are about .3 to .4 milligrams per cigarette.

When we look at consumers, we look at factors of liking and strength, and you're going to hear more about that in our marketing

presentation. So what I would encourage you to do is hear that presentation and see if you still have additional questions, and if so, maybe we can address them there.

DR. HENNINGFIELD: So you have a liking scale and a strength scale?

DR. LEWIS: Yes, we do.

DR. HENNINGFIELD: Thank you.

DR. SAMET: Patricia?

DR. NEZ HENDERSON: Just a quick question for Dr. Lewis. In terms of the synthetic menthol that is used, is there degradation similar to natural menthol?

DR. LEWIS: I’m not sure that I know very much about that. I know that we look -- we check for purity to ensure that there is a certain purity level of what we use, and that will range between 97 and 99 percent. So I’m not sure that I understand your question. They’re very similar materials. They’re primarily l-menthol.

DR. NEZ HENDERSON: Okay. So the degradation, as it’s burning off or as it’s being

consumed, it's the same, basically?

DR. LEWIS: Okay. I misunderstood your question. When menthol transfers into smoke, it transfers as l-menthol. It does not degrade. It's volatile.

DR. NEZ HENDERSON: Okay.

DR. LEWIS: And when the heat hits it in the rod, it transfers as l-menthol to smoke.

DR. NEZ HENDERSON: Okay.

DR. SAMET: Greg?

DR. CONNOLLY: Dr. Ogden, can I ask you a couple questions? On Chart 16, it's a presentation of the Kool data, and I'm looking at a pack of Kools here, called Kool Flow and Kool Groove. And you have one line for the brand family, but within the product descriptors, they argue that the bold and upbeat Kool Groove, you can be expressive. But with the Kool Flow, it's smooth and laid back and expressive. Is there a difference in menthol content between those two brands?

DR. OGDEN: Can you allow me to get some

backup material?

DR. CONNOLLY: Okay. Then I'll ask you a second question while you're doing that.

DR. SAMET: Why don't you let him --

DR. CONNOLLY: It's a similarly related question on the Camel family.

DR. OGDEN: I may be able to answer your question. I'll just see if I have any of that information with me. I apologize. I don't see any information here on the Flow and Groove stuff.

DR. CONNOLLY: Maybe you could supply it to the committee at the next meeting.

Then on the Camel signature brand, it states on the Frost, Camel Signature Frost is extremely cooling with a crisp, clean taste. Now, on Camel No. 9, it states with just a touch of menthol. And I have to go back in and clarify that.

Do you have the levels of menthol for the Camel Signature Frost and for the Camel No. 9?

DR. OGDEN: I believe it's true that we no longer make Camel Signature Frost. I'm quite

confident of that. The 9s, we do still make. I don’t have that information in front of me.

DR. CONNOLLY: But could we get that data as a committee?

DR. OGDEN: Sure.

DR. CONNOLLY: Okay. So we break down the brand family by character.

Now, for the Lorillard representative, may I ask you a question, sir?

DR. OGDEN: If I could follow up with that, all of the current styles that we make, that information has been submitted to FDA in the ingredients.

DR. CONNOLLY: Okay. But could I assume you vary the menthol level within brand families, depending upon a target within that brand family?

DR. OGDEN: Target meaning the particular style of cigarette?

DR. CONNOLLY: Let’s assume demographic by age.

DR. OGDEN: No.

DR. CONNOLLY: You don’t?

DR. OGDEN: There are a number of styles within a family ranging all across the tar range, and those tar numbers vary for the design reasons that we've already talked about.

DR. CONNOLLY: Just one question and I'll stop, Jon. I just want to read from the result section of the Kreslake article that you referenced. It did have a chart in it, but the results, conclusion, "Newport maintained a lower level of menthol during the 1970s and early '80s, and Newport's competitors attribute its historical success among younger adults to its lower menthol content."

It didn't conclude that there was an increase. Those were numbers without confidence intervals, without significance testing. All that was making was observations. But when I go back and I look at the SAMHSA data for the year 2002 and year 2003, I looked at that among 12- and 17-year age groups, Newport comprises 20 percent of the 12- and 17-year age groups, while only 7 percent of 26 and older. And that's true in --

DR. SAMET: Greg, are you leading up to a clarifying question?

DR. CONNOLLY: Yes. The question is, why is your brand lower and more popular with 12- and 17-year-olds than a Kool brand, which only has 1 percent of market among 12- and 17-year-olds, which has twice the amount of menthol?

DR. TRUE: We don’t poll. We don’t look.

DR. CONNOLLY: You don’t know why?

DR. TRUE: We don’t look. We have no idea.

DR. CONNOLLY: You have no idea why your brand is so popular with teens?

DR. SAMET: Okay. So this is quick and clarifying questions.

DR. CONNOLLY: Thank you.

DR. SAMET: And actually, other questions from the -- yes?

DR. BAUER: I would just point out that in the Philip Morris document, Table 1.3 lists all the menthol levels.

DR. CONNOLLY: And if you go through the

lists, you'll see the Newport levels are about one-half the levels of Kool. They're about medium between the levels of menthol. And they parallel use rates among 12- and 17-year-olds in the SAMHSA data, which I find interesting and I think you may find that very interesting, also.

DR. SAMET: Other clarifying questions?

Yes. Dr. Clark?

DR. CLARK: Dr. Lewis, you mentioned that menthol is in smoke, is not affected by the pyrolysis. But others have found that the pyrolysis of menthol at high temperatures results in the formation of carcinogenic polycyclic aromatic hydrocarbons. I don't understand your comments about the effect of pyrolysis on menthol and those other findings.

DR. LEWIS: Yes. There was a C-14 labeling study done a good number of years ago of menthol in cigarette smoke, and I believe that reference is in the materials. And that's the materials that we're relying on. We looked at menthol in smoke and saw that essentially 99

1 percent of the l-menthol transferred as is.
2 DR. CLARK: So does that mean that
3 there's some disagreement in the field about
4 pyrolysis of menthol at the temperature of burning
5 tobacco?
6 DR. LEWIS: Yes, I guess there is. And I
7 think you'd have to look at the studies and look
8 at the science and see how those studies were
9 conducted.
10 DR. SAMET: Maybe just in follow-up then,
11 if I understand, you described -- and remember,
12 I'm just an epidemiologist -- that preservation of
13 C-14 mass labeling is what you described. But
14 that would be regardless of any chemical
15 transformations, if I understand your comment.
16 DR. LEWIS: I don't --
17 DR. SAMET: I'm just trying to clarify
18 the basis of your response to Dr. Clark.
19 DR. LEWIS: I'm sorry. I don't know the
20 particular details of that study. I think that
21 reference is in the materials, so I'd advise you
22 to look at the -- there may be more information in

the submission and look at that particular reference to understand the study that was done.

DR. SAMET: Okay. Dan, can you clarify?

DR. HECK: I do know the answer to the question, if it’s appropriate for me to try to answer.

DR. SAMET: Yes. Please.

DR. HECK: I think the early study that Dr. Clark was referring to is the Schmeltz and Schlotzhauer study of 1968, that was pyrolysis in a laboratory oven under a stream of nitrogen, not under conditions of burning cigarette. That study by the methods of the day, which included like paper chromatography, I think, identified benzo(a)pyrene as a pyrolysis product.

The subsequent studies with radio-labeled fade studies in actual cigarettes did not see that at all, and there have been about -- well, both radio-label as well as chemical analysis, I’d say about four to six studies since then by modern methods that demonstrated, quite clearly in my view, that the transfer of menthol in actual

cigarettes is 99, 99 plus percent intact as the apparent molecule.

DR. SAMET: Thank you.

I have, Dr. Ogden, one last question for you. If you could go back one slide, and in this you were describing menthol and non-menthol cigarettes. The bullet about -- can be directly added to provide a fresh taste or brighten the flavor -- can you elaborate on that?

Is that actually done in some of your products, and ideas about if you do that -- can you describe concentration or give us some idea about how this is -- how often this is done?

DR. OGDEN: Sure. Yes, I can.

Reynolds does add menthol to some of its non-menthol styles at the trace level definition that I gave you earlier, which we’ve defined for process purposes as 50 parts per million or less. Reynolds adds menthol at levels below 50 PPM, generally quite a bit below 50 PPM, to approximately 50 of its non-menthol brand styles.

DR. SAMET: Okay. Thank you.

DR. OGDEN: You're welcome.

DR. SAMET: I think Neal, last question here.

DR. BENOWITZ: A follow-up about the pyrolysis issue. You were talking about milligram amounts of menthol, so if you transfer 99 percent unchanged, that's fine. But if you have 1 percent of menthol at milligram amounts, and if that's being pyrolyzed to benzo(a)pyrene, which is carcinogenic in microgram amounts or less, that's not reassuring to me.

So how do we know that that 1 percent is not being pyrolyzed to carcinogens?

DR. LEWIS: I think the way that I would look at that is I would go back to this toxicological evaluation process that I described, and on the break, we discussed this. With what we do with that process is, we make data-driven decisions. So when there are data in the literature, we rely on those. If there are not data available, we generate those data. So menthol may not have gone through all of those

steps, but there’s a lot of information about menthol.

If you look at the epidemiology between menthol and non-menthol cigarette smokers, you don’t see a difference in disease risk, which I think in end is the final answer. That’s really, in the end, what it comes down to and what matters.

DR. BENOWITZ: And can I just ask if the company has data? In the C-14 studies, did anyone look for C-14 benzo(a)pyrene?

DR. LEWIS: Dr. Benowitz, I don’t know all the details of that study, but it’s published, so we could provide it.

DR. SAMET: Dan, please?

DR. HECK: Neal, to your question, both the C-14 studies -- and there were either two and possibly three, I think heard recently, although I’m not familiar with the third -- and subsequent work with chemical analysis of smoke by, I think, Philip Morris and others, looking at benzo(a)pyrene and other Hoffman-lists

1 constituents, specifically in the smoke of, in
2 some cases, identical cigarettes differing only in
3 menthol, in other cases a less well-matched --in
4 several instances -- and I'm recalling it with
5 R.J. Reynolds' work.
6 I believe I recall it correctly --
7 benzo(a)pyrene and the other pyrolysis products
8 reported by the 1968 early work were actually
9 lower in the menthol cigarette than in the non
10 menthol. I don't recall whether the Carbon-14
11 label studies, which did look for benzo(a)pyrene -
12 - I'm thinking they may not have -- those were
13 done in the late '70s. But the subsequent
14 chemical analysis work -- there has been no
15 indications of elevations in benzo(a)pyrene.
16 DR. SAMET: Greg?
17 DR. CONNOLLY: Post-adoption of the New
18 York standard, there was a study looking at
19 emissions under, I think, it was ISO conditions
20 for five brand families. The sample size was
21 small. I'll grant you that. But what did pop on
22 that study was that the Newport brand did show a

significant increase in gas-phase carcinogens. This was right after the New York adoption. Now, maybe when you adjusted menthol content, you were looking at trying to correct that problem. But there was a significant increase, and it was isoprene and two other gas-phase carcinogens. And it was because it was a lower burn temperature --

DR. SAMET: And your clarifying question, Greg?

DR. CONNOLLY: I'm just trying to add to what Dan is, in trying to respond to his question, and the fact that Newport now has subsequently adjusted menthol. But we have to look at menthol on a per-milligram basis in its contribution because it is such a large constituent and that, yes, if some does pyrolyze, it's going to have to effect the entire amount of smoke emission. Now, I don't know if that relates to exposure but emission. I'm done.

DR. SAMET: Okay. I think we're going to move on. Again, remember, we have time for further discussion at the day's end. But to keep

us roughly on track -- and we're doing well -- we'll move on to the industry presentations on clinical effects of menthol.

I guess, Dr. Ogden, you're leading off.

DR. OGDEN: Thank you, Mr. Chairman.

Good morning, ladies and gentlemen. I'd like to lead off the next of the five general areas of questions that the FDA asked us as industry representatives to address today, and that is the issue of clinical effects of menthol.

From RJR's perspective, we have data and studies on point in two areas, smoking behavior and sensory evaluation. And it's my pleasure to go through some of those data here this morning.

So my review, I will review RJR studies that have been conducted on sensory evaluation and consumer acceptance. I also will look at human smoking behavior studies and yield in use. I will make the caveat that particularly in our smoking behavior studies, we have biomarker data as well, but I will not cover that in the context of this presentation. I will cover that resulting from

the same studies in the context of the next presentation in the next section.

I will also talk about sensory evaluation and improvement of products that is fundamentally the same that is done in other consumer product goods companies. Some of those issues came out in the discussion in the clarifying questions to the previous session. And our studies show either equivalent or reduced smoking intensity and exposure for menthol cigarettes.

In general, R.J. Reynolds does not study a direct comparison of menthol and non-menthol smokers. However, there are data available from several unpublished RJR studies that can provide information on this comparison. And I will review four types of those studies, again, in the sensory arena, both sensory evaluation and consumer acceptance, which are generally two types of what I would call sensory studies, the smoking behavior, and the yield in use which is a measure of mouth level exposure to smoke.

In the sensory area -- and there are four

types of studies that Reynolds has conducted -- I've categorized them in these four ways, the benchmarking and product improvement, fundamental research, product maintenance, and specification tolerance.

The benchmarking and product improvement types of studies are used to determine if design changes impact the sensory characteristics or improve acceptance. And I'll show you some of the attributes of those ballots that we've already talked about earlier today.

In the more fundamental area, we look at the relationship between some design parameters and perception. In the product maintenance area, we determine the impact of perhaps ingredient and material changes on smoke perception. One example of that, which I will cite as well, is the product maintenance that was required to maintain acceptance when the move to fire-standard compliance cigarette paper became prominent over recent years.

Then a fourth example in the

specification tolerance, we look at the manufacturing variability of the process and try to establish tolerances for ensuring that there's not a consumer-noticeable difference with manufacturing variability.

This is some information that we talked about earlier. But we do measure menthol and non-menthol cigarettes using sensory attribute ballots, and they are completed by the smokers. In fact, the majority of attributes on these sensory ballots are common to both menthol and non-menthol cigarettes. I give you some examples of that. I don't show you examples of the actual ballots, but those are available. We've referred to those. Those will be in our production of documents later in the summer.

But the draw of the cigarette, tobacco flavor, papery, woody, bittersweet, later draw, and various after tastes. There are some menthol-specific attributes, but we only evaluate those in cigarettes marketed as menthol cigarettes, the minty flavor, cooling sensation, medicinal flavor,

and overall balance between tobacco flavor and menthol.

As I described earlier in response to a question, the sensory evaluation program at Reynolds over at least my tenure there, over 25 years, has used this quantitative descriptive analysis tool, in which a trained panel of smokers basically defines the ballots. So these are terms that they define. There’s also a backup definition of those terms that is on the ballot that they have defined as well. So these are not industry terms. Whether other companies use same or similar terms, I don’t know. But these are the internal ballots that were developed by, what I would call our expert smoking panel.

In benchmarking and product improvement-types of studies, this is the type of research that’s common, as far as I know, to most consumer product goods companies. Basically, we measure our product acceptance relative to our competition. We use a standardized methodology in order to track changes over time.

We use two specific product improvement protocols. One, we term sensory evaluation and another, we term consumer acceptance. In sensory evaluation, we use a trained panel of adult tobacco consumers. We complete a test ballot. It does profile the product’s taste characteristics in much the way I described earlier. My understanding of the sensory world is that it’s not good to bad. It’s basically a numerical scale low to high, because what may be low to one consumer could be preferred. Something high to another consumer could be preferred. So you just try to rate it more in absolute terms rather than relative terms.

This ballot does not give an acceptance measure because it is a fairly small sample size. We would use a consumer acceptance test, which would be a much larger sample size, if we wanted to infer an overall acceptance for a particular type of product.

In the consumer acceptance test, the basic difference is we use large pools of adult

tobacco consumers, and this does again provide product rating characteristics. And I'll show you some examples of how we use these tools in product development on the next slide.

Product development, as Reynolds has practiced it, is an iterative process. That means you try something, you learn something, you try another. It's back and forth. So this is a way that we try to benchmark the performance of a specific Reynolds product relative to competition. The sensory evaluation studies are conducted to evaluate prototypes that are designed to address any deficiencies.

So, for example, in a benchmarking type of study, we may get information that one of our brand styles is deficient in some way to a competitive brand style. We would attempt to make product design modifications to address that. So those could then go back to a sensory evaluation study, again, a smaller panel, more of a trained panel to see if we're making improvements in the acceptance scores.

Then any potential improvements that come out of that first smaller-scale study would then be evaluated, perhaps further, in a consumer acceptance study. And then, assuming there was improvement in consumer acceptance for our style against its historical benchmark, or perhaps against competition, that particular improvement may be scheduled for implementation.

In the fundamental research area, in the product development and improvement, one way that we would use these tools would be to assess the perceptual impact of an ingredient or material change. And there’s some examples of those. One is if a material becomes no longer available, and we require a substitute. Another one is if there becomes a lower-cost alternative available. We would evaluate it to make sure there’s no differences perceived to the consumer. And the third one, we’ve already covered several times, perhaps regulatory changes in the example of fire-standard compliant cigarette paper. There would be some evaluation done to assess performance of

post-FSC versus pre-FSC.

Hopefully, it’s obvious. The goal of this type of work is to ensure that there is no or minimal perceptual difference after the change. Adult tobacco consumers, like all consumers, develop certain taste preferences and characteristics. So they are obviously buying our brand because they prefer it. We would like not to change that, unless we are trying to improve it based on a deficiency-type of measurement. And these types of tools could use one or both of the sensory evaluation or the consumer acceptance methodology.

We have done fundamental research on menthol perception. Some of our studies include the perception of menthol in clean air at various levels. And the reason I emphasize clean air is this is using olfactometry, which is basically a way of generating a small amount of pure chemical in clean air. It’s not cigarette smoke, so this is a menthol-specific study. I referred to this earlier, also in comments to clarifying questions.

1 That results of that study showed that
2 menthol leads to the perception of an increase in
3 nasal airway openness, but in fact, there is no
4 actual change and there is possibly even some
5 minor constriction. In fact, we've done two
6 studies. In one study, it showed no change, and a
7 second study, it did show a statistically
8 significant reduction in openness of the airways.
9 Those results are very consistent with the
10 published scientific literature that we reviewed
11 in our written comments and have been discussed
12 earlier.
13 We have done two studies that I'm aware
14 of, looking at menthol and nicotine irritation,
15 where cigarettes were designed specifically at
16 combinations of menthol and nicotine to evaluate
17 the irritation potential of menthol versus
18 nicotine. The results show that higher menthol
19 levels are not perceived as soothing, but rather,
20 they're perceived as irritating. And nicotine is
21 less of a driver of irritation.
22 This is work that dates back into the

early ‘80s, and I will say the ingoing hypothesis of the study was not this. The hypothesis was that nicotine would be more irritating than menthol. The first study showed it the other way around, that menthol levels were not soothing, but in fact, were more irritating. So a second larger study was then planned and conducted that confirmed the earlier results. So menthol contributes more than nicotine does to the perceptual characteristics, and it is perceived as an irritant.

There’s another type of study that uses sensory endpoints that is termed “just noticeable difference” or a JND study. I’ve given you one example on the bottom of the slide of a publication in that area that basically, we have used it to set tolerances for manufacturing variability. So if you look at the pack menthol, it gauges, using the sensory tools, the level of menthol change that would be required before a certain percentage of the smoking population would notice a difference. So in our studies, we’ve

used 10 percent, so it's a fairly sensitive test. So what kind of change would you have to have before 10 percent of the pool of smokers would be able to rate that as different? That amount of change in pack menthol varies with the tar level but generally, on the order of .1 to .3 percent.

I'll now move to the smoking behavior studies. These are types of studies in general that have been conducted by Reynolds for 25 years or so. They are used for product development, most especially for our tobacco heating cigarettes, first Premier in the late '80s and now Eclipse, these cigarettes that primarily heat but don't burn tobacco.

They are typically crossover studies where test subjects would come in, all adult, all regular, usual smokers that would come in and test on their usual brand, and then they would switch to a test product. In some cases, we would follow those for generally one to two weeks. In some cases -- and I'll show you examples -- we've done a couple of long-term studies of smokers on their

usual brand where there was no switching.

Our smoking behavior studies include measures of consumption, product attribute ratings and smoking behavior. Those are the attributes that I thought were relevant to this particular section of the agenda, so I will cover those. There are other measures in these studies on biomarkers, as I said. I will cover those in a subsequent presentation on biomarkers.

Here’s a brief description of the six studies that we found that could be analyzed for menthol and non-menthol comparisons. There’s an appendix in the presentation. If you have the printed copy, that gives a little more detail. This hopefully would be helpful in allowing you to match up these studies with our written comments and our subsequent production of documents to FDA.

But basically, there are six studies. You can see the time range, generally the late ‘90s. I’ll just briefly go through some of the acronyms, but the first study, for example, looked at the time-of-day effect on carboxyhemoglobin.

The products studied were a tobacco-burning usual brand. On the right-hand column, you can see the number of subjects. As I said, these are generally small studies on the order of generally two, three dozen subjects, in some cases smaller. These were not specifically designed to examine menthol, but as we've looked through our data, as usual brand smokers come into our study, we can characterize them or certainly split them. And we've done these post-hoc analyses specifically to address TPSAC's question.

So I won't read through all of them, but you can see there is menthol, non-menthol comparison. There are six studies, and I'll show you briefly the top-line results of those studies in a moment. Let me tell you about the other type of study first. I would also give you information on yield-in-use studies. These collect information about mouth-level exposure to nicotine and tar for specific cigarette brands with ad-lib smoking, which means these are not laboratory experiments.

I’ve put a bit more detail in this presentation because I was specifically asked about these type of studies at the end of March meeting of TPSAC. But we include generally 30 to 50 subjects for each brand style. We collect cigarette butts after the smoker smokes them for one full 24-hour period. We extract those, measure tar and nicotine in the butt. We relate that to the amount of smoke that came out of the cigarette through a calibration mechanism that’s performed in the laboratory using multiple machine smoking regimens. And we get certain endpoints from these types of studies that include butt length, cigarette consumption and nicotine and tar yields, both per cigarette and per day, since we collected butts for a full 24-hour period.

There are three studies that have been conducted each of the last three years. The internal working project description is National Yield in Use 1, 2, and 3. You can see that the products studies, the first was one 26 brand styles, both Reynolds and, in many cases, Reynolds

and competition. The second study, we looked at specifically the new FSC brand styles or the fire-standard compliant. And then in a later study, 12 brand styles. A fairly large number of subjects, you can see on the order of 1,000 subjects each, again were broken against brand styles. There's generally 30 to 50 subjects per each brand style.

We'll now go into the results of those two types of studies. In fact, there are some similar -- the reason I broke them up that way, I described the studies first because there's some of the outcomes that can be combined for results purposes. So if we look at cigarette consumption, overall, the studies show no difference or reduced consumption for menthol versus non-menthol cigarette smoking.

In the smoking behavior studies, we've seen significantly fewer menthol cigarettes smoked in one study with full flavor usual brand smokers. We've also seen it in black usual brand smokers. We've also seen it in Eclipse usual brand smokers. In the yield-in-use study, we've seen

1 significantly fewer cigarettes smoked per day for
2 menthol light smokers. And I'm pointing out only
3 the differences here. The bottom line, no other
4 significant differences in cigarette consumption
5 were observed between menthol and non menthol in
6 any of the studies that I've reviewed here today.
7 If we look at menthol and product
8 attributes, overall, few differences in attribute
9 ratings of menthol and non-menthol smokers when
10 smoking their usual brands. Menthol full flavor
11 subjects rated their usual brand cigarettes as
12 being more harsh than non-menthol full flavor
13 subjects. The acceptance rating was higher for
14 Eclipse non-menthol subjects than it was for
15 menthol subjects. And no other significant
16 differences in product attribute ratings were
17 observed between menthol and non menthol in any of
18 the studies reviewed.
19 If we look at smoking behavior, overall
20 results show no difference or less intense puffing
21 for menthol smokers than for non-menthol smokers.
22 We've seen significantly lower total puffing time

among menthol usual brand subjects. We've seen significantly shorter time lit and smolder time. These are terms that we define based on the smoking topography experiment. We've seen again shorter time lit and smolder time for menthol. The results there are consistent for both the tobacco burning cigarette, and also, the Eclipse tobacco heating cigarette. Overall, no other significant differences in smoking behavior observed between menthol and non menthol in any of our smoking behavior studies.

If we switch to yield in use, overall results show no difference or reduced yield in use for menthol versus non menthol. If we compare yield in use and the Cambridge filter method yield using regression models, we see no significant effect of menthol, although the trend line -- and I'll show you an example in a moment -- for menthol smokers, falls below the trend line or the regression line for non-menthol smokers across the range of tar yields.

If we use the regression models that

1 include terms for other cigarette design factors,
2 they also show no significant effect of menthol.
3 In one study, we have a head-to-head comparison of
4 Pall Mall menthol and non-menthol styles, which
5 they are the same cigarette with the inclusion of
6 menthol. There is a nominal, but not
7 statistically significant, reduction in yield in
8 use for the menthol style. We saw a similar
9 nonsignificant reduction in cigarette consumption
10 observed for the Pall Mall menthol.
11 Continuing the yield in use, if we look
12 at menthol and non-menthol cigarettes in a two-way
13 analysis of variance model that includes other
14 factors, including tar category, we found a
15 significantly lower tar and nicotine yield in use
16 per cigarette and per day for menthol. Light
17 cigarettes showed similar significant differences
18 with an additional significant reduction in
19 consumption for light menthol cigarettes.
20 Those differences were not statistically
21 significant for a similar comparison of the full
22 flavor or the higher tar cigarettes.

Menthol was not significantly related to cigarette butt length in a regression model that included cigarette length and tar category. And pack menthol is strongly negatively correlated with Cambridge filter method yield, which means that pack menthol is not associated with an increase in yield in use.

I'll give you one example. Some people process information better visually. So this is a chart that shows yield-in-use tar on the left axis in milligrams per day. So it's calculated per cigarette, and then multiplied by the number of cigarettes that they smoked that day. You can see across the tar range across the bottom, the number of points on a vertical line are the number of smokers of tar category that corresponds to that number. The blue line is the regression line for the non-menthol cigarettes. The green line is the regression line for the menthol cigarettes. And you can see again not statistically significant, but the trend line does fall below.

So key takeaways, Reynolds conducts

sensory evaluation and improvements of its products, in fundamentally the same ways as do other consumer product goods companies. Menthol vapor, in our studies, has been determined to be irritating, not soothing. And menthol does not increase the openness of the nasal airways.

If we look at effects of menthol on smoking behavior, there are no significant differences or reduced consumption of cigarettes for menthol smokers. There are few attribute differences between menthol and non-menthol smokers when they rate their usual brands. There is no significant difference or reduced puffing intensity for menthol smokers, no significant difference or reduced yield in use for menthol smokers.

So in conclusion, smoking behavior and smoke exposure studies conducted by Reynolds are consistent with the published scientific literature. Studies show that for menthol versus non-menthol smokers, there’s equivalent or reduced measures of smoking intensity and equivalent or

reduced measures of mouth-level exposure. Based on smoking topography and smoke exposure, there's no basis to regulate menthol differently than non-menthol cigarettes. Thank you.

DR. TRUE: With respect to Lorillard's product research and Lorillard's product development, the TPSAC has asked for information from the industry on several topics related to some specific clinical effects of menthol. Lorillard has not conducted research in most of the areas in which the TPSAC expressed interest. We simply seek a balance between tobacco and menthol taste, and we use our internal expert panel to design cigarettes to match consumer preference.

I want to highlight that as we saw earlier, our products have been defined and developed decades ago with few or no changes in menthol levels over that time. And this was far prior to the maturity of some of these areas of study of chemosensory receptor sciences and neurobiology, with receptor sciences not coming

1 into much more prominence until 2002.
2 For traditional cigarettes, the process
3 of identifying opportunities for developing new
4 products is not highly technical, and I understand
5 there have been a number of questions seeking to
6 understand a little bit more specificity and
7 engineering design and so forth that might be very
8 typical of other industries, but not this one.
9 Cigarette taste is highly subjective and
10 cannot be precisely engineered. Lorillard focuses
11 on taste and overall adult consumer acceptability
12 in developing their products. And as I mentioned
13 earlier, our unique cigarette taste is defined
14 primarily by special select grades of tobacco.
15 The menthol in Lorillard brands is simply
16 intended to complement the tobacco taste
17 signature, plain and simple. Lorillard's product
18 developers try to maintain a particular balance
19 between the tobacco taste and menthol taste for
20 each distinct brand. So for Newport, for example,
21 with the most premium grades of tobacco that we
22 have, that perfect balance is defined by the

consumer in terms of the back and forth between our product developers, who have the ability to understand which design parameters of a cigarette can affect the various aspects of taste.

The assertions that Lorillard's use of menthol is intended to create a specific or measurable physiological response in smokers is not correct. Our product development staff are very, very capable staff that typically have degrees in general chemistry or flavor chemistry or something of the like. They are not familiar with these emerging fields of chemosensory receptors, et cetera, and neurobiology.

Our expert smokers have defined terms, as many others have, to assist them in expressing taste characteristics of cigarettes being evaluated. As you can imagine, when you're tasting food, when you're tasting any type of consumer product, what one person calls one word or one flavor, someone might sense as something different. So it's critically important for these expert taste panelists to develop their

vocabulary. And “harshness” is a classic example of one word that has been developed as part of that vocabulary.

But I would like to make perfectly clear, relative to product developers, is that the word harshness does not have a connotation of good or bad. It is a characteristic of what they taste in the cigarette, and each brand, whether it’s a non-menthol brand or a menthol brand -- if you look at the competitive products in the marketplace, there’s a whole wide spectrum of harshness that might be perceived in these, and it’s not attributable to one type of cigarette. And clearly, that menthol has not been used to cover that up.

The primary factors, as I mentioned during the Q&A earlier, that affect cigarette harshness are clearly the tobacco blend itself, the moisture -- nothing is more harsh than a stale and dry cigarette -- and filter ventilation which tends to bring in a lot of, again, air that’s not as moist as from the cigarette product. Menthol

is clearly not used to decrease or mask the harshness of the cigarette.

In terms of some internal Lorillard research that we’ve conducted over the last 12 to 18 months, we’ve submitted some detailed summaries in the written materials on some fairly complicated studies. All of these studies are in vitro, so that is a qualifier. But we were trying to get a little bit of a sense on whether or not menthol inhibits the metabolism of nicotine, PAHs, nitrosamines.

Well, we studied a little bit further menthol cytotoxicity and genotoxicity on human lung cells, A-549 cells. And what we found generally in all of these studies is that the levels of menthol delivered by a typical menthol cigarette affect neither the metabolism of the nicotine, PAHs, nitrosamines, nor the cytotoxicity or the genotoxicity.

In one special measure, we found that menthol significantly inhibited an index of double-strand DNA breaks induced by cigarette

1 smoke exposure.
2 If we turn to look at the perception of
3 risk amongst the smoking population, this chart
4 shows the percentage of menthol versus non-menthol
5 smokers who believe smoking presents a great risk
6 of harm. And as you can see, especially in recent
7 years, menthol smokers actually perceive that
8 smoking presents a greater risk of harm. And if
9 you look at that same information from a
10 demographic perspective, in fact, the Hispanic and
11 African American would be the purple and green
12 lines on top, perceive smoking presents a great
13 risk of harm at significantly higher rates than
14 the general population and from white smokers.
15 Smokers do not perceive that menthol
16 cigarettes are less hazardous than non-menthol
17 cigarettes. In a recent publication that I'd like
18 to turn your attention to, Wackowski of 2010, 30
19 percent of menthol smokers believe that menthol
20 cigarettes were more risky than non-menthol
21 cigarettes, and only 2.4 percent of menthol
22 smokers thought menthol cigarettes were less risky

1 than menthol cigarettes.
2 So to summarize, our section on clinical
3 effects of menthol, we recognize the interest that
4 the TPSAC has in understanding the potential
5 effect of menthol on public health. We believe
6 very strongly, these interests are best addressed
7 by appropriate research that seeks to directly
8 measure the exposures and effects resulting from
9 smoking. And we believe biomarker studies of
10 exposure and putative risk provide the most
11 relevant information to inform such risks. And
12 the industry will provide more information in the
13 next section on the biomarkers. Thank you.
14 DR. LEWIS: There’s a lot of information
15 that I’d like to cover here in this particular
16 topic, just due to the combination of topics that
17 were included in the meeting notice. I will do so
18 at a fairly high level just due to time
19 constraints, but I will spend a little bit more
20 time on the mechanistic studies. We’ve got a
21 couple of Philip Morris studies there that were
22 funded by Philip Morris USA that are still to be

published. I'll spend a little bit more time with detail on those.

One of the topics in this section was on dependence and cessation together because it's kind of hard to separate the two. They're very closely linked in the public literature.

I do refer you to our submission, both the March submission and the June submission for more complete information on these topics that I will cover at sort of a high level.

We've spent many, many years trying to reduce the risk of cigarettes. And as a result of that program to do that, we've developed quite a bit of expertise and experience in a variety of scientific areas. We have analytical laboratories and analytical chemists that have experience with validating methods and standardizing methods. Our laboratories are ISO-17025 accredited.

We have a statistics group that assists us with sampling plans, design of experiments. When we get ready to do a clinical study, we'll do a statistical analysis plan. That group will

assist us with that. And then when the data's been generated and results are available, they will help us do the analysis and determine where the statistically significant findings are from those studies.

We've done an extensive review of our ingredients resulting in many, many studies in peer-reviewed publications. We've shared some of that information with public health agencies such as the CDC. We've shared information on menthol with the CDC in 2001.

There's a number of peer-reviewed publications that have resulted from this work. Our scientists attend scientific conferences and meetings so that they can engage with other scientists and get feedback on the work and the science that we're conducting. And we do careful reviews of the published literature. We don't just read it. We analyze it. We analyze the data so that we can inform our thinking by science that's going on out in other organizations.

Let me move now to the mechanistic

studies on sensory effects. There have been literally hundreds of studies on menthol, per se. In airways, those studies have focused on local anesthetic effects, cooling sensation, desensitization to irritation, or desensitization to other molecules in the presence of menthol to irritation and pain.

A local anesthetic effect is known to be something that blocks sodium ion movement through sodium ion channels and neurons. And that blockage of sodium ion movement thereby blocks action potentials responsible for nerve conduction. And we did a study here, and again, this was all in the context of reduced harm. And what we found is when we tried to significantly reduce the risk of our cigarettes is that, typically, we end up with a taste deficit. Our consumers give us feedback when there’s a taste deficit. So we tried to develop additional sensory tools to understand that at a more sophisticated level.

So there was a study done on the local

anesthetic effect. There were cells from a trigeminal nerve from a rat that was in a culture, and there was a current applied to those cells. And you can see here in the black curve, the resulting action potential and then the cell recovering from that flow of sodium ions.

Menthol was added to the culture. The current was applied. You can see the red curve that resulted. The action potential again occurred. And then the cells were removed to a new culture absent menthol. Current was applied and there was a recovery curve there in blue. So the action potential occurred in each and every case, regardless of the presence of menthol.

Now, there is a slight effect in the hyperpolarization region of this curve here, which has not been studied and is not understood. But from this experiment, I think you can see that menthol, per se, menthol itself does not block the current induced neuronal action potentials. So it does not have a local anesthetic effect.

Menthol is known to interact with a TRPM8

receptor causing a cooling sensation. There are two different receptors here. It’s also known to act with a different receptor, the TRPA1 receptor, to cause a feeling of irritation and pain. So it has a couple different actions that can occur.

There is information in the literature from cell culture studies again on menthol, per se, looking at that TRPA1 channel to see, does menthol desensitize the TRPA1 channel to the irritating effects of compounds such as nicotine. And there have been results that show that again nicotine per se, menthol per se -- this is not done in smoke, but that nicotine and menthol do compete at the TRPA1 channel.

In that first experiment, it was found that menthol therefore can desensitize the TRPA1 channel to the irritating effects of nicotine. But what the authors further found was that there are other compounds such as mustard oil that can irreversibly bind the TRPA1 channel and prevent either nicotine or menthol from interacting with that receptor. There are compounds such as

1 acrolein, which are found in cigarette smoke, that
2 also can irreversibly bind the TRPA1 channel.
3 So the evidence from this study, then, is
4 that, yes, menthol and nicotine do compete. But
5 there are other compounds that can irreversibly
6 bind this channel. And in cigarette smoke, keep
7 in mind there are probably 5,000 chemicals in
8 cigarette smoke, many of which are reactive. And
9 acrolein is certainly present there.
10 Moving on to clinical studies, a little
11 bit more representative of the human situation,
12 there was a study done in the literature by the
13 Dessirier team that looked at pretreatment of the
14 tongue with menthol to see if that desensitized
15 the tongue to the irritating effects of nicotine.
16 And they did find that that occurred.
17 Philip Morris USA funded a study with the
18 Renner Group -- and this work is to be
19 published -- where they used an olfactometer to
20 apply materials to the nose. Now, there’s more
21 information in your submission. I’m not going to
22 go through all of that here, but what they looked

at was two different levels of nicotine and four different levels of menthol, one of which was a placebo. So that is in your submission.

The experiment is shown here. An olfactometer was used to deliver pulses of nicotine to the nose of participants. Every one minute, a one-second pulse was applied. Participants were calibrated first with the CO2 and to describe a level of burning pain, and they were told that that was to be 100. And then they were asked to rate the level of burning pain from these nicotine pulses relative to that response to CO2, which was defined as 100.

So for 15 pulses, there was nicotine here that was pulsed in, and respondents rated the level of burning pain. And you can see the increase and then the subsequent decrease. At 16 minutes, a background tonic stimulus of menthol was applied to the nose, and participants continued to rate the level of burning pain due to nicotine. And you can see those responses here.

When you compare that to the placebo

experiment, in the placebo experiment at 16 minutes, a placebo was applied as a background tonic stimulant rather than menthol. Those data are shown here with the red stars. And you see again the increase in the burning pain levels and then the subsequent decrease. And upon statistical analysis, there was no statistically significant difference between the placebo experiment and the menthol experiment in the level of burning pain experienced by the participants from the nicotine.

So in this particular clinical study, menthol itself, menthol per se does not desensitize the nose to pain caused by nicotine. And the menthol here was applied at the level that participants described as a cooling level. Remember, there were different levels of menthol. This particular experiment I showed you was at the level participants described as a cooling level. So there was no desensitization.

So then to summarize, these mechanistic studies with menthol per se, it did not have a

local anesthetic effect in the studies that have been done. In the desensitization, there was some desensitization with just menthol and just nicotine, but in the presence of other compounds, that reaction was blocked. And then in the clinical studies, the tongue showed a desensitization effect, but the nose did not, in the studies that were done.

Importantly, none of these studies have been done with smoke really due to the complexity of the airway system. There’s multiple integrated receptors in the airway system, and smoke is a very complex mixture to work with.

Moving on to health effects, when you start thinking about topics such as health effects, dependence, cessation and disease risk in general, there are a lot of factors to consider, important variables to consider. When you’re trying to determine if there’s an effect of something like menthol and you look at a population of people, menthol versus non-menthol smokers, typically, you find those are not

homogenous populations. There are differences in those populations, and I list a few of the factors here, things like race, gender, age, socioeconomic status.

So you really need to consider those confounding variables if you're trying to sort of tease out an effect of menthol. What is the effect of menthol itself on those two populations in terms of disease risk? You have to look at those confounding variables and make sure you've accounted for those.

This chart I showed earlier, this is again a summary of the epidemiological data that I'm relying on to draw conclusions related to health effects. And so I'm just going to summarize now, and there's quite a bit more information in the submission. But just from time constraints, I'm just going to summarize the health effects information.

Menthol cigarettes do not result in increased toxicity in nonclinical toxicity testing compared with non-menthol cigarettes. Smoking

menthol cigarettes produces no consistent effect on human puffing and inhalation behavior. And in the submission, there are some studies cited there that specifically looked at human puffing, inhalation studies, and found no differences between the two groups.

You're going to see an upcoming presentation in the biomarkers topic from Dr. Mohamadi Sarkar, and he's going to talk to you about the Philip Morris USA Total Exposure Study. And he's going to share quite a bit of data with you and results and findings. And in analysis of that data, we saw no differences in biomarkers of exposure between menthol and non-menthol smokers, no differences in biomarkers of potential harm between menthol and non-menthol smokers. Dr. Sarkar will show you this was quite a large study with many, many smokers.

We've also done an analysis of the metabolism of nicotine and NNK in the Total Exposure Study, and Dr. Sarkar will discuss that. And we found no differences in the metabolism

results between menthol and non-menthol smokers. Then I've reviewed the epidemiological data that suggests there's no effect of menthol on smoking-related disease risk.

So overall, our analysis of the published scientific literature and internal studies concludes that menthol added to cigarettes does not increase inherent health risk of smoking.

Moving on now to dependence and cessation, a widely used test to measure dependence is the Fagerstrom Test for Nicotine Dependence. Within that test, there are two questions that are also relied on pretty heavily, cigarettes per day and time to first cigarette. There's a lot of information published in the literature about this. But also, and Dr. Sarkar will cover this for you, there was no statistically significant effect of menthol status on the Fagerstrom Test for Nicotine Dependence in the Total Exposure Study. We did administer that test and found no differences between menthol and non-menthol smokers.

1 There are four other studies cited here
2 that use the Fagerstrom Test for Nicotine
3 Dependence that found no difference between
4 menthol and non-menthol smokers. And there are
5 other measures besides the Fagerstrom Test for
6 Nicotine Dependence such as the Diagnostics
7 Statistics Manual, DSM-IV criteria for dependence;
8 the Fagerstrom Tolerance Questionnaire, which is a
9 broader questionnaire than the Fagerstrom Test for
10 Nicotine Dependence; the Nicotine Dependence
11 Syndrome Scale, the Minnesota Withdrawal Scale
12 Scores. Again, using these tools, these measures,
13 there was determined to be no difference between
14 menthol and non menthol smokers.
15 Recently, the US Department of Health and
16 Human Services provided a 2008 update on their
17 clinical practice guidelines for treating tobacco
18 use and dependence, and this was quite a
19 comprehensive piece of work. A number of factors
20 were looked at. A number of populations and
21 subpopulations were considered as they looked at
22 cessation treatments and the effectiveness of

those treatments. And in that update, there was no mention of menthol in relation to dependence, cessation, or relapse.

There are also literature available on intervention studies where folks have come into the clinic seeking treatment for cessation, and there are nine published smoking cessation treatment studies that show no difference between menthol and non-menthol smokers on cessation outcomes.

Then finally, looking at large national surveys, these surveys have a lot of people in them, from 1,500 people to 19,000 people, and there’s some results cited here. I’m not going to read through all of them, but I’ll give you just a minute to look at them. But these are quite large studies, and they’ve generally found no difference in cessation outcomes between menthol and non-menthol smokers.

So then overall, to summarize here on clinical effects, based on evaluation of published and unpublished information about menthol, we

conclude that menthol, per se, has airway sensory effects. It does cooling and irritation. It can cause irritation or pain as well as cooling. In desensitization studies, it showed mixed results. If you have menthol and nicotine, you do see desensitization of nicotine from the menthol. But when other compounds are involved, that can block the TRPA1 channel.

Menthol added to cigarettes does not increase the health risk of smoking shown in nonclinical studies, clinical studies, epidemiological studies. Menthol does not increase cigarette dependence, and it does not affect smoking cessation.

I’m just going to show you -- that’s the end. Thank you.

DR. SAMET: Thank you. Thank you for the presentations.

I think we are very close to the lunch hour, and I think rather than starting questions now and interrupting, I think I’d prefer to have us ask clarifying questions in a block. So what

I’m going to suggest is that we break for lunch and reconvene at 1:00 p.m. here for the clarifying questions.

As a reminder to the committee members, you can eat your lunch, but there must be no discussion of the meeting topic during lunch, either amongst yourselves, with the press, or with any member of the audience. Thanks, and see you back here at 1:00. And take any personal belongings you may want with you at this time because the room will be locked.

(Whereupon, at 11:51 a.m., a luncheon recess was taken.)

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

DR. SAMET: Good afternoon. If everybody will take their seat, we'll go ahead and get started again. So we are now going to have a half hour for asking clarifying questions about the presentations that we heard on clinical effects of menthol. So again, this time, I'm going to start right. And let me ask how many of the panel have questions just to get a sense.

So let's make a pass. Pick your highest priority question. You're going to get one on the first pass. No disguised multiple choice-part questions that come as one.

So questions, John? Okay. Dr. Clark, Ursula, Cathy?

DR. BACKINGER: Yes, I had a question. This is for Dr. True. I think in your presentation -- and it was in several places -- you talked about internal expert smokers. And I don't know what an expert smoker is, so I would like some clarification on what is an expert smoker.

DR. TRUE: Okay. An expert smoker is typically a flavor chemist or other staff member in R&D that has a particular sensitivity to detect various flavors at the different levels. So it'd be like someone who can be able to taste wine and be able to give a very full descriptive characteristic of a wine versus someone that can just drink wine and say I like it. Our expert taste panelists, internally for cigarettes, are basically about the same type of thing.

DR. BACKINGER: These are assigned people that work for the company or from the outside?

DR. TRUE: Our internal expert panel are internal --

DR. BACKINGER: Employees.

DR. TRUE: -- employees within R&D, yes.

DR. CLANTON: My question goes to the entire panel and has to do with the various ideas of irritation and harshness and heat perception and cold perception. At least when I was in medical school, I learned that virtually all of those are fundamentally a part of the pain

pathway, those sensations. There may be different receptors, but ultimately, all of the sensations are about pain. And the other thing we learned about pain is that you can apply a painful stimulus or a noxious stimulus or an irritant stimulus that ultimately diminishes a second painful or noxious stimulus.

So on this idea of cross-desensitization, is there any data that you guys have looked at that looks at menthol's ability as an irritant that actually makes other irritants and noxious agents in tobacco smoke more tolerable? And if you do, let us know about that because there's certainly data looking at menthol desensitizing the effect of capsaicin, which is a pain stimulant. And we know that it does desensitize or cross-desensitize other painful stimuli. So what can you tell us about menthol and its ability to desensitize the pain response to nicotine or other potential noxious agents in cigarette smoke?

DR. LEWIS: I went through some fundamental studies that had been done in sort of

pure systems with menthol per se, or nicotine per se, or other irritants, but those types of studies have not been done in cigarette smoke just due to the complexity of that material. So I don't have -- I'm sorry?

DR. CLANTON: There's no data?

DR. LEWIS: There's no data. Right.

DR. SAMET: Other comments on that?

Dr. Clark?

DR. CLARK: Yes. I have a question to Dr. Lewis, similar to that question. The mechanistic studies that you cite have the administration of nicotine first, and subsequently with menthol. Are any studies when they're both administered concomitantly since that's -- the menthol is in the cigarette, so it's consumed at the same time and not sequentially?

DR. LEWIS: Yes, there's no data for that from this study. This study was not conducted that way.

DR. BENOWITZ: Yes. There's a question that I have that's something that I actually have

been trying to figure out in my own research for years, and it sounds like maybe someone has figured it out.

The comment was made that the concentrations of menthol that produce cytotoxicity in test systems are much lower than those that are seen in human smokers. My question is -- what is the level of menthol in the lung of human smokers? Because that’s the concentration that really affects epithelial cells and I’ve not been able to find any data on what that concentration is.

DR. LEWIS: Dr. Benowitz, we don’t have any data on that as well.

DR. BENOWITZ: Wouldn’t that be what you really need to have if you’re going to extrapolate from cytotoxicity studies in vitro to say that menthol’s not having cytotoxic effects in humans?

DR. LEWIS: I guess the way I would answer that is that the cytotoxic studies or the cytotoxicity studies are one set of studies, but what we look at is a total battery of studies.

And that’s one study that we look at, so there’s a total battery of studies. And you’ll see some work coming up from our Total Exposure Study and biomarkers of potential harm and then the epidemiological study. So we look at that total battery to assess menthol, not just one test.

DR. HECK: Just a comment, actually, in the spirit of Neal’s question as well. I know probably all the companies have really tried to get at that same very thing that you mentioned. I think your own estimates of menthol exposure were pretty accurate from one of your prior papers. We do have an idea of the systemic exposure from menthol smoking. It’s about 1 micromolar systemically.

But in terms of local concentration effects, I know there have been attempts to calculate or reasonably estimate those by fluid volumes and all kinds of things. And I don’t know that there is a satisfactory model to approximate that, but there’s no measured value that I’m aware of.

DR. SAMET: Melanie?

DR. WAKEFIELD: There’s lots of evidence from the product marketing literature that you can kind of change people’s sensory perception by giving them or by raising their expectancies of what they’re about to taste. You haven’t mentioned anything to do with psychological factors in sensory perception in your presentations. And I’m wondering whether some of the consumer testing that you do is blind to the brand.

So is the brand concealed or is it unconcealed? And when do you blind consumers to brands and when do you unblind them? That’s probably a question for all the companies.

DR. OGDEN: Reynolds does perform both blind and branded taste testing. Exactly why you would do one versus another, I may not be able to elaborate today. But you do have different findings when you want to test the absolute characteristics of a cigarette. We would often do it in an unblinded fashion.

When you overlay that with brand information, that does shift, and you do get -- I would guess in direct answer to your question, that psychological input so that things that may test A higher than B on a blind basis may, in fact, go B higher than A on a branded basis. And we do see that and have seen that for decades.

DR. SAMET: Dorothy?

I'm sorry. Dr. True?

DR. TRUE: I was just going to comment as well that for Lorillard, we do very little unblind testing. And most of what we do is blind testing in that occasionally, the unblind testing, of course, begins to introduce the expectation of brand loyalty is what we would normally expect. And getting into other psychological responses and everything else is not something that we look at, but the vast majority of ours are definitely blinded.

DR. SAMET: Dorothy?

DR. WAKEFIELD: And Philip Morris?

DR. LEWIS: We do do branded and

unbranded testing. So in some of the tests, the consumers know which brands they're smoking and sometimes they don't. It depends on whether we're trying to look just simply at the product and how it's perceived absent the brand or with the brand information. But again, we don't get into psychological tests as well. It really comes back to their taste preferences and their ratings of those brands.

DR. WAKEFIELD: And just to follow up, do you find that there is a great difference in the blinded versus unblinded testing?

DR. LEWIS: Yes, there can be. Brand does influence the results.

DR. SAMET: Dorothy?

DR. HATSUKAMI: Dr. Lewis, you can still stay up at the podium. Dr. Lewis, I'm going to ask you a question. So what you have presented in your presentation is that menthol does not increase cigarette dependence. And yet, in the tables that were provided by Altria, it seems like there is conflicting evidence as to whether

there's higher levels of dependence with menthol cigarettes versus non-menthol cigarettes. And I was particularly struck by your Table 7.2, in the materials that you had handed out to us, that there certainly are studies among the underage population that show that some of the underage smokers do have higher scores on some of the dependence measures.

So I was wondering if you can elaborate or comment on what you had said, which was that there was no evidence of cigarette dependence with menthol, and yet, some of your tables that you had presented, in the materials that you had sent, don't necessarily support that.

DR. SAMET: Are you ready? I was going to say you can take a little time but okay.

DR. LEWIS: There is a lot of detail in this submission that I didn't cover. What I would say in general with these studies is that again, it's very important to look at other confounding variables in these studies. And if you're trying to determine whether there's a menthol or non-

menthol effect, you have to take into consideration things like race and age. You will see race effects. You will see age effects. You will see effects due to socioeconomic status. But if you correct for those, typically, you're not going to find a menthol effect.

DR. SAMET: Jack?

DR. HENNINGFIELD: This is for all three of you. We are here because of the serious questions that have been raised about making and marketing menthol cigarettes with respect to public health. Any time you consider risk for almost any product or product feature, it's in the context of benefit. In this whole clinical section, every once in a while, one of you would allude to a potential benefit of menthol. But that wasn't clear, and I guess I'm wondering, are there any benefits of any sort that you could put forward to justify why menthol should be allowed in the cigarettes?

DR. SAMET: Jack, I think as a clarifying question, was your question, are there effects

demonstrated that might be construed as not adverse or beneficial in some extent?

DR. HENNINGFIELD: Well, any kind of benefit that would mitigate as we go --

DR. SAMET: Yes, why don’t we stop the question there, I think is the point, and if there are any effects that have been demonstrated that might be construed as nonadverse --

Yes. So Jack’s question, just rephrasing it, has the research demonstrated any effects of the presence of menthol that might be construed as beneficial? I think I assume you mean in the direction of potentially reducing the risk of the smoke mixture itself all together. Okay. That’s the question.

DR. HENNINGFIELD: Or dependence.

DR. SAMET: Or dependence.

DR. HENNINGFIELD: Any effect that could mitigate any of the health consequences that we’re talking about, that we’re concerned about, with respect to menthol.

DR. OGDEN: I’ll attempt to answer

1 Dr. Samet's clarification of the clarifying
2 question. In terms of not adverse events, I think
3 there are many. The smoking behavior literature,
4 both the published literature and the Reynolds'
5 studies that I showed you tend to show either no
6 effect of menthol or reduced consumption. The
7 same for smoking topography, either no effect or
8 reduced puffing volumes, puff time lit, et cetera.
9 You'll see in a subsequent presentation
10 on biomarkers that again, the same trend holds,
11 either no effect or in some cases, reduction of
12 menthol. In terms of benefit, as a consumer
13 product goods company, our attempt at Reynolds is
14 to make products that satisfy our consumers'
15 wants. And it's clear over the last several
16 decades that nearly 30 percent of the adult
17 smoking population prefers menthol. So that from
18 a marketing consumer product goods perspective, I
19 think that is a benefit. It's a strongly
20 established taste preference, and we try to meet
21 that preference.
22 DR. SAMET: Comments from anyone else?

DR. TRUE: I support very much Dr. Ogden's response, but one thing I did want to point out as well is that as you look at the complexity of a lot of these studies, when you start to look at much of the internal data, oftentimes there are some trends that aren't quite statistically significant which would show less of a health impact on menthol cigarettes relative to non-menthol cigarettes. We don't believe they've established a statistical significance, and so we don't tout them in a big way. But in general principles, it's important to understand that there could potentially be some benefits there.

DR. SAMET: Patricia?

DR. NEZ HENDERSON: This question goes to any of you that are in the back. The graph where it shows that Hispanic and African American menthol smokers perceive a greater risk of harm from smoking than white menthol smokers, since perception is a key component to the production of menthol cigarettes, what is your take that African Americans and Hispanic have a perception that it's

more dangerous for them? And I guess this could go towards the marketing question when marketing is discussed, and how is that being addressed by the industry?

DR. TRUE: In terms of the chart that we showed earlier, this was not internal company research. This was information taken from the NSDUH report, and we pulled that out just to highlight the fact that we could see a differentiating difference. There have been a number of discussions and potential allegations that ethnic groups have been targeted, and maybe targeted with messages, and left behind with the belief that menthol cigarettes may be less harmful. And so we felt like this data was compelling to show that, in fact, these ethnic groups were considerably and statistically considering this to be more harmful.

In terms of the marketing aspects, we'll have a section coming up on marketing. I think you can address those questions at that time.

DR. SAMET: Greg, this is your one

question?

DR. CONNOLLY: Yes, one question. I feel like I've been in the forest this morning, and I really can't see the bigger picture. I've been walking down different definitions and lexicon and terminology, and I'm not sure what we're comparing here. I think if we had drug companies here presenting on a drug, we'd have common lexicology and we could look at data and look at it much more clearly. And I would hope that as we evolve over time, that we have a lot of ability to interact better than just looking at one receptor and making these statements, so on and so forth.

I think Jack asked this question. When you look at smoking, my perception is you look at impact as an important variable, and that impact is related to nosio stimulation by nicotine. In Philip Morris research, it appears by menthol in certain cases. You look at irritation, which is not impact, but it's sort of a long-term more tingling affect. Then one looks at smoothness.

So we have three variables that in

looking at industry literature, it appears to be important to what makes cigarette important.

Am I getting closer to a bigger picture here? Anyone can respond.

DR. LEWIS: I don’t understand your question.

[Laughter.]

DR. SAMET: Well actually, then I was actually going to ask if you needed clarification of the clarifying question because I was a little puzzled, too. Try again.

DR. CONNOLLY: Let’s go back to the receptors. We have gustatory receptors on menthol, TS2Rs, affect the tongue. Documentation from Philip Morris would indicate that these are kind of important. They give us a minty flavor and a bitter flavor, but for overall experience, we’re more concerned with another group of receptors, TRPME, which is a smooth receptor. So it gives us coolness. Let’s call it analgesia, if we could. There are other receptors that give us irritation or impact, nosio receptors.

In looking at Philip Morris materials, in particular -- Lorillard, I'm still intrigued by your Alive with Pleasure campaign. I'm glad you adhered to the voluntary code. It seems that you're balancing chemosensory receptors that affect smoothness, impact, and irritation by varying dose of menthol. And I'm looking at the chart in one of your presentations where you very nicely show that. And I think R.J. Reynolds' stated results show higher menthol levels are not perceived as soothing bur irritating, which I take as irritating or impact.

So it hits the posterior pharynx, and maybe it sends some dopamine to the brain about something that's coming. It may be a cue. And then R.J. Reynolds said menthol contributes more than nicotine to perceptual characteristics. So I sort of got one picture from -- I was trying to tease it out from R.J. Reynolds and then a different picture from Philip Morris.

But I'm just trying to look at the forest here. And in looking at documents and what Jack

1 was saying, it appears the industry is balancing
2 impact on nosio receptors with irritation with
3 another set of receptors with feelings of coolness
4 or smoothness with another set of receptors. And
5 menthol is being altered to affect that. Now,
6 that's just my gut from listening and trying to
7 synthesize everything that's been this morning.
8 And I know Lorillard appears that they're not into
9 this area, but the other companies do seem. Is
10 that any more clarifying? Because I wish I was at
11 a Philip Morris meeting to get a better --
12 DR. SAMET: Okay. So I think you've --
13 DR. CONNOLLY: I'm done.
14 DR. LEWIS: I'm not sure it's any more
15 clear, but let me take a whack at it. Some of the
16 mechanistic studies that I described, we have
17 conventional cigarette product development, which
18 I described in the characterization talk, where we
19 have cigarettes with and without menthol that we
20 talk to consumers and we get feedback on taste and
21 strength of taste. And they tell us, "I like this
22 combination of flavors. I don't like this. It's

too strong. It’s not strong enough.” And that’s how we design conventional cigarettes. That’s the technology. As sophisticated as it is, that’s how we design cigarettes. And I think you heard a pretty consistent picture from the other folks.

In the context of reduced harm, what we’ve learned at Philip Morris USA is that when we dramatically change cigarettes -- we learned this the first time with our denicotinized cigarettes. We removed nicotine from those cigarettes, but we didn’t only remove nicotine. We also removed a lot of natural taste compounds in tobacco and aroma compounds. And we were not able to -- we created a sensory deficit for our consumers, and we were not able to make that up with our conventional techniques and our knowledge at the time.

We relearned that in our Accord program, our electrically heated cigarette smoking system. Again, a dramatically different system, dramatically different smoke with a pretty significant taste deficit for consumers, and we

1 were not able to make up that taste deficit. And
2 then we relearned it a third time with our carbon-
3 filtered cigarettes that were designed to try to
4 reduce harm, and, again, we created a taste
5 deficit that we couldn't come back with, with our
6 conventional techniques.
7 So what we've done is try to develop more
8 sophisticated sensory tools to use in the context
9 of these reduced risk products to try to
10 understand what's going on and understand what
11 consumers are telling us in order to compensate
12 for those taste deficits. But we don't use these
13 mechanistic studies in designing and developing
14 conventional cigarette products.
15 DR. CONNOLLY: This is just a clarifying
16 question because I am confused. I'm looking at a
17 project dart which describes your denicotinized
18 program, statement from 1988. And in it, you
19 state, "In addition to its pharmacological
20 effects, nicotine stimulates neural fibers called
21 fast-acting nosio receptors. Stimulation of these
22 fibers produces inhalation impact," which I

referenced earlier and I'm trying to differentiate impact from irritation from smoothness.

Apparently, menthol also stimulates these nosio receptors. Philip Morris in 1988, Bates No. 2031426437, in a chart where as you reduced your nicotine, you increased menthol and you measured impact. Now, I'm confused with what you just said. I'm very, very confused.

DR. LEWIS: That work was done earlier in the context of our denicotinized cigarette program. I didn't discuss that here today, and I'm really not prepared to go into a lot of detail. We did generate some documents. Those are available, and I think you're very familiar with those. So I'm still not sure I quite understand your question.

But we have found some methodological flaws with that work that was done quite a time ago, and so we don't -- I would be careful drawing conclusions from that work.

DR. SAMET: We'll have an opportunity, I think, for additional discussion.

1 The FDA, do you have questions? Corinne?
2 DR. HUSTEN: Yes, I have one clarifying
3 question for Dr. Ogden, particularly looking at
4 slides 18 and 20, where it was talking about no
5 significant differences in cigarette consumption
6 between menthol and non-cigarette smokers studies,
7 and then, basically no significant differences in
8 smoking behavior in menthol and non-menthol
9 smokers. So my question was whether these
10 analyses controlled for age, race, and gender, or
11 if it was just overall comparisons.
12 DR. OGDEN: Dr. Husten, can you again
13 refer me to which slides you're commenting?
14 DR. HUSTEN: Eighteen and 20. I had the
15 question about some other ones, but those were the
16 two that I think I really wasn't clear.
17 DR. OGDEN: Okay. Certainly, on slide
18 18, which shows findings from both human smoke and
19 behavior studies and yield-in-use studies, the
20 smoking behavior studies, to my knowledge, did not
21 attempt to make any correction for any of the
22 other variables that you mentioned because, as I

indicated, those were very small studies. The ones I charted there range from 5 menthol smokers to -- I think the maximum in one study was 51.

That information is in the appendix table, which I may not be able to read without my glasses, but there were definitely some imbalance in those other factors. The studies were not designed to balance those factors.

In the yield-in-use studies, which was also on slide 18 that you mentioned, I presented the regression modeling techniques. There was adjustments made there, and I pointed out the significant differences. Now, whether any of the specific factors you mentioned were adjusted for, I can’t answer as I stand here today, but if that would be helpful, we will research that information and get that to you.

DR. HUSTEN: I think that would be helpful because as your colleagues pointed out, there are quite a bit of differences in terms of these behaviors by these various factors of age, race, gender. So I think it would be helpful to

see adjusted analyses.

DR. SAMET: David?

DR. ASHLEY: My question was covered a little bit by Patricia already, and it is really for Dr. True. And it goes back to slide 9, which showed the difference between the different race/ethnicity groups who were concerned about smoking and the health effects of smoking. And it’s interesting to me that those groups that are more concerned about the health effects from smoking are the groups that smoke more menthol cigarettes. And I guess the question I have is kind of an extension of that, is whether there’s any indication that those people that were concerned about smoking have turned to menthol cigarettes instead of quitting.

DR. TRUE: I’m not familiar with any details in the studies that would indicate that that’s the case, and we certainly don’t have any information internally that would suggest that that’s the case.

DR. SAMET: Actually, Dr. True, I have

one simple, answerable question for you. You described ongoing research at Lorillard -- and I guess the same question to the other companies. Your intent to publish this in the peer-reviewed literature -- is that something you --

DR. TRUE: Absolutely. Yes. In the slide that I referred to, we’ve got probably two or three different studies, manuscripts in preparation that should be published shortly.

DR. SAMET: Okay. And do the other companies have research in the pipeline that you intend to publish in the peer-reviewed literature?

DR. LEWIS: Yes. We always have a pipeline of research coming out of our research center that we’re attempting to publish. We have publications in press, but then others on the way, certainly.

DR. OGDEN: We certainly have information as well that we intend to publish, not for the smaller smoking behavior studies. Many of those have not been published, and they’re older studies. There’s no intent to do that. The

biomarker studies, the larger one that I'll talk about coming up, there is an intent to do that. Certainly in the population effects area, we have three manuscripts. The drafts of those were submitted in our written comments, and those are in internal review now with the intention to be published.

DR. SAMET: Thank you.

Okay. Let me see. I know Jack has an interest in a follow-up question.

How many potential follow-up questions?

[Show of hands.]

DR. SAMET: So four. All right. Brief questions, please.

Jack?

DR. HENNINGFIELD: In all of your questions about acceptance and liking or whatever all you've been collecting, have any of your questions addressed the issue of what the panelists or menthol smokers [sic] would do if menthol smokers were not there? In other words, do you have any idea that if menthol cigarettes

were not available, that they would stop smoking?

DR. TRUE: As far as Lorillard consumer panels go, we’ve had pretty similar questionnaires for a long period of time, and we have not addressed that question at any point in time.

DR. LEWIS: We don’t have any information on that.

DR. OGDEN: For Reynolds, in our consumer acceptance test, we do have questions about intention to purchase. For example, we ask the question again on a scale from 1 to 5, ranging from definitely would buy these if they’re available to definitely would not buy them if they were available.

But specifically in answer to your question about the hypothetical if no menthol were available, we have no questionnaires or surveys that have been done historically with that question. We certainly anticipate there could be a number of unintended consequences, and we’ll be fully prepared to comment on those at a future time.

DR. HENNINGFIELD: So if I understand that, you have no concern that you would lose smokers if you stopped making menthol cigarettes? None of you?

DR. OGDEN: I don’t believe that’s what I said.

DR. SAMET: I think, Jack, we’ll move on. This is not clarifying.

So, we have Neal.

DR. BENOWITZ: I’m trying to figure out still how the currently marketed cigarettes sort of got there. And my question is, what kind of strategies do the tobacco companies use when you’re thinking about modifying a menthol level? How do you figure out for the next consumer test what to do? Are you trying to get cigarettes that are less harsh? I know what happens when you test them, but someone has to think, “Well, should I modify the menthol level in the next cigarette that I’m going to test.” And why would you do that? What are you trying to change in the cigarette?

I'm curious again about the harshness issue because, as we talked about before, many high-tar cigarettes are also high in menthol, or are the menthol characteristic cigarettes. And you would think that if menthol makes cigarettes more harsh and tar makes cigarettes more harsh, why would you have both together? So the question is really, what's your thinking when you manipulate menthol in a cigarette for the next test. What things do you think about? I'm not sure who would answer that question.

DR. TRUE: Well, first of all, for Lorillard, we don't conduct a consumer panel for the purposes of trying to figure out how we want to adjust menthol in a future product. The large majority of our consumer panels are what I'm going to call competitive monitoring just to understand if the Newport franchise, for example, continues to rate the product similarly as they did in the past against the competition. And we monitor that for a long time.

We have a very conservative history in

terms of making changes to our product, like I highlighted earlier, not only with menthol levels and everything else. About the only time that we have to make changes to our product are when we have to go through raw material supply changes, which might impact a little bit of the paper porosity or some other taste characteristics that come along with it.

So in terms of specifically what's our thought process, our thought process is to leave our products alone.

DR. BENOWITZ: Could the other manufacturers comment on that?

DR. LEWIS: You're going to hear more of this from the marketing presentation, but what we're trying to do is with adult cigarette smokers is influence brand choice. So for the adult cigarette smoker population, we would prefer them to choose our brands over competitor brands, so when there's a competitor brand that's being particularly successful, we try to -- we'll compare new brands. We may come up with new ideas

and say, “Does it really compete effectively with that brand?”

So we may talk to consumers that are Newport smokers, for example, and offer them something else and say, “How do you rate this brand compared to that brand?” But again, it’s trying to influence brand choice within that smoker population.

DR. OGDEN: I would certainly agree with Dr. Lewis that Reynolds’ approach is to compete for adult cigarette smokers among our competition. I think I described reasonably well in my presentation on sort of the iterative process of design and product development.

If we go back and draw that together with an answer to a previous clarifying question about the sort of the consumer acceptance scales and few, if any, of these -- there’s not a right answer. There’s not a good or bad scale because what may be overly smooth to one consumer may be overly harsh to another.

I’ll give you just some examples in minty

flavor. We ask about the minty flavor on a scale of 1 to 7, to none to a lot. And then we ask, was the amount of minty flavor entirely too much, just right, not enough, not nearly enough.

We have similar questions for the amount of menthol that you tasted. This is on the menthol-specific ballot. And then going down to overall tobacco flavor, is it low? Is it high? And then ask them to rate whether it’s entirely too much all the way down to not nearly enough.

So when we approach design or redesign, it’s really in response to marketplace trends. If we find, as I showed you on some graphs, some of our brands are losing market share to competition, they’re switching to another menthol style, then we try to understand that with a sensory evaluation test. What’s the balance of all of these attributes that might explain that? And then based on some science, but a lot of art, in cigarette design, which Reynolds in combination with former Brown and Williamson has nearly 80 years of experience, they use their collective

product development expertise to say, “Are there ways we can make blend changes or perhaps menthol changes to satisfy a smaller market share that may be all of a sudden choosing a competitor’s product?”

DR. SAMET: Mark?

DR. CLANTON: My question is for Dr. Lewis, and it takes us back to page 4 of your presentation. It has to do with the mechanistic studies for desensitization. The first slide sort of parses the effect of pain versus cooling between the TRPM8 receptor versus the TRPA1 receptor. You made it clear that there is some cross-reactivity at the TRPA1 receptor between menthol and nicotine, and there’s some desensitization because of that.

What do you know about or what can you tell us about nicotine and its interaction with the TRPM8 receptor, since that’s principally the menthol receptor? Do we know anything about what happens when nicotine -- does nicotine competitively inhibit itself with that receptor,

or does it react with it? And then, what happens as a result of nicotine and menthol at the menthol receptor?

DR. LEWIS: We've not studied that interaction, the TRPM8 receptor specifically, and I don't believe it's addressed in the literature, either.

DR. SAMET: Dorothy?

Dr. HATSUKAMI: I'm going to ask a question that I asked before because I don't think it was necessarily addressed in this, your presentation, Dr. Lewis. And I don't mean to pick on you, but what I had asked before was whether Altria or any of the companies conduct abuse liability studies in animals, looking at whether the combination of menthol plus nicotine results in quicker acquisition of self-administration, slower extinction, and so on, compared to administering nicotine alone.

So especially in light of the fact that you had mentioned that your company's very concerned about introducing a product that's more

harmful, I wanted to know if you do, in your portfolio, actually do abuse liability testing as well. And also, in light of the fact that you raised this whole issue of confounding factors, this might be a good way to address some of those confounding factors. So anyway, that's my question.

DR. LEWIS: We have not done that kind of research that you're describing.

DR. HATSUKAMI: And why is that?

DR. LEWIS: What we look at is the battery of tests that I've described in menthol and non-menthol cigarettes. We look at what's available in the literature in terms of epidemiology. We've got a lot of clinical data that you're going to see, exposure data, biomarkers of potential harm. And so, there's a lot of literature that says that menthol cigarettes are not more harmful than non-menthol cigarettes. So we've not really pursued that further as you're suggesting.

DR. SAMET: Okay. Greg, the last

question?

DR. CONNOLLY: Jane, don't go anywhere. You're back in the snowstorm in Boston.

I want to get back to Jack's question about benefit because I think it was an intriguing question. And I asked this question at the last meeting, and I sort of got a mixed response.

But it's my understanding as prior to the formation of Altria, there was a group called Philip Morris Companies of which Philip Morris USA and Philip Morris International were part of, and that they entered the Japanese market, which was a charcoal market, and charcoal extracts menthol. So it was really a non-menthol market, 1980, '82, '83. And that Philip Morris entered the market and to have benefited, it would appear their intent was to market menthol cigarettes -- and I can read from a series of quotes -- to younger women. And I'll provide you the Bates numbers, if you want to look at those.

Then based on research by Osaki, smoking of menthol among adolescent girls rose from '96 to

2000 from 17 percent to 48 percent. And Japanese traditionally, women didn't smoke. And from 1991 to 2004, 20 to 20, our female --

DR. SAMET: Greg, is there a clarifying question lurking here?

DR. CONNOLLY: Well, the question is, did the entry of Philip Morris with menthol cigarettes into a nonsmoking market in Japan that had an increase, did that benefit Philip Morris' cigarette sales by bringing menthol cigarettes into Japan? Was that a benefit to the Philip Morris companies? Was the introduction of menthol cigarettes into Japan a benefit to the Philip Morris company sales?

DR. SAMET: Remember, this question is not directed at clinical effects, per se.

DR. CONNOLLY: This is marketing on initiation. This relates directly to initiation.

DR. SAMET: We do have marketing presentations to come.

DR. CONNOLLY: Okay. Well, I saw a discussion of initiation in this section.

DR. LEWIS: And I would just further add that that was Philip Morris International and not Philip Morris USA, and we're here today discussing Philip Morris USA.

DR. SAMET: Okay. Thank you for your responses to our clear, clear clarifying questions. We're going to move on to the next segment of industry presentations on biomarkers of disease risk.

DR. SARKAR: Good afternoon. My name is Mohamadi Sarkar, and I am here from Altria Client Services speaking on behalf of Philip Morris USA.

What I'm going to do today is share with you some of our analyses. You heard Dr. Lewis mention several times about the Total Exposure Study which was a large multi-center cross-sectional observational study. And I'm going to show you some of the key findings from this study. I'm not going to go into any details because a lot of the work has been published in peer-reviewed literature, as well as presentations have been made at scientific meetings. Some of the

committee members might even remember the SRT presentations that we made earlier this year.

Just to give you kind of an overview of what I'm going to talk about, I'm going to start my presentation with giving you a little bit of background of why we did this analysis, describe to you some of the elements of the study design and how we conducted the study. And then I'm going to share my analysis and the findings, comparing the adult menthol and non-menthol cigarette smokers as it relates to the demographics, but focusing on the biomarkers of exposure, our analysis of the metabolism as well as the biomarkers of potential harm, and the nicotine dependence scores. And I'm going to end with some summary and concluding remarks.

So there have been several studies reported in literature which have used various measures of smoke exposure and trying to assess differences between menthol and non-menthol smokers. Most of these studies have found no differences, and there is few that report some

differences. So that kind of prompted us to use the Total Exposure Study to try to answer the question whether menthol smokers have any different exposure.

Furthermore, there is also research that has indicated that menthol might inhibit the metabolism of the TSNA, the nitrosamine NNK and/or nicotine. And that has led to the hypothesis that this metabolic inhibition may be responsible for some disease risk and/or smoking behavior. So we chose to use the Total Exposure Study data to shed some light on this topic as well.

So this study that I’m referring to is the Total Exposure Study -- and I’m going to abbreviate as the TES for the rest of this talk -- was conducted by Philip Morris USA and this describes the elements of the study design. It was a stratified multi-center cross-sectional observational study. And you can see from the map that participants were recruited from across 31 states and 39 investigative sites, and there were more than 3,500 adult smokers and more than 1,000

nonsmokers were recruited in the study.

This is just kind of a snapshot of some of the study-conduct-related topics. The participants were generally healthy adult males and females, age verified to be 21 years or older. The study was approved by IRB and conducted in accordance with GCP.

The smokers were all daily smokers of at least one commercially available cigarette at that time, smoking for at least a period of a year. And blood and urine measurements were collected on the samples that were collected from the participants. And also, I want you to know that the number of cigarettes smoked per day was determined based on the cigarette butts returned over the 24-hour period that the urine collection was conducted. And the time frame of the study conduct was around 2002, 2003 time period.

This slide shows the objectives of the study. The primary objectives were to answer the broader question of estimating exposure as well as to investigate the relationship between machine-

measured tar delivery and exposure. And the secondary objectives are also listed underneath, and you can read through that.

The biomarkers of exposure that we measured in this study are listed, and they were broadly selected to capture the gas phase and the particulate phase. Now, the biomarkers were either the smoke constituent itself or its metabolite. I'm going to show you data from carboxyhemoglobin, nicotine which we measure as nicotine and five of its metabolites expressed as a molar-sum equivalent -- and I'm going to abbreviate that as nicotine equivalent or NE -- as well as the NNK metabolite, total NNAL. All these biomarkers have been well established and have extensively been used in literature.

Now, this slide is a list of some of the biomarkers of potential harm, primarily representative of the mechanistic pathways related to smoking diseases. In addition, the participants also completed a multi-item questionnaire. The adult smokers particularly

1 were asked to fill in the information about the
2 smoking history, as well as the Fagerstrom Test
3 for Nicotine Dependence was administered to the
4 smokers. We also measured smoking topography in
5 this study using this hand-held device that's
6 shown here to estimate the puffing parameters.
7 So the results starting off with the
8 demographic characteristics between the two
9 groups, this slide shows the demographic
10 characteristics of the menthol smokers compared to
11 the non-menthol smokers. And of note is the
12 sample size of menthol smokers was more than 1,000
13 and non menthol was about 2,200 or more.
14 The demographic characteristics are
15 generally representative of what's been observed
16 in literature regarding the two groups of smokers,
17 the distribution of women versus men in this
18 group. But also we observed as has been often
19 reported in literature that there is a
20 preponderance of African Americans in the menthol
21 smokers, but the majority of menthol smokers are
22 white.

Also, it’s been known that menthol smokers tend to smoke fewer cigarettes than non-menthol smokers, and as Dr. Benowitz has pointed out a couple times, that they tend to prefer to smoke a higher tar-yield cigarette.

Due to the racial disparity, I’m showing you the data broken down by race. So if you look at the demographic characteristics by race, I want to point out that this is perhaps, to the best of my knowledge, one of the largest studies which has a large enough group of non-menthol African American smokers with such an extensive array of biomarkers measured in the study.

Once again, you see the same distribution. That it’s very well reported that African Americans consistently smoke fewer cigarettes compared to the whites and the preference for a higher tar-yield cigarette in the African American group of menthol smokers compared to the non-menthol smokers.

So noticing the heterogeneity between the groups when we did the analysis of the biomarkers,

we took that into consideration in the statistical models.

This slide shows the biomarkers of exposure. What I'm showing here is the daily excretion of nicotine equivalence and the NNK metabolite, total NNAL, as well as serum cotinine and carboxyhemoglobin. And this is the mean and the standard deviation for the two groups. And as you notice that the daily excretion is lower in the menthol group compared to the non-menthol group, and these values were on a univariate comparison by Wilcoxon Rank-Sum Test. Some tests were lower, significantly lower, but when you adjust for the different confounders, there is overall no statistically difference between the two groups for the biomarkers of exposure.

This slide breaks down the exposure biomarkers by race. Once again, you see the nicotine and total NNAL daily excretion, along with the carboxyhemoglobin and the serum cotinine data. Of note is that is as you saw in the demographics slide, the African Americans smoke

1 far fewer cigarettes than the white, and that is
2 reflected in the overall exposure is lower in
3 African Americans compared to the white. After we
4 do a statistical analysis adjusting for all the
5 confounders, once again, there is no difference
6 between menthol and non-menthol smokers,
7 regardless of how you break down by race in whites
8 or in African Americans.
9 But I want you to note that the serum
10 cotinine levels in the African American menthol
11 smokers tended to be higher just directionally,
12 but there were no statistically significant
13 difference, which perhaps has led to some of the
14 hypothesis about menthol probably inhibiting. So
15 we further investigated that in looking at the
16 metabolite ratios.
17 When we investigated the metabolite
18 ratios -- before I show you the results, let me
19 just very briefly kind of walk you through how we
20 set up the different metabolite ratios. So this
21 first slide shows the major metabolic pathways for
22 nicotine, and I just wanted you to note that

nicotine is predominantly metabolized to cotinine. This audience is probably very familiar with this.

So what we did was we looked at the ratio of the trans-hydroxycotinine to cotinine as a measure of the oxidated metabolic pathway. Since we had measured nicotine in all five of these metabolites, we also measured the ratios of the glucuronide conjugate to the unconjugated compound. So the ratios of the oxidated metabolism and three ratios of the Phase 2 conjugating metabolism with the idea that if at all there was any inhibition of this metabolic pathway, then these ratios would be smaller.

This slide illustrates the metabolism of NNK. And you note that NNK undergoes this carbonyl reduction to form NNAL and subsequently gets detoxified by these glucuronide conjugates. So we looked at the ratio of the glucuronide conjugate to the unconjugated metabolite with the understanding that if there was any inhibition, then these ratios would be smaller because if there was any inhibition of this glucuronide

pathway, the ratio would be smaller. And the hypothesis has been that this inhibition of this glucuronide conjugate would shunt the pathways towards metabolically active compounds like the alpha hydroxylation. But note that there are many other pathways for these NNK and NNAL to be eliminated.

So just to give you a recap, the way we set up the metabolite ratios with the Phase 1 was the ratio of the trans-hydroxycotinine to cotinine. And we looked at the three Phase 2 glucuronidation ratios for nicotine and then the NNK, the NNAL glucuronide ratio. All of these were set up as glucuronide conjugate or unconjugated.

What did we find? So what I’m showing you is the results from the statistical models, so these are the LS-means for the oxidated metabolite ratio comparing the menthol versus the non-menthol groups. And there is no indication of any inhibition by menthol, and there were no statistically significant differences between the

1 two groups.
2 If you then also look at the glucuronide
3 conjugates, the first three rows are the
4 glucuronide conjugates of nicotine and the last
5 row is the NNAL glucuronide ratio. And if you
6 compare between menthol and non menthol, there is
7 no indication of reduction of this ratio. There
8 are no statistically significant differences
9 between the two groups, suggesting that there is
10 no inhibition of any of these metabolic pathways
11 by menthol.
12 Due to the interest and the attention
13 that has been paid in literature around the
14 potential of inhibition around African Americans,
15 we also looked at this breakdown by race. And we
16 find some interesting observations, not unlike
17 what has been reported in literature, that African
18 Americans on the whole tend to metabolize slower
19 than whites and there is no menthol effect.
20 Matter of fact, if you look at the differences
21 between menthol and non menthol for both these
22 subgroups, there is no statistically significant

difference as it relates to the oxidated metabolism.

Furthermore, then we look at the glucuronide conjugate ratios. There is no inhibition of any of these glucuronidation pathways, either for the nicotine metabolite or for the NNAL conjugated metabolites, regardless of when we look at the whites or African Americans, but you note that for all these metabolite ratios, African Americans tend to be slower metabolizers than whites. And there is no menthol-related effect. There’s clearly a race effect. And that could be one of the reasons why the literature seems to point towards menthol because there is not a large enough group of non-menthol smokers that are investigated in literature.

What I’m showing you in this slide is the ANCOVA model, the statistical model for serum cotinine, to try to understand what are some of the primary drivers for exposure to serum cotinine. And if you just walk through this first row, these are the statistically significant

parameters, except the last one. This row is the F-ratio, which is a statistical term that can be used to kind of rank order or weight each of these parameters. And the p-values are listed in the last column.

What you see is that the predominant driver for serum cotinine is number of cigarettes per day, which kind of is intuitive. It makes sense. Followed by machine-measured tar yield and the two metabolite ratios that were responsible for the conversion of the cotinine to the trans-hydroxycotinine and the glucuronidation are statistically significant. But to note that menthol is not a statistically significant parameter in this model for serum cotinine.

Now, despite the differences that we see between the two race groups, the clinical relevance of these small changes in metabolite ratio is unclear. And it has been reported in literature. There was a stud by Darby where they looked at the metabolite ratios, as well as the NNK metabolism in three subgroups with

differential lung cancer risk, and they found no effect from that. It has also been reported that while there might be some inhibition, the consequences with respect to addiction or health effects is unclear.

The last point that I want to make is that when I showed you the metabolic pathways, I showed that there are multiple, different pathways by which the constituents can be metabolized, as well as the involvement as several isoforms for these metabolic pathways. That will lead one to believe that even if there was some inhibition, it’s unlikely that it would have a significant impact on overall exposure, particularly considering, for example, NNAL only accounts for about 15, 20 percent of the total NNK dose.

So I’m kind of summarizing now this particular section of my talk, where what we found was that based on these selected biomarkers of exposure that we investigated, there was no statistically significant difference between menthol and non-menthol smokers. And the second

finding was that menthol does not appear to inhibit the metabolism of either NK or nicotine.

In the next segment, I want to talk about the biomarkers of potential harm. Now, just a reminder, as I showed you in that first table, we used biomarkers that were representatives of the mechanistic pathways like oxidative stress and inflammation. I'm not listing all of them, but I'm just going to show you a selected few. Details are provided in the written submission.

But if you just look at some of these, the data that I'm showing you is menthol, the unadjusted mean and standard deviation for the menthol compared to the non menthol. And there is no indication that any of these biomarkers are either statistically significant or different or even tending to be in the clinically unfavorable direction. On the contrary, if you look at some of the CVD markers, they tend to be moving in the favorable direction. And I think it makes sense because remember, I showed you that menthol smokers smoke fewer cigarettes than non-menthol

smokers. So this is probably an effect of lower number of cigarettes.

So we went on and did a statistical model to adjust for the confounders. And when we looked to see if there is any menthol effect in the statistical model, there was no statistically significant effect of menthol on the biomarkers of potential harm that we investigated. And if you kind of try to understand what are some of the highest factors in the statistical model, what you find, not surprisingly, is BMI and number of cigarettes per day, along with the number of years smoked and age and gender are some of the highest-ranking factors that drive the relationship with the biomarkers of potential harm. And nevertheless, all these statistically significant factors account for a relatively small amount of the variability.

The last set of data that I want to show you is linked to the measures of dependence, the Fagerstrom Test for Nicotine Dependence scores. What I’m showing you on this chart is the raw

data. It’s a frequency histogram of menthol and non-menthol smokers against the number of participants in the raw Fagerstrom Test for Nicotine Dependence, FTND score, for these two groups. And if you just generally look for patterns, menthol smokers did not appear to have higher FTND scores.

Furthermore, then when we go ahead and do a statistical comparison, and in the literature, you’ll see several ways in which people analyze these FTND scores. So we kind of looked at the various ways in which it’s been reported, either by breaking down the Fagerstrom scores into five categories, three categories or two categories. And no matter how you look at it, menthol smokers don’t have any statistically higher odds of scoring higher on the dependence scores compared to the non-menthol smokers.

One of the elements of the Fagerstrom Test for Nicotine Dependence is the time to first cigarette, and so we separated out the times to first cigarette to determine whether there was any

1 difference between menthol and non-menthol
2 smokers. And our analysis, we did a logistic
3 regression. We found that the menthol smokers
4 didn’t have any odds of smoking their first
5 cigarette any quicker than non-menthol smokers.
6 So there was no statistically significant
7 difference in the time to first cigarette between
8 menthol and non-menthol smokers.
9 So in summary, just kind of recapping
10 what we have seen so far, so the four key
11 takeaways that we gather from this analysis is
12 that there were no differences in those selected
13 biomarkers of exposure between menthol and non-
14 menthol smokers. Menthol did not appear to
15 inhibit the metabolism of NNKR nicotine. And the
16 biomarkers of potential harm that were
17 investigated were not significantly different
18 between menthol and non-menthol smokers.
19 Then, our analysis of the Fagerstrom Test
20 for Nicotine Dependence score showed that menthol
21 smokers did not have a higher dependence score
22 than non-menthol smokers. And collectively, this

1 evidence that we have gathered from this analysis
2 from the Total Exposure Study is very much in
3 agreement with the epidemiological reports that
4 adult menthol smokers are not at any greater risk
5 of smoking-related diseases than non-menthol
6 smokers. And that's all I have to say.
7 DR. OGDEN: Good afternoon, ladies and
8 gentlemen. My name is Mike Ogden with R.J.
9 Reynolds Tobacco Company, where I hold the
10 position of senior director in the regulatory
11 oversight department.
12 I'd like to address the TPSAC area of
13 category of interest on biomarkers by reviewing
14 RJR studies that had biomarkers outcomes, and
15 there are two types of studies that have those
16 outcomes. One is we refer to as human smoking
17 behavior studies, and a second general category is
18 clinical trials. The results of these studies
19 will show that using biomarkers, there's
20 equivalent or reduced smoke uptake for smokers of
21 menthol cigarettes.
22 In general, RJR does not study direct

comparisons of biomarkers for menthol and non-menthol smokers. However, there are data from unpublished Reynolds studies that can provide information on that comparison, and again, I provide you with data on two types of studies that we have conducted.

First is the smoking-behavior-type studies. These are used for product development, especially in the development of our tobacco heating cigarette, which was first Premier in the late ‘80s and now is Eclipse. We have been conducting smoking behavior studies for well over 25 years. Typically, these are crossover studies, meaning they’re switching studies with a control, which is often the usual brand or the usual preferred brand of smokers, which I’ll abbreviate UB. And then switch over to a test product. Occasionally, there have been a couple of long-term studies of smokers while smoking just their usual brand; that is, that does not involve a switch or a crossover.

These are typically short-term studies on

the order of one to two weeks for either evaluation or then for crossover to a test product before they're evaluated again. These are the same types of studies. As a matter of fact, these are the same studies that I reviewed in the earlier presentation on smoking behavior, but now I will focus on the outcomes from those studies that have biomarker measurements. In some cases, those studies include breath, carbon monoxide, blood, carboxyhemoglobin. And in two of those studies, I've even included serum nicotine.

This is the same overview as presented earlier, that basically just gives a brief description of the types of studies. Again, you can see that these particular studies were conducted in the late 1990s.

A brief orientation to some of the acronyms used. TB is a tobacco-burning cigarette which would be a more traditional type of cigarette. UB is usual brand. I've broken down and given you the number of subjects in these studies with M designating menthol and NM

designating non menthol. So many of these studies typically are relatively small in comparison to larger clinical trials, with typically on the order of one or two dozen subjects per study arm.

There is an additional table in the appendix that I won't cover in your written handout. And this will provide some more information to link these studies, if you wish, to the information that was provided in Reynolds' written submission and also, information that will be provided as a result of FDA's document request on menthol later in the summer.

As an overview of the clinical trials area, clinical trials that include biomarkers from a Reynolds' perspective generally evaluate differences in potential health-related endpoints. They certainly can include biomarkers of exposure and potential biomarkers of effect or harm. They generally include blood and urine matrices for evaluation of biomarkers.

Typically, there's a measurement at baseline. That is, if smokers come in on their

usual brand, they're evaluated at baseline. If there's a crossover or switch in general to a test product and after some period of acclimation, they're evaluated again. There are varying numbers of subjects depending on study objectives.

One particular Reynolds study allows for comparison of menthol and non-menthol subjects. And we have conducted an analysis of that particular study for the questions posed by FDA. That particular study goes by the internal project name of Quality of Life Study or QoL. It was a 24-week biomarker study, nearly six months.

The primary outcomes of this study, it was a switching study for smokers of tobacco-burning cigarettes. They were randomly assigned to one of three study arms. One is an ultra light cigarette, a 5-milligram product by the Cambridge filter method; a second study arm was switching to the tobacco-heating Eclipse cigarette; and a third arm was switching to a smokeless product called snus.

That study began in early 2007 and was

1 completed in 2009. It was also conducted
2 according to good clinical practices. There were
3 also patient-reported outcome measures in this
4 study, including questionnaires regarding health
5 endpoints. I don't have any information in this
6 deck based on those endpoints. We have not yet
7 reanalyzed the data in that way. But they did
8 include 24-hour urine collections for measurement
9 of urine biomarkers and blood biomarkers at
10 baseline, 12 weeks and 24 weeks. But since
11 there was no switching that involved menthol, the
12 only data available from this study to address
13 TPSAC questions were from smokers on their usual
14 brand at baseline in that study. The final
15 subject numbers included 131 smokers. There were
16 100 non menthol, 31 menthol, and they were
17 compared. All exclusive smokers of tobacco-
18 burning cigarettes in the study sites were
19 eligible for participation. There was no
20 inclusion or exclusion criteria based on menthol
21 or non menthol.
22 So now I've described the studies. Let's

1 look at the results. In the smoking behavior
2 studies, the overall results suggest no difference
3 in nicotine uptake for menthol compared to non-
4 menthol smokers. And in the table of studies I
5 showed you, only two of those studies contained
6 serum nicotine measures. And they were
7 significantly lower baseline serum nicotine
8 observed for menthol versus non-menthol full
9 flavor usual brand, full flavor meaning the higher
10 tar category. So as they are smoking their usual
11 brand, when they come into the study site in the
12 morning, the menthol smokers had a lower baseline
13 serum nicotine.
14 The way that we do our studies for serum
15 nicotine, this is in a controlled laboratory small
16 clinic setting, and we sample blood over a number
17 of minutes, generally from just before lighting a
18 cigarette until approximately 30 minutes after
19 lighting the cigarette. And for serum nicotine
20 measures, we take timed measurements generally on
21 the order of 1 to 5, seven and a half, 10 and
22 sometimes later minutes after lighting.

So we analyze all of those samples separately. So we have the baseline before lighting. And as I've showed you, serum nicotine was lower for menthol versus non menthol. As you look at the individual time points, there was an incremental increase at those timed points after lighting on two of the time points in one study at 7 and a half and 10 minutes. But the total serum nicotine means were not significantly different seven and a half or 10 minutes after lighting. So they came in at a lower level. After smoking a cigarette, there was no difference.

That effect in that same study, if you refer back to that table, there were smokers in three tar categories, the higher tar, the middle tar, and the lower tar. That effect was not observed in any category other than the full flavor. And no other significant differences in serum nicotine measure were observed between menthol and non menthol in either of those two studies.

Those two studies and all of the others

included carboxyhemoglobin by the same general technique that I've described to you. We sampled the blood before lighting a cigarette, and then again 25 minutes after lighting the cigarette. Overall, the results show no difference in carbon monoxide uptake for menthol smokers relative to non-menthol smokers. And similar for the serum nicotine, in fact, it was from the same study. There was a significantly lower baseline carboxyhemoglobin observed for menthol versus non; that is, for the full flavor usual brand smokers.

So in the morning, the first session, they had a lower baseline in the menthol smokers. There were greater incremental increases, which is the difference between after lighting and pre-lighting, 25 minutes. The net result of that is that the carboxyhemoglobin 25 minutes after lighting were not different between menthol and non-menthol smokers. And again, that effect was not observed in the middle tar or the light category.

No other significant differences in COHB

1 were observed between menthol and non-menthol
2 smokers in any of the studies reviewed. And that
3 endpoint, as I said, is present in every RJR
4 smoking behavior study.
5 We'll move now to the clinical trial,
6 which we refer to as the Quality of Life Study.
7 Overall, the results showed that there's no
8 significant difference or in some cases, there is
9 a reduced level of biomarkers for menthol versus
10 non-menthol smokers. The blood biomarkers show no
11 significant effect on any of the markers. I'll
12 show you a table of those markers in just a
13 moment.
14 Looking at the urine samples, these are
15 the 24-hour urine samples. Tobacco-specific urine
16 biomarkers were generally lower for menthol
17 smokers than non menthol, but there were no
18 statistically significant differences. For
19 tobacco-specific urine biomarkers, I mean nicotine
20 and metabolites of tobacco-specific
21 nitrosamine, NNK.
22 Looking at other biomarkers, there were

significant reductions of about 20 percent relative to non-menthol smokers observed for several of the biomarkers. That is for the constituents listed there. There are a number of aromatic amines and metabolites, butadiene, crotonaldehyde, and acrolein. And on average, they were about 20 percent statistically significantly lower for the menthol smokers. No other tobacco-related urine biomarkers showed any significant differences.

My intention is not to go through this chart in any level of detail. But what we've done is we've listed all the biomarkers. We've given you the means, the numbers of subjects that had samples that were suitable for analysis. So these are all the data, and we'll give you the p-value in the far right-hand column.

On the subsequent chart, you'll see where I will highlight in yellow any places there are statistically significant differences. So for none of the blood biomarkers were there any statistically significant differences for these

biomarkers.

Looking at the urine biomarkers, again, you can see the first line is the total nicotine equivalence, which in our case is the sum of nicotine and nine metabolites and molar sum. And there’s a 7 percent reduction but not significant for menthol versus non menthol.

We’ve got the individual metabolites listed there. I’ll focus your attention on the bottom four rows where again, this particular chart shows the aromatic amines with statistically significant differences. And you can see the numbers in the second from the right in terms of reductions for menthol of that range from 17 to 24 percent.

A second table of urinary biomarkers, again, the statistically significant reductions for menthol versus non menthol are highlighted in yellow. There are no other menthol effects. So in this chart, there are three biomarkers, 1 metabolite of butadiene, 1 metabolite of crotonaldehyde, and 1 metabolite of acrolein. And

again, that 17- to 24-percent reduction for menthol smokers was observed.

So in conclusion, the biomarker studies conducted by RJR are consistent with the published scientific literature. The studies show that for menthol versus non-menthol smokers, there’s no overall difference in serum nicotine or CO uptake. That was measured in our smoking behavior in lab trials. There’s no significant difference or reduced levels of blood and urine biomarkers that was measured in our larger clinical trial conducted under good clinical practices.

Based on biomarker measurements, there’s no basis to regulate menthol differently than non-menthol cigarettes. Thank you.

DR. TRUE: Great. Now, shifting to wrap up on the biomarker section, Lorillard has a couple of unique studies that were conducted by Lorillard.

The first one is a parallel arm study comparing menthol and non-menthol smokers, which was a Heck publication in 2009 which was a study

of 112 subjects, African American, white, male, and female. And I highlighted in red a particular feature of this study, something we found to be absent in other clinical studies to date on this subject. And that we went through extra pain in recruiting smokers that smoked their usual brand, and those usual brands, we did everything we could to match them in terms of the tar, nicotine, CO, and NNK deliveries of those products. Secondarily, we also went and actually measured and verified that the cigarettes that were used in the study to ensure the deliveries matched what the claims were.

Looking at carboxyhemoglobin, urinary nicotine, five metabolites, urinary NNAL, and glucuronide, we found that across the board, menthol and non-menthol smokers had essentially identical levels of the biomarkers of exposure.

Later, and this is a study in which the manuscript is under preparation, we took some leftover urine from this clinical study that we had available to us and wanted to ask the

1 question, because there’s been a lot of discussion
2 about the role of oxidated stress in promoting
3 disease conditions that might have already been
4 pre-established. And 8-oxo-2-prime-deoxyguanosine
5 is generated by oxidative stress. And in fact,
6 there is a substantial difference between the
7 amount of 8-oxo-dg that exists in nonsmokers
8 versus smokers.
9 So again, we were able to use this same
10 matched cigarettes and constituent yield because
11 it was basically the same study. And we found no
12 statistical differences in 8-oxo-dg levels were
13 observed across all the different ethnic groups.
14 And we found overall that menthol smokers had
15 between a 4 to 21 percent reduction actually, in
16 8-oxo-dg excreted than non-menthol smokers,
17 although this was not statistically significant.
18 This bar chart basically breaks that up.
19 You can see that the lines on top of each of the
20 bars is the statistical confidence level, and the
21 overlap indicates that in a couple of cases
22 they’re very close to being statistically

1 significant. In other cases, there’s considerable
2 overlap.
3 So to wrap up this entire menthol
4 biomarker section, our conclusions overall are
5 that we feel very strongly that biomarkers are
6 highly quantitative and direct measurable outcomes
7 of smoking. Biomarker studies integrate all of
8 the diverse elements of complex human smoking
9 behavior, including the cigarettes per day, puff
10 intensity, percent of cigarettes smoked, and any
11 filter vent hole blocking that might take place.
12 The biomarker studies that have been conducted by
13 Lorillard, PM U.S.A., and RJRT show no differences
14 in selected biomarkers of exposure between menthol
15 and non-menthol smokers.
16 As you heard earlier, based on the
17 largest study of actual smokers, the Philip Morris
18 USA Total Exposure Study with over 3600 smokers,
19 this is truly a revolutionary study for this
20 topic. And under normal smoking conditions,
21 menthol does not inhibit the metabolism of
22 nicotine or NNK and does not have any increased

levels of biomarkers.

Internal studies do not indicate that menthol cigarettes are smoked any differently or more intensely than are non-menthol cigarettes. And these studies reinforce the overwhelming weight of epidemiology literature which indicates that menthol and non-menthol cigarettes convey similar risks of chronic disease. Thank you.

DR. SAMET: Okay. Thank you, and thank you for your concise presentations.

We're actually roughly back on time, bringing us to break for 15 minutes.

Committee members, remember to behave yourselves. No discussion of the meeting topic during the break amongst yourselves or with any members of the audience.

(Whereupon, a recess was taken.)

DR. SAMET: We now have a half hour for clarifying questions. And let me just get a sense of how many have clarifying questions. So actually, I'm going to take the Chair's prerogative and ask the first question myself

because I think it's important.

For Dr. Sarkar, if I could ask you just on slide 15, if you could put that up for us. This was the biomarkers of exposure by race. And I may need to appeal to my colleague Neal Benowitz in interpreting the data.

So this slide, I just want to make sure that I understand this. So you have here the total serum cotinine, for example, and the numbers of cigarettes are a little bit different comparing the menthol and non-menthol groups. So when you looked at this, no significant differences, these were without considering the cigarettes smoked, the differences in COPD.

Is that correct?

DR. SARKAR: Right. We actually did two types of analysis, what I'm showing you here, the mean and the standard deviation. The first set of analysis that we did was kind of a univariate comparison, and this was published in the Wang paper. So we did a univariate comparison and then followed up with an ANCOVA model, and in both the

cases, there were no significant differences in the serum cotinine between menthol and non menthol after adjusting for all the other factors.

DR. SAMET: And in your model, the statistical model, I guess one of the questions is, you have the menthol by race interaction.

Did you look at a cigarettes per day by menthol interaction?

DR. SARKAR: We looked for it. It was not significant. But I think when we see this menthol by race interaction, it was just there were other underlying factors that probably account for that.

DR. SAMET: Right. But not shown in this slide. Additionally, you did look at the cigarettes per day by menthol interaction.

DR. SARKAR: Right. What I'm showing you here are the significant parameters that showed up in the final model after the analysis.

DR. SAMET: Okay. Thank you.

Yes? Clarify specifically about that?

DR. BENOWITZ: One thing we talked about

at the last meeting was the issue of the unusual dose response race issue with lung cancer. So for African Americans, the risk of lung cancer in relation to whites is much, much greater at 10 or fewer cigarettes per day and is not much different at 30 cigarettes per day. And one of the things we talked about is the possibility that menthol, at very low cigarette consumption, can facilitate intake. And one thing that we asked last time is could you do an analysis of just 10 or fewer cigarettes per day and looking at biomarkers as a function of menthol?

So I'm not sure that just looking at a simple cigarette by menthol interaction would do it. But what I'd like to see is an analysis of just 10 and fewer cigarettes per day by menthol.

DR. SARKAR: One of the things that if you look at the demographic characteristics, the average number of cigarettes smoked by the African American menthol smokers is about 10 cigarettes per day. But importantly, there are a couple of things that I think we need to keep in mind is

that there are many underlying factors, particularly when you start looking for the various factors that influence disease risk as for lung cancer.

The fact is that actually African Americans, you've got a lot of other factors like socioeconomic factors, gender. In fact, the disparity in the lung cancer is actually a reverse if you just look at the smoking prevalence. In other words, a higher number of women are in the menthol-smoking population, but the lung cancer risk is greater for African American males than in women. Also, if you look at the epidemiology, you don't see the same effect on the other smoking-related diseases like COPD or cardiovascular diseases.

So I think it's a very complex phenomenon, and some of these underlying factors like socioeconomic status, availability of healthcare, et cetera, could be playing a role as well.

DR. BENOWITZ: But I think you're

avoiding the basic question, which is, still, the socioeconomic status things or whatnot, that's going to hold up across all the cigarette consumption levels. What I would like to see is just for 10 or fewer cigarettes per day in both race groups, is there a difference in exposure versus menthol.

I think that's a critical question because that's where the biggest lung cancer signal is, and so there's a biological plausibility that menthol could facilitate more intake when you're trying to just smoke as few cigarettes per day as you can. Maybe you don't have enough money to buy cigarettes or whatever. It could be that menthol allows you to take more when you're really trying to get as much from a cigarette as you can. So that analysis is critical, so I just would ask you to present that.

DR. SARKAR: One of the things that we did -- and I'm not sure on the details of this analysis here -- was that if you look for just a comparison of serum cotinine against number of

cigarettes, and you plot the raw data and look for the regression analysis, and then you compare the slopes, you find that the smoke slopes are not different. But I have not specifically done the analysis which is separate out the 10 or less cigarettes per day. We can certainly do that, look at that.

DR. SAMET: I think actually what Neal is asking is that you just better describe across possibly the range of number of cigarettes, the relationship between numbers smoked and biomarker levels. And the stratification would be one way to do that, and there are others.

So, sorry; having gotten us all out of order, we're going left this time. We'll start with Corinne and move around.

DR. HUSTEN: This is also a question for Dr. Sarkar. I wanted to ask you a question on slide 14. I think it's the slide right before this one.

I was struck, given the size of the study, how large the standard deviations are for

all of these measures. And I guess my question is, is even a study of this size just too underpowered to really see differences in biomarker levels, or is there some other reason that the standard deviations are so large? It seems like it'd be very hard to show a significant difference at all, given those standard deviations.

DR. SARKAR: Well, that's the reason I showed you the slide where I shared with you the primary objectives. The primary objective of this study was to answer a broader question of exposure in the smoking population. But if you just look at the sheer number of the subjects and the fact that these kinds of standard deviations are very typical, you see a lot of variability in the smokers that we recruited were daily smokers of one or more cigarettes per day.

So in the population, we had a wide range of smokers that were recruited in the study, so it's not surprising that you see this difference. Some of this could be manifesting from the fact

that there was this large number of differences in the numbers of cigarette smoked, which is why when you then adjust for that, you can kind of draw some inferences.

I think at the end of the day if you kind of look at the collective body of evidence, you kind of get some inferences around the -- comparing it to what’s reported in the literature and kind of tie it in with the epidemiology as well. The collective evidence is all pointing in the same direction.

DR. HUSTEN: Although most of your slides are showing the unadjusted data, I guess just as a comment, I think it would be more helpful to have these analyses that really segregated out the independent effects of menthol from race, cigarettes per day, maybe differences in metabolism, nicotine equivalence, whatever the appropriate measures are. You did that one slide, but all the other slides are the unadjusted. And I think it just doesn’t really tell us what the independent effect of menthol is compared to these

other confounding factors.

DR. SAMET: Greg?

DR. CONNOLLY: Just to follow up and then I'm going to ask a question. I'd feel much more comfortable if you'd turn the raw data over to the staff of the FDA, who could conduct an independent analysis and answer Neal and Jon's question. So I think we made that request at the last meeting, but give the FDA the raw data, as a drug company would, so they can analyze these questions independently and then present before the board.

You mentioned that there's been IRB approval for the human subjects study. I assume all of the entities that are involved in the study received IRB approval from an FDA-equivalent agency or an FDA-approved agency?

DR. SARKAR: As I had mentioned in my study conduct details, that there were 39 investigative sites and the IRB approval was obtained from all of these sites, yes.

DR. CONNOLLY: And they were all FDA-approved on sites? Well, FDA-equivalent. I deal

with IRB all the time in smokers, and I am very sensitive. And my sense is as we create new paths here as a committee, that we make sure that when research is conducted by the tobacco industry, that the research is done through approved IRB agencies that are in accordance with FDA.

DR. SARKAR: Well, as I showed to you when I'm describing the study that the study was conducted in accordance with GCP, and the study conducted was taking place through a CRO, which is used to doing clinical studies for pharmaceutical companies and gets audited by the FDA; so yes.

DR. CONNOLLY: So we can assume no pregnant women or people with cardiovascular disease or lung cancer or emphysema participated in this study?

DR. SARKAR: Due to the time constraints, I couldn't give you the details of the inclusion and exclusion criteria, but they have been published. And, yes, absolutely.

DR. CONNOLLY: Okay. Thank you.

DR. LEWIS: And I just want to make one

comment based on your initial comment, Dr. Connolly, that if we are requested by the FDA for this data, we will provide this requested proprietary information to the FDA.

DR. NEZ HENDERSON: I just have a quick question. I keep coming back to the mission of what we're supposed to be doing, which is for us to make a recommendation to the FDA on the issue of the impact on the use of menthol in cigarettes on the public health. So I've asked my colleagues around the table, what is your definition of public health, and it was thrown around. So I looked it up. "Science and art of preventing disease prolonging life and promoting health through the organized efforts and informed choices of society, organization, public/private communities, and individuals."

So the information that you have given us all indicate that I guess, in my view, that the way I'm perceiving it, that menthol is just as bad for you as regular cigarettes. So I guess I'm asking you is that promoting public health,

1 particularly for African American communities,
2 where according to the table that you showed, more
3 than 73 percent of them use menthol cigarettes.
4 DR. SAMET: I will say before you answer
5 that, this is not exactly a clarifying question in
6 relationship to biomarkers but one, I think, with
7 broader implications perhaps relating to some of
8 Dr. True's overall comments.
9 So I guess if you have a framework to
10 answer this question within perhaps those
11 conclusory remarks, you might do so. But I think
12 the question certainly goes outside of biomarkers
13 to their implications. And you can also not
14 answer, I think, if you don't have an answer.
15 Okay. Thanks.
16 Thank you.
17 Patricia? Jack?
18 DR. HENNINGFIELD: The first just
19 question to lead into the second is, how long did
20 you track people in the test study? How long were
21 people assessed?
22 DR. SARKAR: As I mentioned to you in my

description, this was a cross-sectional observational study, so it was a cross-section. We didn't --

DR. HENNINGFIELD: Okay.

DR. SARKAR: -- track them there.

DR. HENNINGFIELD: Okay. Well, in any of your studies or any of the studies by any of the others for biomarkers, do you have any data on measures of dependence as a function of age, even if it's only starting with 18 or years of smoking? In other words, it's not surprising that in established adult smokers, you're not seeing differences in dependence as a function of menthol. But what about over time, over age, over years of smoking?

Do you have anything that would tell us about the trajectory of development of addiction as a function of menthol?

DR. SARKAR: This particular study was done in age verified 21 years or older, and it was a cross-section. We don't have any data on trajectories or long-term follow-up.

DR. HENNINGFIELD: But in none of the studies? Again, this was open ended. So do any of the companies have any data on your own data on menthol and the trajectory of addiction?

DR. LEWIS: We don’t have that data, and I believe there’s nothing in the published literature, either.

DR. SAMET: Dorothy?

DR. HATSUKAMI: This is a question for Dr. Sarkar. I was wondering if you looked at FTND by race, the same way you did with biomarkers by race.

Did you look at FTND by race as well?

DR. SARKAR: No, we did not. When we did the analysis, it didn’t come out to be significant.

DR. HATSUKAMI: I’m sorry. So you did not or you did and it was nonsignificant?

DR. SARKAR: It was nonsignificant.

DR. HATSUKAMI: Okay.

The other question is related. I would be interested in just going along with what Jack

was saying as to take a look at FTND by the number of cigarettes smoked. So I'd like to see what the FTND scores are by menthol cigarettes among people that are smoking few cigarettes, like 1 to 5 cigarettes, 5 to 10, and so on.

Would that be possible? It's similar to what Neal was asking, but it has to relate to the FTND.

DR. SARKAR: Right. In the FTND score, numbers of cigarette is the predominant driver.

DR. HATSUKAMI: Yes, that's right.

DR. SARKAR: And if you know the way the criteria are set up, you kind of it's overwhelmingly driven by numbers of cigarettes.

DR. HATSUKAMI: Okay. That's a good point. So maybe time to first cigarette might be --

DR. SARKAR: That's shown in the data, yes.

DR. HATSUKAMI: Yes. Great. Thank you.

DR. SAMET: Neal, did you have additional questions?

DR. BENOWITZ: Some comments. I assume the hydroxycotinine to cotinine ratio were urine based. And urine is reasonable, but there's much more variability in urine ratios versus plasma or serum ratios. And you must have the serum data. I'm just curious to know if you have analyzed the serum hydroxycotinine to cotinine data.

DR. SARKAR: No, we did not. We just had the urine metabolite ratio. I mean the urinary measurements within the table. The only serum measurement that we had was the serum cotinine.

DR. BENOWITZ: And to follow up on Corinne's question, there's a potential sex confounding here that I think is really important because the proportion of menthol cigarettes is greater in women than men, and women have different normal cigarette consumption, normal cotinine intake per day and differences in nicotine metabolic pathways. So it would be really important to make sure that you're controlling for the effect of sex before concluding anything about menthol, per se.

DR. SARKAR: Right.

DR. BENOWITZ: There are a lot of potential confounders by sex.

DR. SARKAR: That’s very true. In fact, there are reports of differences in the smoking, puffing parameters as well. And if you remember the table that I showed you which had all the different statistically significant variables in serum cotinine, I believe gender was one of the significant variables.

DR. BENOWITZ: Right. That was just serum cotinine, but you presented a lot of comparisons of menthol versus non menthol. And I think those really have to be carefully controlled for sex.

DR. SARKAR: Yes, what I showed you was for the Exposure data, I showed you the mean and the standard deviation and the conclusions that I drew in the bottom were from the ANCOVA analysis which took into consideration the age, gender, et cetera, yes.

DR. SAMET: Mike?

DR. CLANTON: My question is for Dr. Sarkar as well.

Page 15 of your presentation, biomarkers of potential harm, C-reactive protein. You may have said this, and I missed it. So my two-part question, one question but two parts, the 8 percent increase for C-reactive protein for menthol, was that statistically significant or not? That’s Part 1, Part A.

DR. SARKAR: That table shows just the mean data for the C-reactive protein, but if you go to the next slide, when we look at the analysis of covariance model, menthol was not significant. It was not significantly different between menthol and non-menthol smokers.

DR. CLANTON: Okay. So the difference wasn’t statistically significant. I was particularly concerned because C-reactive protein of 3 is actually the upper limit of normal beyond which your heart disease risk goes up. So I assume that the 2.9 is a real number, so the mentholated group seems to be getting to that

1 higher risk level. But you're saying there's no
2 difference between menthol and non- mentholated C-
3 reactive protein levels?
4 DR. SARKAR: Right. One of the things
5 that I've not done in that slide is shown you all
6 the data. It's just impossible to show you the
7 results from all the different markers for
8 inflammation. So if you look at them
9 collectively, you probably are very well aware
10 that the C-reactive protein is also very sensitive
11 to some of the acute responses to inflammation, et
12 cetera. So you look at the white blood cell, for
13 example, they don't seem to point in that
14 direction.
15 We had also measured a number of other
16 markers for inflammation. Admittedly, exploratory
17 markers like the interleukin, so none of these
18 others seem to point in this same direction. So
19 directionally, collectively, all the biomarkers
20 for inflammation didn't raise any flags.
21 DR. BACKINGER: I apologize if I missed
22 this. I think Corinne was asking this. This is

again for you, Dr. Sarkar. So on the bottom of page 7, which is, I guess slide 14, which is the results of the biomarkers of exposure, did you or you didn't control for all the demographics that you presented on page 6, which I guess is slide 11 and 12? And they may be a moot point since I think the committee's asked for the raw data to actually do analysis, but did you control for all those demographics?

DR. SARKAR: Yes. Indeed, yes.

DR. BACKINGER: Okay. I apologize.

DR. SAMET: Thank you.

Continuing around? Okay. I have actually a question for Dr. True, and I think just to understand your conclusions and just on your very last slide, you imply that the evidence reviewed shows that the menthol and non-menthol cigarettes convey similar risks. So have we actually seen evidence that's directed at equivalence, or have we not been looking at evidence that questions whether there are differences in risk? To me, they convey very

1 different notions. And if one were to set up an
2 equivalency study, it would be quite different
3 from the evidence that we have looked at, whether
4 in an epidemiological or an experimental context.
5 So tell me a little bit more about your very last
6 bullet.
7 DR. TRUE: Yes. I think when you take
8 all the different types of studies that have been
9 done and you've seen the trends both statistical
10 and nonstatistical across the whole body of work,
11 we reached the conclusion we think it's pretty
12 overwhelming evidence that there's no difference
13 between the health risks conveyed by non-menthol
14 cigarettes and menthol cigarettes.
15 DR. SAMET: So by no difference you're
16 saying that the risks are equivalent to health in
17 your view, based on the review of the evidence?
18 DR. TRUE: On review of the evidence,
19 yes.
20 DR. SAMET: And do you put any bounds
21 around that equivalence in terms of either
22 uncertainty, or say, if one were doing a formal

study, one would look a the difference and put some bounds around it in, let's say, a trial context, head to head with two agents? How do you judge it similar? This is just overall weight of evidence?

DR. TRUE: Yes, yes. Because when you look at the totality of all of the work that's been done, the published studies and the internal studies that have been done to date, as you know, there's a volume of information. There's a lot of complexities involved. And when you take the time to go and look at the underlying data in as much detail as you possibly can and comprehend and pull all that together, you basically in all cases seem to come down to these conclusions.

We're not getting statistical differences. In some cases, we're getting some trends towards less health effects associated with menthol smoking, not quite statistically significant. But in the totality, we would conclude that they're equivalent.

DR. SAMET: Okay. And just one last

question about the bullet, in terms of the overwhelming weight of epidemiology literature, again, to use your phrasing, I see a relatively limited set of studies conducted over a somewhat lengthy time period during which, in fact, in the earlier studies, the studies with Cabot and others, that they came along during a period which there would have been few people with lengthy exposure, for example, to menthol cigarettes due to marketing. And you described for us the rise in use. So again, then there's only limited numbers of studies per potential cancer site and not all health outcomes are represented.

So, again, why overwhelming?

DR. TRUE: Well, we believe that 13 published studies, which, as you say, do in some cases focus on one disease, some across multiple diseases -- we think 13 epidemiological studies is a pretty good set of evidence, especially when you consider how all of them point in the same direction. There's that one subgroup, the male population, out of the Sydney study, I believe,

that again, upon further review by the same authors in the study on follow-up, they were not able to reproduce that effect and they concluded on their own that it was likely due to a chance effect since it was not duplicated in women.

So overall, you basically have 13 very strong studies. Again, the Werley paper was a meta-analysis, which is the 14th, which when you combine all the data together from that study -- and we'll have some information tomorrow on a second meta-analysis that again points in that same direction. So we feel that all -- from the field of epidemiology, as you know, there can be some uncertainty and some studies don't always compound with the same conclusion. In this case, they're all coming together to point in the same direction.

DR. SAMET: Okay. Thank you.

I think we have a moment or two for other questions, if there are.

Yes, Mark? Go ahead.

DR. CLANTON: This question is for Dr.

1 True. I don’t have a page number, but it’s your
2 oxidative stress slide. Well, first of all,
3 obesity, which is overly represented in African
4 Americans, is its own source of oxidative stress
5 and, of course, measures of inflammation. Was
6 there any effort to either control for or describe
7 obesity among the African Americans measured in
8 your oxidative stress test?
9 DR. TRUE: No, there was not.
10 DR. CLANTON: Thank you.
11 DR. SAMET: Dr. Clark?
12 DR. CLARK: I don’t know if this is a
13 biomarker question, but clearly, there’s an
14 epidemiologic difference associated with menthol
15 preferring among African Americans and some
16 Hispanics. And even though you don’t appear to
17 have the biomarkers, Dr. Lewis made it clear that
18 there is no safe cigarette.
19 So given that there is no safe cigarette,
20 and smokers are far more likely to develop serious
21 diseases like lung cancer than nonsmokers, the
22 question that comes to my mind focuses on quit

rate as a function of race and menthol. Have we looked at quit rate as a function of race and menthol?

DR. LEWIS: I believe the studies you're referring to were covered in my earlier talk when I talked about cessation outcomes and success with cessation. And if you look at the studies that are done and there's really a lot of information in our submission, I covered a lot of information really in about three slides. But we're not seeing an effect of menthol on those cessation outcomes.

DR. HECK: Mr. Chairman and Committee, I might add that there will be some more discussion of quitting initiation subsequently in the population effects presentation.

DR. SAMET: Thank you.

Dorothy, last question.

DR. HATSUKAMI: Just I was wondering, it's a question for Dr. Ogden.

Would it be okay if you provide the data for the human studies, human smoking behavior

results? I know that you gave us generally what the conclusions were, but it would be really nice to see the figures or the data from that study.

DR. OGDEN: All of the smoking behavior data that I presented are summarized in internal reports. There are some of those that for the menthol-specific question was originally in the report, and some of those were reanalyzed specifically to address the questions before the committee. It's my understanding that all of that information will be produced as a result of the document request; so yes.

DR. HATSUKAMI: Okay. Great. Thanks.

DR. SAMET: Okay. Then we're going to move on to the marketing presentations. And Leonard Jones is leading off.

MR. JONES: Good afternoon. I'm Leonard Jones, the director of direct marketing and marketing research for the Lorillard Tobacco Company. Before I start my remarks, I want to make one point for clarification. There are three marketing presentations today. Those are

independent presentations. There was no collaboration between the three companies. We believe there was some proprietary information that we did not want to delve into. And we need to take that into consideration. As a result of that, there may or may not be some overlap in the presentations.

There are a number of misconceptions as it relates to the menthol segment volume trends and what we as a company do in terms of marketing our products. I would like to address several of those concerns today and talk specifically about what we do do as a company in our efforts to market our products in a responsible manner.

The first misconception is that menthol segment volume is growing. That’s not true. The menthol segment volume, just like the industry volume, is declining. In fact, over the last 30 years, both the menthol segment volume and the industry volume have declined approximately 50 percent.

Another misconception is that Lorillard

markets its cigarettes to kids. Lorillard has not and does not market its products to kids. Smoking is an adult custom. Kids should not smoke, and we have taken steps to market our products to minimize youth exposure. Lorillard markets its products to adult smokers.

Our core marketing principles that underlie everything that we do from a marketing standpoint, we comply with the guides, the codes, the regulations, the laws as they relate to marketing cigarettes. We have adhered to the cigarette advertising code, the FTC guides, the 1998 Master Settlement Agreement, and the Tobacco Control Act.

Lorillard does not create demand for its product. Lorillard responds to consumer demand. Newport, our number one brand and the number one menthol brand, is number one because the majority of menthol smokers prefer the taste characteristics of Newport over the other competitive brands.

Lorillard’s marketing activities again is

directed towards adult smokers. We do not direct our efforts to nonsmokers nor do we direct them at kids.

There are two core marketing objectives that we follow. Our objectives are to first maintain the loyalty among franchise smokers, and by that, I mean for those consumers who have made a choice to smoke and are currently smoking one of our brands, we want them to continue to smoke one of our brands. Secondarily, for those adult smokers who have chosen a competitive brand as their brand of choice, we would like for them to convert or switch to one of our brands.

Our advertising and promotional activities can be categorized as follows: retail price promotions, which are discounts given to retailers that are then passed on to consumers; direct marketing, which is one-on-one communications with adult smokers; print advertising, which in this case is magazine advertising; and retail point-of-sale advertising. Each of these tools are not unique to our

industry. Other consumer packaged goods companies utilize these same marketing tools, and they are legal.

I want to talk in a little more detail about each of these marketing categories. First, retail price promotions, retail price promotions again, discounts that are given to retailers that are then passed on to consumers. Over 90 percent of our marketing expenditures are directed at retail discounts. Why is that? Over the past 12 years, the price of cigarettes has increased significantly due to increases in local, state and federal taxes. Only legally available to adults, again, these discounts are only available to those who reach the minimum age requirement to purchase cigarettes. In most cases, that’s 18 years of age or older.

How do we determine the level of discount and the duration of discounts that retailers receive? It’s based on a geographic state segmentation. There’s this misconception that we advertise or promote our products differently in

1 different ethnic communities. That's not true.
2 Again, it's based on a geographic state
3 segmentation.
4 Then within the state, the determination
5 is made based upon Newport share development; that
6 is, the share of Newport in that state relative to
7 the national share. So a state that indexes high
8 for Newport development may be eligible for a
9 higher rate of discount.
10 We also take into account state excise
11 taxes. Higher tax states, in conjunction with the
12 level of Newport development, will affect where
13 that state falls in terms of the level and
14 duration of promotions. And we also take into
15 account competitive volume development and
16 competitive promotion activity.
17 Our promotions are not directed to
18 consumers, to adult smokers based on ethnicity.
19 Direct marketing, these are the one-on-one
20 communications between Lorillard and smokers that
21 we have on our marketing database. These
22 promotional offers are restricted. Individuals

have to first indicate they are a smoker. They have to be age verified to be 21 years of age or older, and they have opted in to receive promotional offers from our company. Just like consumers opt in, they can opt out. They can write a letter to the company. They can log on to our website. They can dial a toll-free number, call in to our call center. So they can opt out and be removed from our mailing list.

There are three components to our direct marketing efforts. First and foremost is direct mail, which constitutes over 90 percent of our total direct marketing spending. And that direct mail is primarily coupons that are good for discounts on packs or cartons of Newport cigarettes. So it works in conjunction with our retail discounts. We also have a custom magazine called “Pleasure Scene” which is versioned by age. The content of the magazine is the same in most cases, but it’s also versioned. It has editorial content that’s specific to a particular age group. Those age breaks are 21 to 34, 35 to 49 and 50

plus, all adult menthol smokers.

Ethnicity plays no role in our database in our direct marketing efforts. We do not collect nor do we retain any information on ethnicity in our direct marketing database.

Print advertising. Since the Master Settlement Agreement in 1998, billboard, transit, stadium advertising has been banned. So here what we're talking about is print ads in select magazines, and that is exclusively Newport. We don't have print advertising in magazines for any of our other brands. Magazine advertising represents less than 1 percent of our total marketing spending, less than 1 percent. Remember, 90 percent of our marketing spending is retail promotions.

Lorillard has always advertised Newport in magazines which primarily reach adult menthol smokers. We do not advertise in magazines that have a youth readership of 15 percent or more or 2 million. All magazines are selected on their basis to reach menthol smokers and more

1 particularly, Newport smokers, both groups which
2 are 21 years of age or older.
3 Smoker ethnicity does play a role in our
4 magazine selection. Again, we're trying to reach
5 as many adult menthol smokers as possible. There
6 is this misconception that our ads appear
7 disproportionately in African American
8 publications. That's not true. Most of our
9 spending, our advertising spending, is in the
10 general market. And again, we're trying to reach
11 as many adult menthol smokers as possible.
12 As you can see on this graph which shows
13 the percent spending on Newport magazine between
14 general market, African American, and Hispanic,
15 plotted from the years 1979 through 2008. Since
16 1979, 80 to 95 percent of all of Newport's
17 advertising spending has been in the general
18 market.
19 Retail point-of-sale. This is
20 advertising at the store level. There are two
21 reasons why we utilize retail point-of-sale.
22 Number one is to let adult smokers know that the

brand is available in that store, and secondly, to communicate the price. So it's price communication and brand identification, primarily. Since 1998, point-of-sale spending has declined more than 60 percent.

We spend approximately $8 million on retail point-of-sale, and there is this idea that our advertising is in all of the stores across the United States that sell cigarettes. That's not true. Approximately 34 percent of the retail outlets in the U.S. have our advertising, and there's a store universe of 3 to 400,000 stores that sell cigarettes in this country. So we're in approximately a third of them.

Point-of-sale is available across all geographies, and it's the same point-of-sale. It's the same campaign for Newport. In other words, the Pleasure campaign, even though there are different executions, is available across all geographies. And the availability is dependent upon whether or not that store meets the requirements and participates in our promotions.

It has been suggested that in African American communities, there's more point-of-sale than in other retail outlets in the general market. That's simply not true. I think what you need to do is take a look at the point-of-sale placement and the store location and how it fits within our segmentation analysis. Are they participating in our promotions? Do they have a merchandising contract with our company? How do they index for menthol sales in that store? And then, take a look at the advertising that's placed in those stores.

Another thing you need to keep in mind is that different stores have different requirements in terms of the placement of point-of-sale. A chain store may have different restrictions than an independent store.

So the menthol segment is declining as is the industry. Those trends will not reverse themselves. Lorillard has not and does not market its products to kids. Kids should not smoke. Lorillard has complied with the guidelines, the

regulations, the laws, the Master Settlement Agreement, the Tobacco Control Act as it relates to marketing our products. We believe we market our products in a responsible manner. We believe we follow not only the letter but the spirit of the law in doing so. Thank you.

MS. GRAVES: Hello, I'm Monica Graves. I work for R.J. Reynolds Tobacco Company. My title is director, marketing operations, regulatory oversight. I appreciate the opportunity to talk with you today about the menthol market.

Today I'm going to answer this question: Do marketing or menthol levels explain the recent trend in the menthol category?

First, some background. Government data shows positive trends in tobacco public health factors. There are lower smoking prevalence rates seen, lower consumption levels, and lower to stable initiation rates. What does this mean? It means that fewer people are smoking and those who are smoking are smoking less. Incidence, while difficult to measure, appears to be declining or

at least stable.

Dr. Curtin tomorrow as well as others from the industry will speak to these population effects in terms of how they appear in menthol and non-menthol use. And the analysis will show that there are no adverse population effects in terms of menthol relative to non-menthol use.

Also, as background, I would like to review our guiding principles at RJRT and our marketing practices. Our guiding principles are published on our website, but most importantly, they are at the core of how we approach our business and how we conduct our marketing. I'm going to go through each one individually.

No tobacco product has been shown to be safe or without risk. Quitting cigarette smoking significantly reduces the risk for serious disease. The best course of action for smokers who are concerned about their health is to quit. Minors should never use tobacco products. Adults who do not use tobacco products today or those who have quit using tobacco products should not start.

Specifically, in terms of marketing, we market our tobacco products to current adult smokers. Our policy is that we do not market any of our products to minors, non tobacco users, or former users, and none of these groups are included in our marketing research. We market our brand portfolio to all adults who choose to smoke regardless of ethnicity.

Now, back to the question at hand. Do marketing or menthol levels explain the recent trend in the menthol category? To be responsive, RJRT performed an analysis of industry data. We looked at menthol and non-menthol volume trends. We looked at menthol inclusion levels. We also looked at marketing spend, in particular, advertising, pricing, and promotion.

The analysis is going to show that approximately 70 percent of cigarettes consumed today are indeed non menthol. Fewer cigarettes, fewer menthol and non-menthol cigarettes are sold today, and less are consumed each year.

Recently, menthol cigarette sales have

declined slightly slower than non menthol. The recent softening in this decline rate is not driven by menthol levels or marketing efforts. I'll walk you through each of these points starting with menthol shipment volume.

Like the U.S. cigarette market in total, the menthol segment has experienced volume declines for 25-plus years. During this time period, menthol has declined 53 percent. Non menthol has declined 49 percent. Menthol share of shipments has been relatively stable and has not changed appreciably over this 25-year period. Menthol share of shipments has ranged between 24 and 29 percent during this time period with the changes up or down being only fractional. For the first 15 years, there was a slight decline, stable for five, and then slight growth in menthol share of shipments thereafter.

So overall, the development of menthol has not changed appreciably, although there are slight differences in the recent menthol decline rate relative to the non menthol decline rate.

1 For example, the last 10 years, the decline rate
2 for menthol has been 21 percent and for non
3 menthol, 28. So the result is what we would refer
4 to as a slight preference shift occurring, with
5 menthol shipments increasing for the last five
6 years as a share of shipment from 24 percent to
7 approximately 27 percent. Conversely, non menthol
8 has moved from 76 percent to 73 percent, still the
9 majority cigarette market.
10 In terms of menthol inclusion levels, we
11 talked about menthol inclusion this morning to a
12 great extent and also, the practices associated
13 with menthol inclusion. So this chart is intended
14 to augment that discussion this morning, and to
15 show visually the menthol levels from the
16 perspective of what’s being consumed in the
17 marketplace over this menthol preference shift
18 time period.
19 Keep in mind that the menthol levels in
20 the marketplace range from .3 percent to 2.3
21 percent, and this range is across over 350
22 different menthol styles in the market. So as you

can see, if you weight the menthol inclusion level based on what's being shipped and therefore, primarily what's being consumed, you see complete stability during this time period. The slight uptick in 2009 was addressed this morning as being compliance with fire standards and the impact on the menthol levels. So appears as if the explanation for this slight preference is not being driven by menthol inclusion levels.

Let's move to marketing. Marketing preference shift coincides as mentioned earlier with the MSA. It is highly unlikely, therefore, that marketing would be driving this preference shift that we see in the last few years. The MSA constrained all marketing activities, primarily advertising or advertising in particular, in that billboard, and out-of-home communications were banned. Sponsorships and magazine advertising were severely limited. In addition, the messaging and the mediums used during this time period for advertising has changed very little.

Let's take a look at marketing starting

with advertising specifically. Total industry cigarette advertising has declined significantly during this period of menthol preference shift. Advertising here is newspapers, magazines, and billboards. During this 10-year period, advertising levels went from approximately half a billion dollars down to 50 million. This trend was seen in both menthol and non-menthol advertising.

In addition, if you look at Kool, brand style for Kool, in terms of the advertising spend, keep in mind at this time period is the second largest menthol-only brand in the marketplace, and it’s our brand, so we had data on it. But you see overall, this is a point for correlation. In 2004, you see Kool ad spend ticking up, but yet Kool share of market decreasing. In 2004, you see ad spend going to almost zero, but yet there’s a slight uptick in Kool’s share of market. So no apparent correlation or explanation provided in terms of the menthol preference shift with regard to advertising.

Let’s look at pricing. The pricing strategy also does not appear to be a factor in the shift towards menthol. Menthol products sell at a slightly higher price than non-menthol products, and menthol products follow industry pricing trends.

Let me just also note, this average price here is the price that the consumer actually pays. It’s not a list price. So to the extent that there’s price promotions and discounting and coupons and so forth, it’s reflected in these prices.

In looking at promotion, it also appears as if this is not an explanation for the menthol preference shift. Menthol cigarettes receive less price promotion than non menthol, and the percent of menthol volume that was promoted in 2000 was relatively low and increased slightly for those five years afterwards. However, menthol shares of shipments during that time period was flat at 24 percent. The last five years in this time period where you see the percent of menthol volumes

stabilize is actually when you see the share of shipment preference shift occurring.

In conclusion, and let me just first reiterate, that we take the marketing of cigarettes very seriously at RJRT. And as such, we only market our tobacco products to smokers that are adults, people who have already chosen to smoke and are adult smokers. The analysis that shows, in terms of answering the question do marketing or menthol inclusion levels, explains this recent menthol trend.

The analysis clearly shows, and perhaps again, some misperceptions out there, but menthol cigarette sales are declining just like non-menthol cigarettes. Non menthol is still preferred approximately 3 to 1 in the marketplace. There has been a slight preference slight recently from non menthol to menthol while menthol still continues to decline. This dynamic is not explained by marketing or the amount of menthol in the product.

MR. FERNANDEZ: Thank you. Good

1 afternoon. My name is Pascal Fernandez. I'm the
2 vice president of marketing information and
3 consumer research at Altria Client Services, and
4 I'll be talking on behalf of Philip Morris USA.
5 So first, let me share with you what I
6 think are four key tenets of PM USA's approach to
7 menthol cigarettes. The first is PM USA's
8 commitment to responsibly marketing its cigarette
9 brand by building a relationship between those
10 brand and adult smokers.
11 The second tenet is that PM USA markets
12 its cigarette brand only to adult smokers. And I
13 will be talking about PM USA following a number of
14 business practices designed to limit underage
15 access and exposure to cigarette brands and
16 cigarette brand marketing materials. And finally,
17 that Philip Morris USA markets its menthol
18 cigarette brands and non-menthol cigarette brands
19 using the same marketing approaches.
20 So I wanted to share with you these four
21 tenets, and I will articulate my presentation in
22 two parts for giving you some of the key tenets of

the menthol category and menthol consumers and then tell you how we utilize this for our approach to marketing our cigarette brand at PM USA.

So first of all, this is cigarette shipments. Cigarette shipments is essentially the unit sold in the marketplace, and what I'm looking at here is market share, so just the percentage of this unit sold, if you wish. If you take a long range perspective, what you do see is that the menthol category is a long-established category, essentially accounting for about a quarter of US cigarette industry volume for the past 35 years. And essentially, it has been operating in this fairly narrow band for 35 years.

The second point that I want to make when you look at market data is this is a marketing presentation, so let's take a look at the brands. Brands have come and gone. If you looked at the history of the leading brand in the menthol market, Salem came first, followed by Kool, followed by Newport as a leading brand. Philip Morris USA has never been in a leadership position

in the menthol category, Marlboro menthol being half the size of Newport today.

So let me switch now from market data to what we call our adult smoker study. This is a large-scale quantitative survey that we conduct, and let me just introduce it. This is a survey where we do talk to adult smokers, legal age or older. How do we know that? Well, Question 1 is we ask consumers are you 18 years of age or older. We actually do go to control this study in states where the legal age is 19 or counties where it’s 19 or above. We actually adjust for this.

Then the second question is do you smoke cigarettes? It’s a nationally representative sample of United States, of the continental United States. It’s administered by a third-party market research firm, and that provides key information such as regular brand and switching data.

Let me show you some key information. So when you look now at smoker shares, so the percentage of adults who claim to smoke a menthol brand as their regular brand, what you see is

about a third of adult smokers in the United States today claim to smoke a menthol brand, 33, 35, 34 percent, really no big movement in the last three 3 years.

What’s the second thing that we know? Then that allows us to answer the question who smokes menthol cigarettes and how does that compare with the rest of the industry. Well first, let’s point out that in this study, we see that the gender ratio is 50/50, 50 percent of the menthol smokers are women, 50 percent are men.

From a demographic and ethnic standpoint, what we found is most menthol smokers are white smokers, 58 percent, and about a quarter of the menthol smokers are African Americans. And clearly, that is askew compared to the total industry. And then when we look at Hispanic, essentially, Hispanics don’t have a particular skew on menthol versus non menthol. Then from an age standpoint, what we found is 33 percent of smokers are legal age to 29, but also 27 percent are 50-plus versus 31, 28 when you look at the

total industry.

So that’s what we know about who smokes menthol cigarettes today. Obviously, when you switch the data and you look at smoker share, now you’re going to zoom into a particular ethnic group. It is obvious that over three-quarters of African Americans, when they decide to smoke, are going to smoke a menthol cigarette. That’s what the data shows whether we look at 2007 to 2009. White smokers is 28 percent, and Hispanic is about -- a third of Hispanic smokers choose to smoke menthol cigarettes. So that’s what we know.

I’m going to just take a quick departure here on another study which is a study that I know you’re very familiar with, which is the NSDUH study. Now, the NSDUH study is what I call a more inclusive study because what it does is it talks to adults but looks at past 30-day cigarette consumption to have least smoked a cigarette in the past 30 days, and, therefore, the total number is a little higher than some of the other sources.

When you look at total number of smokers,

these quotes, 56.9 million, which is higher than what you'd find in CDC and NHIS and BRFSS, which range between 42 and 46 million adults in 2008. Nevertheless, there are 19 million adults who have smoked a menthol cigarette in the past 30 days.

So what else do we know? Well, there was some discussion. We've seen in various studies that menthol smokers tend to smoke less than non-menthol smokers. This is the average number of cigarettes per day in this large-scale quantitative study that we conduct, 14.7 versus 16.6. I would also highlight the trends are going in the same directions. So that's what we know about daily cigarette consumption.

I'll make a stop in switching. Now, this is a comparison of brand switching dynamics between menthol and non menthol. So what really we see is it's asking menthol smokers and non-menthol smokers have you switched brand in the past year. And really, I think the key points of this is when a smoker switches brands, they tend to stay in that taste preference, menthol or non

menthol. I think that reinforces through quantitative data what we've learned in consumer research, which is clearly, menthol versus non menthol is a taste preference and an articulation. Some adults like menthol cigarettes, some don't.

Then the second point is switching level, and if you look at the data across time, 2007, 9 percent, maybe a little bit more, are going to 13 versus 11 in 2009. These are really barely statistically significant, so I would really highlight this is about the level that is pretty consistent.

So this is some of the key tenets, if you wish, of what we know about the menthol category and menthol smokers. Now, I'd like to talk to you a little bit about what are PM USA's menthol and marketing practices, and I want to highlight a couple of points. First, which is there is no difference between our approach of menthol versus non menthol; it is the same approach.

Now, what are the goals of cigarette brand marketing for Philip Morris USA? We clearly

understand that this is not like any other consumer packaged goods company. We market a dangerous product, so we clearly have this understanding. So what does that mean? That means as a marketer, there is really one of two things that I can do. I can either work at maintaining my market share by ensuring that those adult smokers that have today chosen the brands of Philip Morris USA, if they're going to continue to smoke, don't switch out, don't alternate purchase to one of my competitors' brands. So that's one goal.

The second piece is growing market share, especially for a brand that is not the category leader. I'd very much like to ensure that if an adult is going to choose a menthol cigarette, then I'd like them to switch to Philip Morris USA's menthol brands or alternate purchase to Philip Morris USA's menthol brands.

So that's really the tenet as a marketer of what is the focus. That's quite different than what you'd see in other CPG for the right reason

when you'd market a dangerous product.

Let me just -- not to oversimplify but perhaps to really clarify marketing. What do we do when we do marketing? Well, the first act of a marketer is to define its audience. That's what's called targeting in a broad way. And so, our target is adult smokers, and for the specific question on menthol, it is menthol audiences, which is adult smokers who are interested in menthol cigarettes. So that's the first tenet of a marketing approach.

What's the second tenet? It's to track some of this marketplace data, and I shared some of that with you. The third thing you do is you actually go engage in conversation through qualitative research with adult smokers. And in the case of Philip Morris USA, when we engage in conversation through qualitative research with adult smokers, we've actually placed on ourselves the additional age, if you wish, where we only talk to 21 plus adult smokers. And why is that? It's to take yet an additional buffer between the

legal age and 21. And we study what they want.

Obviously, we utilize this information to design marketing programs and products. You've heard a lot of discussion of products earlier today. To respond to adult smokers want, we've learned that there is a variety of taste preference. And then we develop through an iterative process this idea, and we go test it. And we go test this ideas. Dr. Lewis talked about blind product test or branded product test to 21-plus adult smokers to understand if the idea has some merit, if you wish, among the intended audience of adult smokers. And then the true test is if the idea is good enough, you do introduce it in the marketplace and you measure the market performance.

So that's a simplification of the process. So how have we done over time? How has Philip Morris USA done if this is the same-scale, large-scale history? Well, the first point I want to make is really until Marlboro menthol started to get some market share movement in the mid

1990s, Philip Morris never had much market share success in the menthol category. The most market share we ever got was in the mid 1980s. I think Benson & Hedges for a brief period of time reached about 2-share points of market. Most of the other brands stayed at 1 share point or below.

So Marlboro menthol -- how do we explain Marlboro menthol growing market share? Well, there is really, as a marketer with the principle that I expressed before, really there is kind of two things, two approaches. One is you really have to, once you understand your audience, develop awareness among your intended audience. For us, it’s adult smokers. Try it among your intended audience, adult smokers, purchase and conversion. This is a traditional, classic marketing process. For us, the intended audience is and continues to be adult smokers.

The second thing that Marlboro menthol has done is to actually introduce a certain number of line extensions. And for many years, in fact, from 1966 to 1988, Marlboro menthol essentially

had one full flavor, if you wish, regular Marlboro menthol packing. Its further line extended in 1988 to provide the light tasting version of the Marlboro menthol and then further line extended in the mid 90s with a neutral light-tasting menthol. And then we actually through some consumer research found that there was some interest in slightly different taste within our menthol and then we launched Marlboro Milds.

We also found there was a number of consumers who were interested in a slightly shorter cigarettes that could be used for promotional purposes to provide value, to be able to compete in the marketplace and go try to attract some of this competitive menthol smokers to switch to Marlboro menthol. We launched Marlboro Menthol 72s. And then most recently, we introduced two other new products, Marlboro Smooth in 2007 which was yet a slightly different taste and last year, Marlboro Brand No. 54.

So really, this has been the approach that, if you wish, being the driver of Marlboro

1 menthol market share growth so that today, it's
2 about a 5-share brand.
3 So what's the result of all of this?
4 Now, when we take a look at the demographic of PM
5 USA's menthol brands, well, we have a 51 percent
6 of PM USA's menthol smokers are women, which is 49
7 percent women; 72 percent, three-quarters,
8 essentially are white smokers; 9 percent are
9 African Americans, are clearly lower than the
10 balance of the menthol category, and 12 percent
11 are Hispanics, which is, I'd say, really within a
12 noise level of the 11 percent of the industry.
13 Then from an age standpoint, the legal
14 age to 29, 36 percent are legal age to 29 and 20
15 percent are 50 plus. So I'd say a fairly broad
16 demographic range for PM USA menthol brands today.
17 So what else? I told you we are living,
18 rightly so, as a marketer of dangerous product
19 with a set of restrictions. Obviously, this group
20 is quite familiar with the Tobacco Settlement
21 Agreement of 1998, which really clearly changed
22 the way cigarettes are being advertised and

1 marketed and sold in the United States.
2 Obviously, you know that we do not do outdoor
3 advertising, billboard, stadium, transit ads, that
4 we do not distribute merchandising bearing the
5 cigarette logo with our promotion. And we do not
6 do any paid product placement for our brand. And
7 obviously, this group is quite familiar with the
8 new requirement of the Tobacco Control Act.
9 I want to point out, though, that in
10 addition to this set of regulatory and legal
11 restrictions, we've taken additional steps at
12 Philip Morris USA, additional business practices
13 to further limit our cigarette brand marketing.
14 And I just want to highlight a few.
15 When we do engage into one-on-one direct
16 communication with adult smokers, we go beyond the
17 legal age requirement to limit this one-on-one
18 communication to adult smokers 21-plus. So I told
19 you about this three years' buffer in qualitative
20 consumer research. Well, here again, there is a
21 three years' buffer when we do a one-on-one
22 communication with adult smokers.

As a matter of fact, the Marlboro has not been in any print media for the past eight years. So while we could, we don't. And it's been eight years since Marlboro has been in any print media. And, in fact, it's been six years since any Philip Morris has been in print media.

Then I'll talk to you about our consumer research practices where we really only talk to adult smokers because that's what the marketing group really should study. That's really these adult smokers, and that's what we do.

So then remaining, I think a next question as a marketer -- and those who are familiar with marketing -- and that's where we also have quite a departure versus kind of a classic CPG marketer, is in terms of how do we connect, how do we communicate with adult smokers?

Well, there is one or two ways. It's that straightforward. We either conduct on one-on-one communications with adult smokers 21-plus with these three years' buffer, and we ensure that our brand are present in retail stores through

brand retail programs toward adult smokers over the legal age. And really again, menthol/non menthol, it's really the same approach.

I'll give you a little bit of texture in the time that I have about one-on-one communication, what do I mean by one-on-one communication. It's really one of three things. It's either the form of direct mail or electronic mail sent to adult smokers 21-plus. These are adult smokers who have raised their hands and said they're interested to receive marketing material and promotion from a PM USA cigarette brand. And we have a fairly convenient process to be able to opt out if that's something that you want to be able to do.

Secondly is we've made available advertising on the Marlboro-branded website. It's an age-restricted website. Actually, when the team took me through the process of age restriction, it was quite a stringent process of age verification to ensure that these adult smokers are 21 years of age or older. They need

to enter their password and their name, so on and so forth each time.

Then finally, we conduct a certain number of consumer engagement programs in adult-only facilities where we know adult smokers are 21 years of age or older. So that’s a summary of one-on-one communication.

Cigarette brand retail program, obviously, these 42, 45 million adult smokers go purchase cigarette brands in retail stores, and we want to ensure that our brands are available and the prices are clearly communicated to adult smokers.

We’ve developed a retail merchandising program that you might have heard about called the Retail Leaders Program. It’s really a category management program that allows to have alignment between the trade and Philip Morris USA. Obviously, if the retailers want to sign the agreements, that allows PM USA to be in the best position in the store behind the counter. It allows to allocate the merchandising space

1 according to PM USA's fair share, if you wish, to
2 clearly communicate the price and the promotional
3 offers that might be available so we can work on
4 our strategies. And we've also utilized these
5 merchandising programs to really incent the
6 retailers to really put in place a more stringent
7 limiting access programs to underage purchasers,
8 so to really make an impact in that directions.
9 That's a summary of brand retail programs.
10 If I could only leave you with five
11 points, and I know you will have questions, I'd
12 say the menthol cigarette category has remained
13 essentially stable in the U.S. market for 35 years
14 in well-established categories. Millions of adult
15 smokers who smoke like the taste of menthol
16 cigarettes. PM USA markets its cigarette brands
17 only to adult smokers. PM USA markets its menthol
18 cigarette brands using the same marketing
19 approaches as it uses for its non-menthol
20 cigarette brands. And obviously, PM USA limits
21 its cigarette brand marketing and remains subject
22 to significant oversights and enforcement

mechanism. So these are my formal remarks. Thank you.

DR. SAMET: Okay. Thank you for your presentations and being on time. I noted a similarity amongst your presentations so in spite of your not getting together, I think for those of you who have been watching “Mad Men” on television might consider yourself as marketing experts now. I’m up to the third season. Let’s see. I think we will start on the right side this time with clarifying questions.

MR. HAMM: I have one.

When you consider that a menthol cigarette is probably less likely to be counterfeited, when you consider the other volume of flagship brands, is it possible in the way that you account for total market share, that menthol cigarettes may be considerably less than is currently estimated?

MR. JONES: I’m not aware of any information that suggests that mentholated cigarettes are counterfeited any less than non-

menthol cigarettes.

MR. FERNANDEZ: I'm not sure. I can't talk about counterfeit cigarettes.

But there is a variety of source to measure market share. And I shared with you today the cigarette shipment, which is really a methodology that was built in the 1970s through a common reporting to an outside company called MSA, the cigarette shipments. So it shows 25 to 27. But there is other measurements using various retail takeaway services. I think they all point in a fairly similar direction, so that's really my overall conclusion, fairly similar consistent trends.

DR. SAMET: Okay. Continuing on, Dr. Clark?

DR. CLARK: Mr. Jones, under the direct marketing statement you made, you said that smoker ethnicity plays no role in Lorillard's direct marketing strategies. But you used direct mail marketing, and if you use direct mail, you obviously have marketing databases. And those

databases, are they not tied to ZIP codes and areas in communities where you know there's going to be high consumption rates?

MR. JONES: Yes. We have addresses on the database.

DR. CLARK: Right.

MR. JONES: But we do not segment the database by ZIP code for marketing.

DR. CLARK: But you don't segment the database by ZIP code?

MR. JONES: No.

DR. CLARK: That's a strange direct marketing strategy then.

DR. BAUER: For both Reynolds and Lorillard, you both stated that you didn't target your marketing based on ethnicity. But, of course, race is different from ethnicity, and I'd just like you to clarify that you don't target your marketing based on race.

MR. JONES: We do not target our direct marketing efforts based on race. It's based on meeting the criteria that you're an adult smoker

21 years of age and older. You have opted in, meaning that you have asked to receive these promotional offers. If you meet those qualifications, you're put into our mail stream, and you receive those promotional offers.

DR. BAUER: And that goes for your non-direct marketing as well, your other types of promotions?

MR. JONES: Absolutely.

MS. GRAVES: And the same for RJRT, all of our marketing efforts when we speak to including -- not excluding any demographic populations, ethnic groups, race as well. I mean, we market to any current adult smoker, regardless of what they look like or where they live.

DR. CLARK: Do you segment by ZIP code?

MS. GRAVES: ZIP code? No. We don't.

DR. CLARK: When you mail stuff, you don't put a ZIP on it? You don't know where those ZIP codes go to? You don't have any demographic information about -- you don't use the US Census data at all?

MS. GRAVES: No. The way we have adult smokers on our database -- third-party age verified, just like my cohorts here presented for their companies. When we mail, we pull for a menthol product, we would go to the database and look at the smoker's preference, if they currently buy menthol products or they occasionally use menthol products, then that's who we mail to. And, yes, our addresses have ZIP codes, but we're pulling people who have already expressed interest, not only in smoking but in menthol products.

MR. FERNANDEZ: I know you may not ask me, but if you see the type of question that I found, those who might not be familiar in the bowers of marketing find, well, how does that work? That's not what I read. And I'd say we do not do that, either, by ZIP codes. But you have to think or so, you're in a very mature category. We are focused on converting competitive smokers and keeping those who are going to continue to decide to smoke to our brands.

So therefore, you've already most likely have already mailed to these individuals in the past, so really response rate and previous response rate is really a key driver. And so I thought I'd just add that perspective. That's very good information for a marketer to know, what happened last time, right?

DR. CLARK: But knowing you live in certain areas and you're a previous consumer, your mailing list can't be eternal, so it degrades with nonuse. So who is more likely to use, a consumer in a given racial or ethnic area who's using is more likely to continue to use. Is that not true?

MR. FERNANDEZ: Well, you have a number of individuals who are no --

DR. CLARK: Your mailing list can't be eternal.

MR. FERNANDEZ: No, that's correct.

DR. CLARK: So it degrades, so you want to preserve the active list.

MR. FERNANDEZ: Sure. And you would find that there is many individuals who actually do

raise their hands and want to be part of the programs and that's --

DR. CLARK: Yes.

MR. FERNANDEZ: And so they're coming in as others come out.

DR. SAMET: Let's go back to Ursula.

DR. BAUER: So Ms. Graves, on your presentation, slide number 14, you talked about your pricing strategy and you showed the price per carton of cigarette. I wonder if that same trend that holds for carton, holds for pack price.

MS. GRAVES: It was actually industry pricing. It wasn't just RJRT pricing strategy. It's the pricing that appears in the marketplace. And, yes, the same trend does hold for pack prices.

DR. SAMET: Cathy?

DR. BACKINGER: Yes, I think this is for all three. I think all three of you stated that, and explicitly, that you do not market to youth and that all of your marketing, advertising and marketing is only directed to adult smokers over

the age of 21 or the legal age. But I'm wondering whether any of you have done any research or collected data to support that, to look at whether youth, in fact, are not receiving your marketing and advertising messages to assure that. So didn't know if you had any data on youth, anybody to look at the reverse?

MR. FERNANDEZ: No. No, I do not. As I told you, we solely focus our consumer research efforts towards, in fact, legal age plus and any qualitative research investigation towards 21-plus. And we've got the two mechanisms that I explained to direct our marketing.

DR. BACKINGER: All right. But you see what I'm asking, though? You say you only market to adults, but how do you know that you're not marketing to youth if you're not checking that? So is anybody checking that?

[No response.]

DR. BACKINGER: Okay. Thank you.

DR. SAMET: Mark?

MR. JONES: Because we only market to

adult smokers 21 years of age or older, and because we don't conduct consumer research among any smokers younger than 21 years of age, we do not have that kind of information.

DR. SAMET: Mark?

DR. CLANTON: My question goes to anyone who's offering either a price promotion or a discount for mentholated cigarettes. I'm assuming that a discount is recognizing that there is a price sensitivity when it comes to tobacco consumption. We know in general, of course, that the higher the cost of the cigarette, the less likely someone is to consume that cigarette.

But there are subgroups like children, adolescents, women, African American young males, and lower socioeconomic groups who are very sensitive to price. So my specific question is, are mentholated cigarettes discounted at a greater degree or greater rate than are non tobacco products, either because your companies sell both, or because you have general data that recognizes the comparison or mentholated versus non-

mentholated products? So is there a differential discount of mentholated products?

MR. FERNANDEZ: Sorry. I want to make sure I'm clear. You're asking a comparison between menthol and non-menthol cigarettes or between menthol and other product categories? You're asking between menthol and non menthol, both?

DR. CLANTON: Correct, both.

MR. FERNANDEZ: Look here. I explained to you when I shared that marketing information, that in the case of the menthol category, Philip Morris USA is a distant second to the competitors. Therefore, we have an interest -- we do compete to present our brand with, if you wish, an incentive to try these brands among competitive menthol brand. That's usually the way price promotions are now being used. So if you were going to introduce a new product in the market for a period of time, you might provide a value that is a better value. That really is the way product promotions mostly are now being used. And each

are different, but that's really kind of my key point there.

DR. CLANTON: And I think I understand your response, but in the end, there's an economic reality. The lower the price, the more people will consume tobacco products, and there are plenty of studies showing it. But what I'm asking is, are any of you aware of circumstances, whether on purpose or accidentally, that there is a higher discount for mentholated products as compared to non-mentholated products?

MR. JONES: For Lorillard, between 85 and 90 percent of our cigarette volume is concentrated in one brand, Newport. Newport's average price is higher than other menthol brands across the country. That's based on a study that was conducted by Bank of America and Merrill Lynch.

DR. CLANTON: I appreciate that, but that does not answer the question about a differential discount of mentholated versus -- I'm finished, but it's clear -- okay.

MS. GRAVES: If I understand your

question correctly, that was what was demonstrated in the charts, the average price of a pack of menthol that the consumer pays versus non menthol, as well as the percent promoted volume. The list price at RJRT for menthol versus non menthol is the same. So therefore, by looking at percent-promoted volume and the average price after discounting, you can clearly see that there's no price advantage to a consumer if he's buying menthol versus non menthol.

DR. CLANTON: I'm not looking at the final price at point-of-sale. I'm asking at the margin. It's a marginal analysis. Is there a bigger discount applied to the mentholated cigarette versus the non-? I'm not looking at the final price so that was nonresponsive.

MS. GRAVES: No. The list price is the same; therefore, the percentage discount at the margins is the same.

DR. CLANTON: Thank you.

MS. DELEEUW: Mr. Fernandez, you went over the slide about switching rather quickly. Is this

slide saying that menthol smokers are less likely to switch to non menthol than the reverse?

MR. FERNANDEZ: So this is what the slide says. I gave you three years of data so you could compare over the years. So if we pick in 2008, in 2008, 11 percent of menthol smokers switched brands during the year -- that’s what it means -- while 9 percent of non-menthol smokers switched brands during the years. So what you would say is of the 11 percent -- actually, there is a bit of rounding here. But if you wish, 70, 75 percent came from another menthol, while about 30 percent came from a non-menthol cigarette. Now, if you go the other way around, I guess you’d say it’s a 90-10 ratio, so it’s slightly different.

I think that’s the question you’re asking, right?

MS. DELEEUW: I think so.

MR. FERNANDEZ: Right. So, yes. It sounds like in these data, most of the switching takes place within the taste preference, right, from a menthol to a menthol, from non menthol to a

non menthol. But in a ratio standpoint, one would be 70 percent versus 80, 90 percent in non menthol. I'm not sure it's statistically significant, but that's what the data shows.

DR. BENOWITZ: I've got a question, but I want to make sure I understand this. Would the orange be switching to non menthol or switching from non menthol?

MR. FERNANDEZ: So here's another way to look at this, and I know it's not the most intuitive. So it says 11 percent of menthol smokers switched brands last year, 2008. And essentially, it says 7 percent of menthol smokers switched brands from a menthol to another menthol and 3 percent switched from a non menthol to a menthol.

DR. BENOWITZ: Okay. So it's more switching to menthol than from menthol.

MR. FERNANDEZ: It's switching to.

DR. BENOWITZ: More switching of regular to menthol than of menthol --

MR. FERNANDEZ: A little bit, a little

bit in that data.

DR. BENOWITZ: Okay.

MR. FERNANDEZ: Most of the dynamic is still within flavor, but you're right to point out that the 3 is bigger than the 1 on the other side.

DR. BENOWITZ: Okay. So the question I have is actually related to this. I assume that if you're marketers, you want to know why people are smoking your cigarettes. And so I'd like to know is what information do you have about -- and even though you're studying people who are 21, you're studying people who started smoking for the most part before they were 21.

So what data do you have on why people selected menthol cigarettes in the first place? And what data do you have on why people switched to menthol cigarettes later on? You must ask them why. And so what can you tell us about that?

MR. FERNANDEZ: Right. In this data -- this is one chart. When you ask the question, why did you switch brands, there is a variety of reasons. These are brands, but the number one

reason is taste. Taste always comes back as really a number one reason for why a smoker would switch brands. In times where, if you wish, the economy is in a tougher condition, price and value tends to go up. So price, taste, and then brand I like- --, that’s also some of the key reasons why smokers would switch brands.

DR. BENOWITZ: But just a follow-up, if someone is a non-menthol smoker and you say they’re switching to menthol because of the taste, how did they get exposed to that in the first place and where? I’m curious to know why people want menthol cigarettes.

What do they get from the menthol cigarettes when they switch?

MR. FERNANDEZ: The primary learning that I’ve had -- and sorry to be over simplistic. The primary reason was really the taste. The taste is something that these adult smokers at this point in time liked. That, in my experience, has been the primary driver of choice when switching to a menthol brand or choosing a menthol brand.

DR. BENOWITZ: I'm still not getting the question answered. If you look, say, at the youth data, there's a much bigger percentage of menthol smokers among underage smokers than legal smokers. So they must be switching from menthol cigarettes to non-menthol cigarettes, which is actually different than what you show here.

What is it about menthol cigarettes that people like? You must have asked that question. But beyond just taste, there must be some thing that makes people want to smoke menthol cigarettes, then they get older, to switch from menthol to non menthol.

Do you have any data about the details of that?

MR. FERNANDEZ: First of all, let me just remind you, this is only among adults, and that's the only data that I do study. And I'm sorry to be so simplistic, but really the primary reason that's talked to for switching to, is consumers like the taste of menthol versus non menthol. And I think the switching data shows that when

switching occurs, despite the kind of multiple dynamics that takes place around switching, the switching tend to stay within one of these two types, if you wish, of flavor profile of menthol versus non menthol. And that seems to have been the case for a very long time in the U.S. cigarette industry. And I'm sorry if I don't have more, but really, that's the primary driver, in my experience.

DR. SAMET: Thank you.

Melanie?

DR. WAKEFIELD: Thanks. The first question is for Lorillard. I'm interested to go back to the price promotions issue. And you indicated that you segment your price promotions based on Newport share, state excise taxes, and competitive volume. So in relation to state excise taxes, what you're suggesting is that you tend to use price promotions more to kind of cushion the impact of a tax increase because I suppose we all know that when there is a tax increase people are going to cut down on their

consumption and they're more likely to quit smoking. So you're using price promotions in a targeted way to kind of cushion the impact of a tax increase.

Is that my understanding there?

MR. JONES: That is a true statement, but the state excise tax is not the primary driver of that segmentation. The primary driver is the share development for Newport.

DR. WAKEFIELD: Right. And so then, that means that you kind of go where your Newport smokers are actually.

MR. JONES: That is correct.

DR. WAKEFIELD: Right. And then by state because you kind of have an over-representative percentage of African American smokers who smoke Newports, this really does end up being more price promotion in states with a higher proportion of African American smokers.

Yes? Am I wrong about that?

MR. JONES: I don't believe that's true. In fact, there are twice as many white menthol

smokers as there are African American. There are about 8 million white menthol smokers.

DR. WAKEFIELD: I'm aware of all those statistics, but because there are a variable proportion of African Americans across the states, you're going to have a varying proportion of African Americans who smoke your brand by state.

Yes?

MR. JONES: I would say that's true.

DR. WAKEFIELD: Yes. So I think therefore, it means that you are actually, ipso facto, when you use price promotions, you are exposing more African Americans to those price promotions because you're targeting in that way.

MR. JONES: I don't think it's disproportional, though, because again, the level of discount and the duration of the discount is based upon where the store falls within the segmentation.

DR. WAKEFIELD: Okay. Next question is just getting a bit more to the price again. What's the average price paid for a pack of

Newport before a price promotion? And what is the average price paid after a price promotion?

MR. JONES: I don’t have that information with me.

DR. WAKEFIELD: Could you get that to us?

MR. JONES: Yes.

DR. WAKEFIELD: That would be very helpful. And also, how does that differential compare with non-menthol brands that you sell? Can you get that to us as well?

MR. JONES: Well, again, Newport is our number one brand.

DR. WAKEFIELD: It is, yes. But --

MR. JONES: It represents 85 to 90 percent of our volumes.

DR. WAKEFIELD: I know all those statistics, but I think that would be helpful to us.

MR. JONES: What is your request? I’m sorry.

DR. WAKEFIELD: So first of all, what is the price paid on average for a pack of Newports

before a price promotion; and what is the price paid after a price promotion; and what is the price paid for an average brand that you sell that's not menthol before a price promotion and after a price promotion?

MR. JONES: Okay.

DR. WAKEFIELD: Okay. My second question is really to all of the companies, and I was really surprised that none of you mentioned packaging. And I would have thought that, in this kind of regulatory environment, where you are limited in what kind of marketing strategies you can use, packaging becomes so much more important as a marketing strategy, and yet none of you mentioned anything about packaging.

So I think we know from a lot of your own documents and the literature that what appears on the pack can really influence consumers in terms of what they think about that brand and so forth. And so I just wanted each of the companies to respond to that. Thank you.

MR. JONES: Newport is the number one

menthol brand. It has been since 1993. We have not changed the packaging on Newport full flavor, which represents the bulk of the volume, because we are the menthol leaders. There's no reason to change the packaging.

MR. FERNANDEZ: So really, time was the reason why I didn't talk about packaging. Look, adult smokers buy brands. Brands are really the sum of five things, if you wish. It's the positioning. It's the product. It's the packaging. It's a set of promotions that are used for the brands, and it's a particular price.

Certainly, the packaging is an important component that's used to carry the product and to be able to clearly identify. Most of the menthol product carry a green color or a blue color that's often associated with menthol. So that's -- now, there has been limited innovation, I'd say, in the cigarette on our part around the cigarette packaging. That's why I didn't highlight it in my presentation.

DR. WAKEFIELD: Just a follow-up

question, there have been changes in the menthol packaging in Marlboro menthol. You are increasing your share.

MR. FERNANDEZ: Yes.

DR. WAKEFIELD: What kind of research do you do on your packaging, and can you share some of that with us?

MR. FERNANDEZ: Sure. Here’s the type of research that we do, and there again, it’s a fairly iterative process. I told you that defining your target audience, which in our case is adult smokers who are interested in menthol cigarettes. We spend quite a bit of time in qualitative research and consumer research talking to adult smokers 21-plus to understand, to listen to what their preferences are, which leads to an iterative development of a new product idea.

Then in the same way, this new product, if you wish, has been given a certain packaging with a certain packaging design that is going to be matching the product attributes. And then the research you do, essentially Dr. Lewis talked to

you about blind product tests. Really, what the branded product test is, is the part in the process where you do take the entire bundle of the new product, if you wish, which is the brand name with a certain packaging design that's been selected in a certain product. And you present it to adult smokers, and they rate this proposition, which includes the packaging, on a variety of scales. And that's what allows us to come to a conclusion that this is indeed an idea that is worth pursuing and launch in the marketplace. So that's the type of research we would do.

MS. GRAVES: For RJRT, packaging changes are typically done if we feel like there's a brand that needs a little bit of updating or refreshing and so forth. Packaging changes are very expensive. They typically would create confusion in most cases. Your franchise smokers think, "Okay, this is different," retailers confused in terms of being able to recognize it and so forth. And given those potential challenges, relative to what we believe would appeal to a competitive

smoker, we're not so sure that packaging is really what would make somebody interested in trying one of our products that is currently smoking a Newport or a Marlboro menthol.

DR. SAMET: Okay. Thank you.

Dorothy? You've had your microphone on all day. You just turned it off.

DR. HATSUKAMI: Good thing I didn't say anything bad.

[Laughter.]

DR. HATSUKAMI: I think it's Mr. Fernandez.

If you can just refer to your slide number 5 that talks about the fluctuations in terms of key menthol brand share history. And you do see a significant increase with Newport since 1955, I believe, a more steep increase since 1985. And then you see an increase in Marlboro, but you see decreases in other brands of menthol cigarettes.

I just want to understand why there's been such an escalation among some brands like

Newport and Marlboro menthol whereas others have decreased in brand share. Is it because of the, as you say, maybe the Lorillard and Philip Morris is more aggressive in terms of price promotion? I just want to understand the etiology or what's causing the fluctuation because we know it's not the menthol levels from our previous presentations.

MR. FERNANDEZ: Let me just put the slide up. Obviously, I did not market the Salem, Kool, and Newport brands. And I think I gave you a basic explanation of the drivers behind Marlboro Menthol. I'd say as a marketer, it's not unusual that brands go through certain life cycles, if you wish, where a certain brand grows in market share for a period of time and then comes down and then another brand replaces it.

As each relates to the specific reason for the growth of Newport, I would hesitate to say, my colleague -- my competitor might be better off answering that question. I understood there was some reformulation, but I think you probably

would be better off answering, if that's okay. I'm saying I feel uncomfortable to explain the growth of Newport in front of the marketing director of Newport of Lorillard.

[Laughter.]

DR. HATSUKAMI: I think it's appropriate.

MR. FERNANDEZ: Thank you. I appreciate.

MR. JONES: I like the way you deflected that question, Pascal. I think there are probably many drivers behind the success of Newport and why it's the number one menthol brand. And I don't think it's just pricing. It is a brand that has been consistent over time. I think one of the key elements to the success of any brand across all categories is delivering on a promise to the consumer. If you think about a product that you consume that you enjoy, it's about more than price because if that were the case, private label brands would be the dominant brands in the industry.

So getting back to Newport, I believe it's a consistent product over time, a quality

product. It's a product that touches the consumers who use it on not just a functional level, but on a emotional level as well. It fits into their lifestyle.

We've had a consistent advertising campaign over time. All of these consistencies, you ask about the packaging. The packaging has been consistent on Newport full flavor for many, many years. I believe these are the key drivers behind the success of the brand.

DR. SAMET: Jack?

DR. HENNINGFIELD? Actually, I wanted to talk about that slide, too, because earlier in the presentation, I believe the Lorillard representative said it was all about taste. And did I hear that wrong? But I thought that when you were talking about the dominance, the rise to dominance of Newport, it was about taste. And now you're talking about marketing.

I'm just wondering the degree to which you and/or the other companies think is this about taste or is this about marketing. If it's about

taste, it just seems amazing that the other companies fell so far behind, or if it's really about taste or product design, then that information I think really should be turned over to FDA. If it can't be shared with us, that creates such a difference. Is it about taste? Is it about addictiveness? Or are you folks much better marketers than you seem to be claiming today?

MR. JONES: When I talked about the success of Newport, I mentioned the product. At the end of the day, it comes down to the product. Does it deliver according to consumers' expectations? So I did say earlier that the majority of the menthol smokers who choose a menthol brand prefer the taste characteristics of Newport over competitive brands.

DR. HATSUKAMI: So just as a follow-up question, then that means that the product, the Newport product, has been consistent in terms of product design.

Is that right?

MR. JONES: Absolutely. Newport has been very consistent over time.

DR. HENNINGFIELD: So did the taste change in mid ‘70s, late ‘70s?

MR. JONES: Yes, it did. There was a reformulation in 1972. So since then, there have been minimal product changes to that product. And in 1972, Newport had a market share of less than 1 percent. The brand was introduced in 1957. It had a market share of 1.8 percent in 1961. By ‘72, it had fallen to half that share. So it was either reformulate, reposition the brand, or watch the brand disappear.

DR. HENNINGFIELD: I would request that everything that can be disclosed to the committee about the reformulation, that we get that, because that it is an amazing rise. And if that has anything to do with change in addictiveness, in attractiveness, we should know. And if there’s information that can’t be disclosed publicly, then I assume that FDA has a process like it does with foods and drugs to get the information and examine

it.

MR. JONES: We will certainly consider that.

DR. SAMET: Patricia?

MR. FERNANDEZ: You asked for another point of view? This question about taste versus what more than taste, that's about taste, I think, which is a category choice. It's about taste. There is consumers who like the menthol taste, and there is those who don't. So primarily, that is the category dynamics, I think, is primarily the taste.

That's about brands. And as Dr. Wakefield pointed out earlier, the brand is more than taste. The taste needs to perform, make no question, right? So I would concur that as a manufacturer, you need to make sure that the taste performs in a way that the adult smokers who choose brand like the taste, but you also need to ensure that this is a brand that is communicating position well with the right packaging, the right promotion at the right price. And that's what

generates differences in market share within that category choice. That's my point of view.

DR. SAMET: Patricia?

DR. NEZ HENDERSON: I think my experience is very different from a lot of my colleagues here. And I can say that because we worked primarily with American Indian tribes. I work primarily with American Indian tribes, and there is one quote that I use among my people when I work with them, I say [speaking in Indian language]. Literal translation means that white man's tobacco will hurt the inner essence of who you are and everything around you.

It's pretty powerful when you say that because I'm looking at the numbers here, and this question goes to Mr. Jones.

When more than 70 percent of African Americans are saying that the product is more harmful than regular cigarettes, the menthol, how are you addressing that in terms of your marketing? This is a huge proportion of African Americans that are saying this.

MR. JONES: I don’t believe that 70 percent of African Americans smoke.

DR. NEZ HENDERSON: But of those who smoke?

MR. JONES: Was that your question, of those who smoke?

DR. NEZ HENDERSON: Yes.

MR. JONES: Okay. I’m not familiar with that study, so I can’t comment on it. All I can say is that African Americans who choose to smoke, a majority of them choose a mentholated product.

DR. NEZ HENDERSON: And I know that you don’t have this data right now, but could you give them to us? It’s just how your marketing is broken down by states, like whether it’s the west region, the northwest region, the south, just in terms of where the money is spent?

MR. JONES: So the state segmentation that I referenced?

DR. NEZ HENDERSON: Absolutely, yes. Thank you.

DR. SAMET: Greg?

DR. CONNOLLY: I just want to reinforce the point that you're presenting a lot of data but not the raw data. We're not seeing breakouts by age, and I think if that raw data could be produced to the FDA, it becomes a lot easier for this committee to do its job than just selectively look at PowerPoints. I think it's critical that the FDA has the ability and the staff to look at this data and come back to this committee with reanalysis and then protect proprietary interests.

I'm just pointing at this chart, and what I know is that Newport, over that time period, has kept menthol levels very low and has become the most popular among 12- through 17-year-olds according to SAMAHA, where Kool kept the menthol levels very high, and that has dropped in market share significantly. I know Marlboro has brought in Marlboro Shorts with menthol, and I think you were referencing product changes. And I'd be very curious if the product has changes in menthol concentrations. I do know when menthol shorts were test marketed, they were test marketed

in Philadelphia, in Chicago. And those two communities do not, in my opinion, appear to be necessarily Caucasian.

I heard the statement that R.J. Reynolds didn’t market to blacks, but I think back to the Kool Mix campaign, which was shut down by the attorney generals from -- that that, in my opinion, was a very targeted campaign to a very specific population group.

But what I’ve heard today, which is very interesting, is taste is critical. And when I think of taste, I think of gustatory responses on the tongue to certain neural endings. And I don’t think of chemosensory perception. I think those are other nerves. I did talk about -- and I think Newport presented data -- about Wilkinson Sword No. 23 or 24, where they actually took the taste of menthol out but kept the chemosensory perceptions in.

Would the companies be opposed if we let you keep the taste and had a gustatory response, but came up with like a Wilkinson Sword

alternative analog, where people could taste the menthol but there'd be no chemosensory effects?

DR. SAMET: Greg, can you put that in terms of a clarifying question in relationship to what we've heard?

DR. CONNOLLY: I think my question -- could we have an analog developed, a menthol analog that just had taste but no chemosensory effects? Would you be acceptable with that?

MR. JONES: I'm not a scientist, so I certainly can't answer that question.

DR. LEWIS: I think when you think about that kind of suggestion, some of those products, as you suggested, have been marketed before and have not been acceptable to adult cigarette smokers. I think if you were to mandate something like that, there may be unintended consequences. This is a pretty big adult smoker population that you're talking about, and there may be unintended consequences to be taken into consideration.

DR. CONNOLLY: I'm just trying to reiterate what you told me today about taste being

so important. I'm just trying to help.

DR. TRUE: I think, unfortunately, we're bridging marketing topics and science topics a little bit here. Maybe that's unavoidable, but kind of coming back to the taste that we describe a lot in terms of product development and what that means, keep in mind for the key attributes of the Newport product, it's the tobacco blend.

It's the tobacco blend taste signature that drives the difference, we believe, between our product and everybody else's product. The level of menthol that we have in there perfectly complements that, and that is very unique. We believe that the grades that we select of tobacco are very unique and not typically necessarily used by our competitors. That's very unique and special to us.

In terms of the Wilkinson Sword work that you're referring to, that was a very short study that we did some time in the past. And as I think Dr. Lewis pointed out, the limited amount of testing we did, the consumers did not find those

to be of acceptable taste, and the project was discontinued fairly quickly.

DR. CONNOLLY: Well, if they didn’t find an analog that had chemosensory effects not acceptable but they found menthol taste acceptable, then wouldn’t it make sense then to eliminate the chemosensory effects in a product that just had menthol taste like -- this morning, there was an awful lot of ambivalence about these chemosensory effects, and I really thank you for your presentations that there’s no mechanistic link and they probably don’t make that much difference. But taste is really the critical thing.

So if Wilkinson Sword failed with the chemosensory effects, then wouldn’t it be wise just to have a menthol taste product, a menthol taste analog out there that just affects the gustatory neural receptors?

DR. TRUE: Well, I think in the context of the work that was done, that was done at a time when we were looking at other mint-flavor-type,

peppermint, spearmints, and things of that nature along with these Wilkinson Sword compounds that had a little bit of that cooling effect without maybe the same taste signature as menthol.

So this was done in collection. This was not a chemosensory type of project. This was not looking at what kind of cooling effect was necessarily being done. We were just looking at in the category of minty-type, minty-like flavors, how acceptable might they be as alternatives.

DR. SAMET: Okay. Dr. Ogden?

DR. OGDEN: I think your definition of taste is fundamentally flawed because it’s not simply the impact of a substance on the taste buds because olfaction is a very important component of taste. Anyone who knows that if you hold your nose and take something that’s tasteful, you have no taste. So when we use taste, it’s the total sensory experience. It’s not a physical contact with a substance on the taste buds of the tongue.

DR. CONNOLLY: So we’re coming back to chemosensory perception and we’re leaving the area

of taste then, that's what you're telling me?

DR. OGDEN: I'm telling you the way we use the terminology taste, it was -- as I showed you in my presentations, the sensory attributes, the sensory acceptance.

DR. SAMET: Okay. Moving on.

Corinne?

DR. HUSTEN: Yes. I just had a couple of quick questions.

Mr. Fernandez, I was really intrigued by your slide number 22 where you talked about your Retail Leaders Program, and part of that was incentives to prevent underage sales to minors. I was wondering if you could describe those incentives a little bit.

Then my question for all three companies was if, in fact, you know that a retailer has been found to be selling your products to minors, do you take any actions in terms of financial disincentives?

So first, if you could just describe what the incentives are

MR. FERNANDEZ: So this retail program is a program that has a component, wherefore a retailer to be able to participate in this program and get some of the resources generated by Philip Morris USA, you need to have a certain number of requirements such as obviously, no self service, back bar, a more limited amount of point-of-sales in the store, a placement of a youth smoking prevention sign. And then, when retailers are found to have -- I don’t know how to say that -- violated, if you wish, and there is a certain number of financial penalties associated with that. I don’t have the specific dollars of the program, but obviously, that’s something that could be provided to you.

DR. HUSTEN: Okay. And do the other companies have similar programs?

MR. JONES: If there are multiple infractions by a retailer caught selling cigarettes to a minor, that retailer can be removed from receiving promotions from our company.

MS. GRAVES: Similar for RJRT, to the extent that we have contracts with retailers, which primarily is how you determine that there is a commercial relationship other than the retailer purchasing our product through a wholesaler and selling it, we require that they adhere to all laws and regulations. And our policy is that if we find that they have, for example, gotten a warning from the FDA or something like that and it has not cured, similar with selling to underage, we would pull commercial relationships with that retailer.

DR. HUSTEN: And maybe while you're up there, could you clarify for me on slide 15 what you mean by percent volume promoted? I just didn't understand exactly what that was.

MS. GRAVES: Okay. So if you look at the, on an annual basis, menthol shipments in terms of packs --

DR. CONNOLLY: Could you show the slide?

DR. HUSTEN: It was slide 15.

MS. GRAVES: Okay. The percent promoted

volume, the denominator is menthol shipments if you're looking at menthol percent promoted. So you take your menthol shipments as your denominator, and then the amount of those shipments that had a discount applied to it and so forth. So it's literally, of all the volumes shipped or sold, what percent had some sort of price reduction associated with it.

DR. HUSTEN: Okay. And then just one last quick question for Mr. Jones, you had talked about the retail marketing is just in 34 percent of the retail outlets. And I was curious how you determined whether an outlet would have that kind of advertising or not.

Is it like not in pharmacies or grocery stores, but, yes, in convenience stores and gas stations, or it's some other way of dividing it?

MR. JONES: It varies. But the primary driver for having our point-of-sale at retail would be one of our promotional contracts. So those stores that are on contract with Lorillard who receive promotions are the ones that are more

likely to have our point-of-sale at retail.

DR. BAUER: Since contracts have come up, I'm interested to know what proportion of the 300 to 400,000 tobacco retailers each of the companies has contracts with and what's the average value of those contracts.

MR. JONES: I don't know the actual value of the contracts, but we have promotional contracts with a little over 100,000 of those stores.

MR. FERNANDEZ: As I said to you, the approach that we have on the Marlboro menthol and non menthol is essentially the same. So we have a large percentage. I don't have the exact number with me today. We have a large percentage of these stores being contracted with Philip Morris USA which allows us to have this impact, if you wish, from a youth smoking prevention on a large number of stores.

MS. GRAVES: I don't have that information for RJRT. Typically, our contracts wouldn't have a value amount. It would just be an

agreement in terms of providing discounting and certain agreements from the retailer to put up signage in certain locations and so forth. So it wouldn't necessarily have a value associated with it, but I don't know that number. I'll be glad to get back to you on that for RJRT if you'd like.

DR. CONNOLLY: But just on that slide, it looks like what you're allocating for menthol, the blue line from 2000 to 2003, it looks like you're tripling or quadrupling the amount of promotional expenditures against menthol. Am I interpreting it wrong?

MS. GRAVES: On a percent promoted volume, these aren't dollars. But, yes, during that time frame --

DR. CONNOLLY: So you're putting more money against marketing menthol over the past eight years there or nine years?

MS. GRAVES: Well --

DR. CONNOLLY: You're actually really concentrating on menthol now, it looks like.

MS. GRAVES: No. I think the way to look

at this is the first few years there was more promotion activity behind menthol increasing over the first five years. But the menthol percentage of shipments was flat during that time period. The last five years, promotion levels are stable, higher than they were in the first five years, but they're stable, constant and also consistent, and in some cases, slightly lower than non menthol. And that is the time period where you're seeing a slight share of shipment shift for menthol.

DR. SAMET: Okay. David?

DR. ASHLEY: I was told this pretty clearly that you do not market to children, and I was just wondering what steps you go through to prevent children who enter retail establishments from observing point-of-sale promotional material.

MR. JONES: Children who enter retail outlets where point-of-sale is visible, there's really no way we can keep them from being exposed to that advertising. However, it's incumbent upon the retailer to ensure that anyone who purchases a pack of cigarettes is of legal age. So it's their

responsibility to make sure they're not selling cigarettes to kids.

MR. FERNANDEZ: Here's what we have to do -- and you asked to know the percentage of stores who have signed a retail agreement. I said a large percentage. I don't have the exact number with me. But certainly, what this has allowed us to do is put in place a system or encourage a system by which we're able to reduce the amount of visibility of our brands in the stores. And I'd say that's the approach we've taken.

Though the strict answer to the question, "How do we do to make sure that they can't see," that's really a more complex -- we make sure that we direct our marketing work towards adults. We put our emphasis in these directions, and we work with retailers to have a more responsible visibility in the store.

MS. GRAVES: In terms of point-of-sale, we at RJRT have historically had a policy where we do not place any advertising outdoor within 500 feet of schools or playgrounds. And then and

currently, the policy with regard to outdoor advertising is that we are not placing any at all. Within the store, we try to focus our point-of-sale around the counter. In some cases, that would be a situation where you couldn't prevent children from seeing it. But clearly, we wouldn't go out of our way to place point-of-sale on the ice cream bin down the aisle and so forth. We focus it around the point-of-purchase and no outdoor advertising at point-of-sale.

DR. SAMET: Okay. Thank you. I suspect that even this committee has no questions left. Is that true or am I wrong? Okay. We have a lot of last questions left. I never should have said that. You've risen to the challenge.

Who has questions left? Okay. Neal, Melanie, go ahead.

DR. BENOWITZ: In following up on some of this recent conversation, if we consider there's a higher percentage of children who smoke menthol cigarettes than adults, is this a consequence of marketing or is the consequence of intrinsically

having a better taste that's attractive to children? I think that's a really important question because we don't want children to smoke cigarettes, and we need to know why that's occurring.

Are you inadvertently marketing to children or is the taste just so good that children like it better?

MR. JONES: As I stated earlier, we comply with the codes, the regulations, the laws as it relates to marketing cigarettes. And a lot of those are in place to minimize the exposure of kids to cigarettes. I also stated earlier that we only conduct research among smokers 21 age and older. I think to get to the answer of your question, you would have to study kids, which we don't do.

DR. SAMET: Actually, Neal, I think this question, hold the question till tomorrow for our population effects session because I think it fits in very well with the issues we need to explore there.

Melanie?

DR. WAKEFIELD: A question for Lorillard on slide 10 which was on Newport magazine ad spending, it's interesting to me that there was a jump in the amount of ad spending around about 1996, and it kind of doubled from 8 percent to 16 percent, and that was maintained at this higher level ever since.

What was the reason for doing that?

MR. JONES: I don't know the answer to that. I would have to go back and look at the details associated with the actual publications that we had Newport ads in.

DR. WAKEFIELD: Do you know the motivation for it, though?

MR. JONES: I do not know the answer to that.

DR. WAKEFIELD: Okay. Could you get that for us?

DR. SAMET: Greg?

DR. CONNOLLY: Could we go back to slide 5 on Philip Morris?

MR. FERNANDEZ: Okay. Go.

DR. CONNOLLY: From what I've heard today, Newport has kept their menthol level around .4 since '75 or since reformulation, and done quite well. Kool kept it high and went low. Now, Marlboro Menthol brought in a brand, I think it was -- I'm asking market share here. Marlboro Menthol Milds, whose menthol content, is about .3, kind of equal to Newport, about the same area. Of that 5.5, do you know what percent of that is in the range of .4 or similar to the Newport range?

MR. FERNANDEZ: I think Marlboro Milds was about .4, but I think it's in the submission. I don't have that stuff.

DR. CONNOLLY: It's .4. I'm talking about market share. What percent of the 5.4 is comprised with Marlboro Menthol Milds?

MR. FERNANDEZ: Marlboro Menthol Milds, I believe is about four-tenths of a share point, about half of a share point at the most.

DR. CONNOLLY: Again, it would be good for the committee to get data on the menthol

levels with market share over time. So if it is taste and low levels that may be more appealing to children that has driven this Newport, then we can maybe take a look at the Marlboro experience and help you understand this great success story you're showing us up here.

MR. FERNANDEZ: Okay, sir.

DR. NEZ HENDERSON: Can you provide data to what the rate of smoking was in 1975 for African Americans, in terms of those who smoked menthol and those who didn't smoke menthol, Mr. Jones?

MR. JONES: No. I don't have that information.

DR. NEZ HENDERSON: Could you provide that for us?

MR. JONES: I don't know if we have it, but I'll take it into consideration.

DR. SAMET: Actually, Patricia, there are probably other groups that may be better equipped to look for such data if they are available.

DR. CLARK: I have one last question for

Mr. Jones.

DR. SAMET: This is the last, last question.

DR. CLARK: Yes. You refer to the Pleasure campaign. Is there a reason you choose that phrase?

MR. JONES: I don’t know the answer to that. Again, at the time, Newport was reformulated, there was a decision to reposition the brand from a product packaging and advertising standpoint, but I really don’t know the answer to that.

DR. CONNOLLY: Jon, very quickly, it was Alive with Pleasure, not Pleasure, and you dropped the term Alive with Pleasure. I’d be curious, why did you drop the term “alive” since it is such a --

DR. SAMET: This is the last, last, last --

DR. CONNOLLY: -- robust term alive?

What was the reasoning dropping the term Alive with Pleasure?

MR. JONES: I don’t know the reason for dropping the word “alive”. I know that we’ve not used it in our advertising for a number of years, and furthermore, the execution, the themes of our advertising when we dropped alive.

DR. SAMET: Okay. Don’t dare ask another question anyone.

So you might have gathered that I think we’re at the moment for adjournment. Just again, a reminder to the committee, no discussion of the meeting topic this evening either amongst yourselves, ourselves or the press or with any member of the audience.

Remember, that we get back together at 8:00. Take anything you want. You can leave your notebooks, et cetera, here unless you want to review them tonight. And otherwise, we’ll see everyone in the morning at 8:00. Thank you.

(Whereupon, at 5:20 p.m., the meeting was adjourned.]