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FOOD AND DRUG ADMINISTRATION

FDA ACTIONS RELATED TO NICOTINE REPLACEMENT
THERAPIES AND SMOKING-CESSATION PRODUCTS
REPORT TO CONGRESS ON INNOVATIVE PRODUCTS AND
TREATMENTS FOR TOBACCO DEPENDENCE

Part 15 Public Hearing

Monday, December 17, 2012

8:00 a.m. to 3:45 p.m.

FDA White Oak Campus
Building 31, The Great Room (Room 1503)
White Oak Conference Center
Silver Spring, Maryland

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P R O C E E D I N G S

(8:01 a.m.)

MS. SIPES: Good morning to both the attendees in the conference center and to those viewing the hearing over our live webcast. Welcome to the Part 15 hearing on FDA actions related to nicotine replacement therapies and smoking cessation products, and the report to Congress on innovative products and treatments for tobacco dependence.

My name is Grail Sipes. I'm a lawyer, and I work in the Office of Regulatory Policy in the Center for Drug Evaluation and Research at FDA. And I will serve as the presiding officer for this hearing.

Before we begin, I have a few housekeeping announcements to go over. First, I have to ask you to turn off any cell phones and other mobile devices that you have, as they may interfere with the audio in this room. The hearing is being recorded and videotaped.

We ask that all attendees sign in at the table outside this meeting room. The meeting is

1 scheduled from 8:00 a.m. until 5:00 p.m. today.

2 The restrooms are located in the lobby, to
3 the left and the right hallways. If you go out of
4 the room past the coffee to the right, all the way
5 down the hallway, there are some restrooms down
6 there. We are planning to take one 15-minute break
7 during the morning, one during the afternoon
8 session, and an hour for lunch.

9 Today's lunch break is scheduled from 11:55
10 to 12:58, and as you saw, there's a little area out
11 there where food is being sold. There'll be
12 sandwiches, salads, and beverages available for
13 purchase at lunchtime.

14 In addition, as you have probably seen from
15 the abundant signage posted all about, this is a
16 tobacco-free facility. And that means that our
17 policy, which became effective on this campus on
18 January 1, 2012, prohibits the use of all tobacco
19 products, including cigarettes, cigars, pipes,
20 smokeless tobacco, or any other tobacco products and
21 electronic cigarettes, at all times. So I need to
22 remind everyone that anyone violating this policy

1 will be asked to leave the premises.

2 Turning to the hearing itself, the purpose
3 of the hearing today is to obtain broad input from
4 stakeholders on two sets of issues that are raised
5 by Section 918 of the Food, Drug & Cosmetic Act, as
6 amended by the Tobacco Control Act.

7 First, Section 918 requires that the
8 Secretary of HHS consider certain new approval
9 mechanisms and additional indications for nicotine
10 replacement therapy. Several NRTs, including
11 nicotine-containing gums, patches, and lozenges, are
12 already marketed as drug products for smoking
13 cessation.

14 Section 918 also requires that the
15 secretary of HHS, after consulting with recognized
16 scientific, medical, and public health experts,
17 submit a report to Congress examining how best to
18 regulate, promote, and encourage the development of
19 what are referred to as innovative products and
20 treatments, including both nicotine-based and non-
21 nicotine-based products and treatments, to better
22 achieve three goals.

1 The first is total abstinence from tobacco
2 use. The second is reduction in consumption of
3 tobacco. And the third is reduction in the harm
4 associated with continued tobacco use.

5 FDA will consider all the information it
6 obtains at this public hearing and in the related
7 docket submissions in its implementation of the
8 requirements of Section 918, including and drafting
9 the report to Congress.

10 A quick word for members of the press who
11 are here today, in keeping with the purpose of the
12 hearing, which is to obtain input, the panelists and
13 other FDA employees will not be available to make
14 statements to the press. I ask that you not
15 approach the panelists or other FDA employees with
16 questions. If you have any questions or concerns
17 about this, please see Jennifer Haliski.

18 I would now like to ask the FDA panel
19 members to introduce themselves.

20 DR. KWEDER: Good morning. My name is
21 Sandra Kweder. I am the deputy director of the
22 FDA's Office of New Drugs in the Center for Drug

1 Evaluation and Research.

2 DR. NGUYEN: Good morning. I'm Christine
3 Nguyen. I'm the acting deputy director for the
4 Office of Drug Evaluation II.

5 DR. RAPPAPORT: Good morning. I'm Bob
6 Rappaport. I'm the director of the Division of
7 Anesthesia, Analgesia and Addiction Products.

8 DR. WINCHELL: I'm Celia Winchell. I'm the
9 medical team leader for addiction products in
10 Dr. Rappaport's division.

11 DR. LEONARD-SEGAL: Good morning. My name
12 is Dr. Andrea Leonard-Segal. I direct the Division
13 of Nonprescription Clinical Evaluation in CDER.
14 Thank you.

15 DR. HUSTEN: Hello. I'm Corinne Husten.
16 I'm a senior medical advisor in the Center for
17 Tobacco Products.

18 MR. LINDBLOM: Good morning. And I'm Eric
19 Lindblom, director of the Office of Policy at the
20 Center for Tobacco Products.

21 MS. SIPES: All right. Thank you.

22 We have an agenda today of, I believe,

1 22 speakers who have scheduled presentation slots.
2 And in order to keep to the agenda as closely as
3 possible, I just need to go over some ground rules.

4 First, this meeting is informal. The Rules
5 of Evidence do not apply. However, there are some
6 basic rules of the road. No participant may
7 interrupt the presentation of another participant.
8 Only FDA panel members can be allowed to question a
9 presenter. We may recall a presenter for additional
10 questions, assuming that time allows and that the
11 presenter remains available in the room.

12 Public hearings under Part 15 are subject
13 to FDA policy and procedures for electronic media
14 coverage of FDA public administrative proceedings.
15 Representatives of the electronic media may be
16 permitted, subject to certain limitations, to
17 videotape, film, or otherwise record FDA's public
18 administrative proceedings, including the
19 presentations of the speakers today.

20 This meeting will be transcribed, and
21 copies of the transcript may be ordered through the
22 docket or accessed on our website approximately

1 30 days after this public hearing.

2 Each registered speaker has been given an
3 eight-minute time slot on the agenda, with eight
4 additional minutes allotted for the FDA panel
5 members to ask questions. If a speaker goes over
6 the eight-minute time slot, the time allotted for
7 questions may be reduced accordingly. If the panel
8 has questions, we may ask the speaker to stop after
9 eight minutes so that those questions can be
10 addressed within the time allotted.

11 If a speaker ends early or if the questions
12 from the panel do not take the full eight minutes,
13 we intend to move on to the next speaker. This
14 means that speakers may find themselves being called
15 up to present before the time that is listed on the
16 agenda.

17 So if you're scheduled to speak, please
18 keep track of where things stand in terms of the
19 presenters so that you are in the room and ready to
20 go when your turn arrives. We will take the
21 registered speakers in the order in which they are
22 listed on the agenda.

1 One update to the agenda, we just found out
2 very recently that one of the individuals who was
3 scheduled to speak in the morning, Mr. Ronald Ward,
4 will not be attending. So, Mr. Williams, you'll be
5 moving up to his position on the agenda.

6 Now, while the speakers' time slots may
7 move up, as I have just described, we do intend to
8 keep the morning break, the afternoon break, and the
9 lunch break as close as possible to the times that
10 are currently listed in the agenda. So the morning
11 break is currently scheduled for 10:02, lunch at
12 11:55, and the afternoon break at 2:50.

13 For those of you who did not register to
14 make a presentation but would still like to speak at
15 this hearing, you may speak during the open public
16 comment period, which is currently scheduled from
17 3:54 to 4:50 p.m. Those interested in presenting
18 during the open public comment period should print
19 their names clearly on the list, which is on the
20 table outside this room.

21 In the interest of accommodating as many
22 speakers as possible, we will extend this comment

1 period longer if we are able to do so. For example,
2 if we complete all the registered speakers and all
3 the questions from the panel ahead of schedule,
4 which may happen, extra time will be added to the
5 open public comment period.

6 We will try to accommodate as many requests
7 to speak as possible. Please recognize that some
8 panelists may need to leave if the open public
9 comment period goes beyond 5:00.

10 This hearing is not your last chance to
11 comment. The docket will remain open until
12 January 16th. Federal Register notice gave the date
13 of January 2nd, but that date is going to be
14 extended, and I expect that to be confirmed shortly
15 in a notice published in the Federal Register.

16 We strongly encourage all interested
17 parties to comment, and you can see the Federal
18 Register notice announcing this hearing for details
19 on how to submit comments to the docket.

20 Given the full agenda, we request that each
21 speaker keep to the eight minutes allotted so that
22 we're able to stay on time. When you speak, you'll

1 come up to this podium. You'll see that there's a
2 small light on the desk over there, which will be
3 green when you begin. It will go to a yellow light
4 when you have one minute left, and when time is up,
5 it will start flashing red. So if that happens, I
6 may have to ask you to stop. I apologize in advance
7 if I'm interrupting any of you.

8 We thank you very much for your interest
9 and your participation today. I've been very
10 pleased to see, as we put together the agenda, that
11 we have consumers, individuals, the public health
12 community, the tobacco industry, the pharmaceutical
13 industry, the electronic cigarette manufacturers,
14 and others all represented here today. We look
15 forward to a very productive public hearing.

16 So let us proceed with the presentations.
17 The first speaker is Mr. Gregory Conley, speaking as
18 a private citizen.

19 MR. CONLEY: Good morning. Let me first
20 say that I've only drank about a half a cup of
21 coffee this morning, so if I fall asleep at the
22 podium, all I ask is that you don't wake me up until

1 my eight minutes are finished.

2 For more than two decades, one of the most
3 prominent facets of tobacco control in the United
4 States has been the promotion of nicotine
5 replacement therapy products. However, during
6 the entirety of this time period, NRT packaging has
7 perpetuated the false myth that nicotine is the
8 harmful part of smoking by warning users, one, not
9 to use any NRT product for more than 12 weeks, and,
10 two, not to use any NRT in combination with a
11 tobacco product.

12 Approximately two years, the FDA CDER held
13 a two-day scientific workshop on the risks and
14 benefits associated with the long-term use of NRT
15 products. Over the course of those two days, there
16 was wide agreement among attendees that NRTs are far
17 less hazardous than smoking, that use of NRTs beyond
18 the 12-week window currently recommended would be
19 beneficial to some smokers, and that packaging on
20 NRTs should be updated to truthfully inform smokers
21 that long-term use of NRTs is one option that can be
22 considered.

1 Unfortunately, in the two years since that
2 hearing, no action has been taken to improve public
3 health by loosening these unnecessarily rigorous
4 standards. With this hearing, the CDER again has
5 the opportunity to push to revamp the outdated
6 mechanisms that govern NRT products in the United
7 States.

8 It is vital that the panel and the
9 Secretary of the DHHS recognize that Section 918(b)
10 of the Tobacco Control Act does not just require a
11 report to be produced covering innovative products
12 and treatments to achieve total abstinence from
13 tobacco use.

14 Instead, the panel and secretary must also
15 consider innovations and changes to current law that
16 foster two other goals: one, reducing consumption
17 of tobacco, and, two, reductions in the harm
18 associated with continued tobacco use.

19 The fact that a sizeable minority of NRT
20 users wisely ignore warnings and use NRT for as long
21 as necessary to avoid a relapse back into smoking
22 should come as a surprise to no one in this room and

1 no one on this panel. Indeed, early trials of the
2 nicotine gum showed that between 2 percent and
3 9 percent of patients were still using the gum
4 12 months in. Studies of this subset of NRT user
5 population show that in addition to withdrawal
6 relief, long-term users also find that smokefree
7 nicotine products are helpful in weight control and
8 an aid in concentration.

9 Furthermore, a pooling of studies that
10 randomize patients to NRT or placebo for long-term
11 maintenance found that the use of NRT "appears to be
12 effective in preventing relapse following an initial
13 period of abstinence."

14 In regards to the health effects of long-
15 term NRTs, a succinct summary of the evidence was
16 given by Dr. Neal Benowitz to the CDER two years
17 ago, October 26, 2010. Because of the novel nature
18 of NRTs and the lack of studies regarding long-term
19 use of these products, NRT safety has traditionally
20 been judged by examining data on the effects of
21 smokeless tobacco.

22 After reviewing the existing evidence

1 regarding smokeless tobacco user outcomes,
2 Dr. Benowitz noted, "The lack of increase in common
3 cancers in lifelong smokeless tobacco users
4 indicates that nicotine is not a general cancer
5 promoter."

6 On the topic of cardiovascular disease,
7 Dr. Benowitz found that studies of users of Swedish
8 snus, a tobacco product that is low in TSNAs and can
9 be adequately compared to modern NRTs, indicated
10 minimal if any risk of CVD with smokeless tobacco.

11 Furthermore, tremendous advocates of
12 tobacco harm reduction have performed calculations,
13 such as one person speaking today, Dr. Carl
14 Phillips, who found, studying Swedish snus users,
15 that the average snus user loses about one to two
16 months off their life, as compared to smokers, who
17 lose up to ten years or more.

18 This panel should also make two other
19 recommendations as it relates to NRT and Chantix.
20 First, in recognition of the dismal success rates of
21 NRTs when used for the treatment of tobacco
22 dependence and as a smoking cessation aid, the panel

1 should recommend that existing NRTs be unapproved
2 for these functions.

3 Additionally, the panel should act swiftly
4 in recommending that Chantix be unapproved as a
5 treatment for tobacco dependence, and most
6 importantly, that smokers be warned of suicide and
7 cardiovascular risk posed by using the product.
8 Just last week the FDA warned of cardiovascular
9 risk, but they have not done their part to warn the
10 public about the suicide and depression risks.

11 The pressing need for more warnings is
12 demonstrated by the Department of Health and Human
13 Services' outdated and inaccurate "Be Tobacco-Free"
14 website on electronic cigarettes, which recommends
15 would-be quitters use Chantix instead of electronic
16 cigarettes.

17 While the "Be Tobacco-Free" website spends
18 several paragraphs on warnings about the
19 hypothetical risks posed by electronic cigarettes,
20 the Department fails to dedicate even a single
21 sentence to warning smokers of the very well-known
22 and well-documented risks associated with Chantix

1 use.

2 Additionally, the panel should not
3 recommend fast-tracking of any non-nicotine
4 medication intended to treat smokers' dependence.
5 As the Chantix experience has already shown us, a
6 tinkering with smokers' brains can have disastrous
7 and tragic results.

8 Additionally, while not required by the
9 Tobacco Control Act, the CDER should go further in
10 their recommendations. With the recent explosion in
11 the use of electronic cigarettes, and to a lesser
12 extent, snus as well as the publicity firestorm
13 erupted by the tobacco industry's decision to market
14 what are essentially nicotine lozenges as a
15 dissolvable tobacco product, there has never been a
16 moment in our history where tobacco harm reduction
17 has had such wide visibility.

18 There are no signs that interest by smokers
19 in quitting smoking but not quitting nicotine, or
20 simply dramatically reducing their smoking
21 intake -- there is no evidence that this interest in
22 tobacco harm reduction is going to decline. If

1 anything, next year we will see electronic
2 cigarettes surpass NRT sales.

3 With this in mind, the CDER should
4 recognize that all existing evidence points to the
5 long-term use of smokeless tobacco, dissolvable
6 tobacco, and electronic cigarettes being nearly or
7 just as non-hazardous as the use of NRTs.

8 In conjunction with this finding, the CDER
9 should recommend that agencies of the DHHS,
10 including the FDA Center for Tobacco Products and
11 the Centers for Disease Control, stop misinforming
12 the public about the health effects of these
13 products.

14 I would like to thank the panel for
15 seriously investigating these important issues, and
16 I would be glad to answer any questions.

17 MS. SIPES: Thank you.

18 I don't believe there are any questions.
19 Thank you very much.

20 MR. CONLEY: Thank you.

21 MS. SIPES: All right. Our next speaker is
22 Ms. Lorie McClung, also speaking as a private

1 citizen.

2 MS. MCCLUNG: I'm Lorie McClung, owner of
3 Nimble Fingers, a small retail shop offering life
4 choices information and products. I'm not now,
5 never have been, nor do I wish to be a health care
6 professional.

7 My business grew out of my personal
8 experience with smoking and becoming an ex-smoker.
9 During my 28-year relationship with cigarette
10 smoking, I tried the patch repeatedly. The most
11 difficult thing for me was the big decision that
12 loomed each time I considered stopping smoking. I
13 dreaded that deadline and the doing without.

14 I would set a date. I would smoke far
15 heavier on the days leading up to that date. I
16 would start the set date with a patch. I might make
17 it a few days, or even a few weeks, but there was
18 never a time when I didn't want to smoke.

19 Eventually, some event would give me the excuse to
20 light up. Then I would put the patches away and go
21 right back to smoking full-tilt.

22 I believed using NRT products was an all-

1 or-nothing process. I further believed smoking and
2 nicotine were synonymous. In January of 2011, I
3 learned otherwise. After deciding to use nicotine
4 without smoke, I made a switch that changed and
5 probably saved my life.

6 Today my goal is to share with others what
7 I've learned of the relative risks of numerous,
8 everyday items, including personal fragrance,
9 detergents, and soaps; skin and hair care products;
10 and different forms of nicotine, and let others
11 decide for themselves if they wish to make any
12 changes in their lives. The majority of my time,
13 however, is spent with smokers, ex-smokers, and
14 their families.

15 My methods are that through personal
16 interviews, I learn their history with smoking; why
17 they wish to make a change, whether that be
18 professional or health-related; what methods they've
19 tried in the past to make a change; and the results
20 of those methods.

21 At this point, we proceed with these facts.
22 There are real reasons why they've continued to

1 smoke in spite of health consequences, warnings, and
2 costs. The methods they've tried fail over
3 95 percent of the time, stressing it is the method
4 that fails and not the smoker.

5 If they're smoking, they have chosen the
6 most dangerous method of getting nicotine; that all
7 nicotine sources vary greatly, and there are overall
8 risks. If they choose to eliminate nicotine, they
9 should not be surprised if they, like myself,
10 require another product to replace the lost benefits
11 of nicotine such as anti-depressants, anti-anxiety.

12 Then I give them the opportunity to decide
13 for themselves how they would like to proceed this
14 time around. The vast majority decide to try
15 smokefree cigarettes. From there, we go into the
16 training and using equipment and liquid according to
17 their personal preferences.

18 The results of this, all have reported
19 continuing health improvements, often verified by
20 their physicians. None have reported any adverse
21 effects, some with usage in excess of a year.

22 There are over 400 vapers in our area that

1 have either completely stopped smoking cigarettes or
2 have drastically, from packs per day to three
3 cigarettes per day, reduced their cigarette smoking,
4 with the latter being the extreme minority.

5 The same cycle that I went through as a
6 smoker that wanted to stop smoking is not uncommon.
7 I hear it daily. I tried the patch or the gum, and
8 didn't smoke for days or months. Then I just had
9 one cigarette, and I was right back to packs a day.

10 In this recounting, I hear numerous things
11 like, "I was stupid. I don't have the willpower.
12 I'm weak. It's just so hard." We already know
13 plenty of things that don't work: current methods.

14 Some things that do work:

15 Educating smokers about the benefits of
16 nicotine: real reasons for using nicotine that are
17 not in any way related to intellect or income;

18 Sharing the fact that it is the smoke that
19 causes death and premature disease;

20 Treating smokers like adults;

21 Making zero judgments upon smokers and
22 their choices about continuing to smoke or not;

1 Reminding smokers that they are a cash cow
2 and should never sacrifice their dignity, in
3 addition to their health and money, to any person or
4 organization that benefits from their continued
5 smoking;

6 Stressing that the failure lies with the
7 method, not the smoker;

8 Removing comparisons of cigarettes to
9 alcohol and illegal drugs. People don't miss work,
10 cause fatal auto accidents, or resort to physical
11 violence because they are under the influence of
12 nicotine.

13 By admitting it is the product that fails,
14 this relieves the smoker's sense of guilt and
15 failure. How many times can anyone be expected to
16 seek the experience of personal defeat and return as
17 a customer? Feelings of guilt result in increased
18 cigarette consumption.

19 Please stop stating how difficult it is to
20 stop smoking. Can you imagine a coach sending an
21 athlete into a competition with a pep talk like,
22 "Your odds of winning are pretty slim"?

1 Do not impede the availability of anything
2 that results in less use of a product proven to be
3 dangerous and deadly. Stop encouraging smoking.
4 Recognize that the common man has common sense, but
5 is still influenced by your authority. Do not
6 forfeit your authority by insisting the greatest
7 danger to the common man's health lies anywhere
8 other than with burning tobacco.

9 Use your authority responsibly and educate
10 the public about the relative risks of different
11 forms of nicotine, all the while maintaining that
12 burning tobacco is by far the deadliest, most
13 harmful source of nicotine.

14 I suspect that had I not thought of using
15 NRT products as an all-or-nothing choice, and had
16 continued to have the occasional cigarette while
17 wearing the patch, I might very well have continued
18 using the patch indefinitely and eliminated
19 cigarettes entirely. This would only have been
20 possible had I been given information confirming
21 that nicotine without smoke did indeed have
22 benefits.

1 In closing, there's one simple thing I will
2 share with everyone that is or knows or cares about
3 a smoker. Simply eliminate the word "quit" from
4 your vocabulary. Quit is a four-letter word to a
5 smoker. It makes cigarettes the center of their
6 universe. In our minds, quitting equals suffering,
7 and no one willingly goes toward suffering.

8 MS. SIPES: Thank you very much.

9 I don't believe there are any comments.
10 Thank you -- oh, I'm sorry.

11 DR. LEONARD-SEGAL: Thank you for your
12 presentation. I guess that one question that I
13 would have -- it seems like you've done a lot of
14 thinking about this, both on a personal level and in
15 an effort to help other people. We have some
16 nonprescription products that are NRTs that are
17 designed to help people quit smoking. Obviously,
18 you know this. And I'm wondering if, with your
19 experience, you could think of a way that we can
20 enhance the behavioral information on OTC products
21 to help be more informative.

22 You've said, don't tell people it's hard to

1 quit. I think that maybe some people would think
2 that that is an encouraging comment because if
3 somebody has trouble, then they would know that
4 they're not alone, but that this is -- do you have
5 specific ideas for us as to what we could put with
6 some of these products in terms of additional
7 information to help people in their efforts to quit?

8 MS. MCCLUNG: I am going to be submitting
9 written testimony as well. I'll make a note to put
10 something specific like that in my written response.

11 DR. LEONARD-SEGAL: Thank you.

12 MS. MCCLUNG: Thank you.

13 MS. SIPES: Thank you very much.

14 Our next speaker is Mr. Carl Phillips, also
15 speaking as a private citizen.

16 DR. PHILLIPS: Thank you. I'm here as a
17 private citizen, but I've been a long-time advocate
18 and researcher on tobacco harm reduction, probably
19 almost as long as anyone, trying to understand and
20 promote the substitution of low-risk alternatives
21 for smoking.

22 My talk is adhering closely to a couple of

1 the questions. First, question 4.4 asks, what is
2 harm, basically, and which harms are important?
3 Harm -- this is kind of obvious -- does refer to
4 actual harmful effects, which include the increase
5 in the risk of deadly or debilitating disease in the
6 future, or immediate problems of functioning, pain,
7 distress, and so forth, both of which fall into the
8 important category.

9 It's obvious, but what this notably
10 excludes is addiction. Addiction not only is not
11 well-defined, either scientifically or medically,
12 but it's perhaps arguably a reason for a behavior
13 that might be a harm, but it is not a harm in
14 itself. And so if the biggest "harm" from nicotine
15 use absent smoke is addiction, that's hardly a harm
16 at all.

17 Equally important when calculating harm, it
18 must be considered in net terms, as is done for
19 treatment drugs and everything else that the
20 government properly regulates. Nothing is harm-
21 free, but the harm may be low or trivial compared to
22 the benefits.

1 The "this is harm, and therefore it's bad"
2 attitude that you sometimes see from extremist
3 advocates on the Internet makes for terrible public
4 policy about any product. But it's what you get if
5 you don't consider the net.

6 So on the net side, there are psychological
7 benefits from nicotine that improve functioning and
8 treat, in some sense, various psychological
9 conditions, which are highly important advantages of
10 using nicotine rather than being abstinent for many
11 people.

12 But it's not just the medicalized side
13 of things. Acting as if nicotine is purely a
14 treatment for a disease, rather than recognizing it
15 as a consumer good that serves other preferences, is
16 simply out of touch with the obvious reality. Many
17 people use nicotine because they like the effects,
18 which is also highly important when considering it.
19 If the drug side of FDA is not accustomed to dealing
20 with it, you might consider talking to the people on
21 the food side who regulate things, keeping in mind
22 that the purpose of food is not merely to alleviate

1 starvation. It serves many other purposes.

2 The net health benefits need to be based on
3 probability weighted but for choices. So if there's
4 a 20 percent chance that someone would be abstinent
5 but for the option of long-term use of a low-risk
6 alternative and an 80 percent chance they would
7 smoke, they need to be compared not to the
8 abstinence but to a .8 times the risk they would
9 suffer from smoking.

10 It's simply out-and-out wrong to compare
11 the risk from a low-risk alternative to some
12 unrealistic best case world. And again, this is not
13 an odd concept. This is how treatment drugs are
14 always considered from a regulatory perspective.

15 Continuing on that thought, sometimes
16 efforts to achieve abstinence themselves are quite
17 harmful. It's already been mentioned that using
18 Chantix is quite hazardous in itself. And most
19 importantly, I would argue -- and this was slightly
20 misquoted by a previous speaker -- but my previous
21 research points out that someone who tries to
22 achieve abstinence but relapses for just a while,

1 just a couple of more months of smoking, the
2 resulting risk from that smoking is greater than the
3 risk of using a smokefree nicotine product for the
4 entire rest of their life. And there aren't very
5 many people who don't suffer that relapse.

6 With regard to question 4.6, which asks
7 what FDA and HHS can do to better promote public
8 health in terms of these goals, to best promote
9 public health, the most important thing for HHS
10 to do is to stop lying.

11 I've been documenting disinformation
12 campaigns that are intended to discourage smokers
13 from switching to low-risk alternatives for more
14 than ten years, and have found that units of HHS are
15 the world's biggest anti-THR liars. FDA has now
16 joined other agencies within that department in
17 published disinformation that's designed to
18 discourage smokers from switching to low-risk
19 alternatives.

20 The anti-THR messages encourage people to
21 smoke, and no conceivable amount of low-risk product
22 use could cause as much health harm as has been

1 caused by discouraging smokers from switching to the
2 low-risk alternatives over the last decade.

3 The practice of promoting "total abstinence
4 from tobacco use," to quote back from the question
5 that I'm answering, at the expense of discouraging
6 "reductions in the harm associated with continuing
7 use," again quoting from that question, is
8 guaranteed to be bad for public health.

9 Finally, to very briefly address
10 question 4.7, how these broader outcomes can be
11 taken into account in premarket evaluation -- this
12 is a topic I've been working on, and a fair bit in
13 my research over the last six months has been on
14 this topic. I don't have time to go into much
15 detail, obviously, but a couple of points to make on
16 this.

17 Focusing on the net effect on the smoking
18 rate is the key to any such modeling. Everything
19 else is a rounding error. It doesn't matter how
20 many people are using these products compared to how
21 many people are smoking.

22 When doing the modeling, it's necessary to

1 look at actual consumer preferences. People act
2 based on incentives. They are not black boxes that
3 just change behavior for no apparent reason, which
4 unfortunately is the way that most of the models
5 have been done so far.

6 That is it. I originally planned this for
7 the original seven minutes that we had available,
8 and wasn't able to change my slides. So I will stop
9 with that. But obviously, I'm available for
10 questions.

11 MS. SIPES: Thank you.

12 DR. HUSTEN: Yes. I was interested if you
13 could explain a little bit more the data behind your
14 statement that if someone smokes just a couple more
15 months, the risk is greater than from using a
16 low-risk alternative for a lifetime.

17 DR. PHILLIPS: Sure. Well, the key to
18 this -- and the key at the core of that -- is
19 estimating the comparative risk, obviously. And
20 that's based on the estimate that the low-risk
21 alternatives are approximately 1 percent as risky as
22 smoking.

1 This is based on the extensive evidence we
2 have about smokeless tobacco, which is well-studied,
3 as opposed to the relatively limited evidence we
4 have about the products that are the focus today,
5 and e-cigarettes even less so. But it seems safe to
6 extrapolate that number.

7 Once you have that number and you have the
8 widely established estimates about the toll from
9 smoking, it's a fairly straightforward population
10 modeling exercise to compare people who are smoking
11 for two more months, and thus experiencing the
12 fraction of the lifetime risk that would result from
13 smoking, and compare them to that relatively low
14 risk.

15 Now, that 1 percent may even be an over-
16 estimate, frankly, and there's really very little
17 reason to believe that it's an underestimate. So if
18 anything, that's fairly conservative.

19 Did you want me to go into more detail of
20 the net results?

21 DR. HUSTEN: I just had one follow-up
22 question. I was wondering if your model included

1 any assumptions about the number of people who
2 continued to use cigarettes in addition to the
3 alternatives, so become dual users, and in fact
4 potentially increase the duration of their cigarette
5 use. Does the model have any assumptions about
6 that?

7 DR. PHILLIPS: Right. So that particular
8 model, as opposed to the ones that I'm working on
9 right now, didn't actually make any prediction. So
10 it says, if this happens, then that will happen.
11 And, basically, anybody who was a dual user and
12 continued to smoke quite a lot in that model was
13 considered to not have quit smoking, so they were
14 still on the bad side of the equation. They were
15 one of the ones who two months more would be as bad
16 as the complete switch.

17 So this was, again, focused on the complete
18 switch. And, again, the message there was
19 that -- the title of the paper emphasized that
20 pushing for abstinence only is not necessarily the
21 healthiest option because, again, the
22 relapsing -- or the dual using, if that includes a

1 heavy amount of smoking, as you're pointing
2 out -- is worse than, again, the lifetime use of the
3 smokefree product.

4 DR. HUSTEN: So do you have any kind of
5 data about the number or percent of people who maybe
6 would have quit, but instead of quitting, they fall
7 into this category of dual user?

8 DR. PHILLIPS: Yes. Well, that's more of
9 what I'm trying to just start working on now in
10 terms of the predictive models of what people are
11 going to be doing. No, that's quite difficult. And
12 one of the reasons that it's difficult is that
13 second -- or whatever; it would be third, third
14 bullet on this slide right here, which is that
15 people act on preferences as well as on information.

16 There are relatively few people,
17 unfortunately, even today, who understand that
18 switching to the low-risk alternative really is
19 approximately as good as quitting for their health.
20 And so they choose to dual use for any number
21 reasons, time and place restrictions and so forth.
22 And they are not being motivated by the same

1 motivation that they might have to quit, that is,
2 the health benefits.

3 So in terms of predicting what people are
4 going to do, that's entirely depending on what
5 message that they're getting. And to the extent
6 that people are able to start getting the accurate
7 message that dual use is not nearly as good for you
8 as switching entirely to the smokefree alternative,
9 they're likely to continue to do it; whereas if they
10 got a very clear message that the smokefree
11 alternative is basically the same as quitting,
12 whereas dual use a lot like continuing to just
13 smoke, we would see a much greater change. So the
14 prediction is highly dependent on social factors.

15 DR. HUSTEN: Just one last follow-up
16 question. A lot of the marketing that we see for
17 products, really, is more promoting to use when you
18 can't smoke. So it seems to actually be promoting
19 more of the dual usage.

20 So do you have any thoughts about how to
21 minimize the effect of that to get to the end that
22 you're trying to achieve?

1 DR. PHILLIPS: Yes. Well, first off, I'm
2 not sure the characterization that a lot of it is
3 that way is accurate. But certainly some of it is,
4 although some of it goes as far as the companies
5 legally can in order to encourage switching for
6 harm-reduction purposes.

7 But not only is the government actively
8 lying about, not the lack of benefits from harm
9 reduction, but it strictly prohibits merchants from
10 telling people the correct information.

11 So the very straightforward answer to that:
12 allow those who are selling -- pharmaceutical
13 nicotine products, e-cigarettes, smokeless
14 tobacco -- to explicitly point out that this is a
15 lower-risk alternative to smoking; or, better still,
16 change the labeling that's on the packages so that
17 it says that. And also change the labeling on
18 cigarettes, trying to aim people toward the lower-
19 risk alternatives that they could be using.

20 MS. SIPES: Picking up on that question, on
21 Corinne's questions, what about a situation
22 where -- you talk about the manufacturers of these

1 alternative products being able to talk about the
2 lower risk, as you describe it. What if the same
3 person is marketing the combustible and the lower-
4 risk products?

5 DR. PHILLIPS: Well, it's an interesting
6 question. But there seems to be a willingness
7 of those who are marketing both products to
8 cannibalize their own customer base away from
9 the combustible products and to the low-risk
10 alternatives.

11 From what I've seen, I believe that this is
12 extremely genuine on the part of many of these
13 companies. And if they were allowed to -- if they
14 were allowed to say more, they would, and they would
15 be happy to lose cigarette customers in favor of
16 their smokefree business.

17 MS. SIPES: All right. Again, a slightly
18 related follow-up. In your last slide, you talk
19 about an important consideration being modeling
20 actual consumer preferences. And you've spoken a
21 little bit about some of that in the discussion
22 we've just had.

1 Are there other types of consumer
2 preferences that we haven't talked about that
3 you think are important to this discussion?

4 DR. PHILLIPS: Well, right. So there
5 are -- the consumer preference is to consume
6 nicotine rather than not, which is true for many
7 people, many of us in this room. There are -- the
8 consumer preference is to engage in a socially
9 acceptable behavior.

10 So I recently presented a paper which
11 models the use of low-risk alternatives,
12 e-cigarettes in particular, as a bit of social
13 contagion. So, that is, the greater the use of
14 these products, the more people who are using them
15 in one's social circles or that you encounter, the
16 more likely any given individual is to switch,
17 "individual" being, of course, a current smoker
18 who's a potential candidate for harm reduction. So
19 that's n absolutely critical consideration.

20 As I mentioned, there is the information
21 coming from both trusted sources; the government;
22 advertising sources, which people, of course, don't

1 fully trust but do gain some information from. That
2 makes a lot of difference in terms of peoples'
3 understanding and so forth.

4 But I think the real key to keep in mind is
5 that smokers are not idiots. They do not believe
6 that what they are doing is -- they understand that
7 what they're doing is as harmful as we all know it
8 to be. And yet they're still choosing to do it
9 because given the choices just between abstinence
10 and smoking, abstinence is a poor choice for them.

11 If given a third alternative that could
12 trump both of those, then a lot of people would make
13 the move to it. The question is, basically, how are
14 they going to find that out? How is it going to
15 become socially acceptable?

16 It will, I think, in both cases. The
17 answer is, it will happen. The question is whether
18 the U.S. government, among others, is going to help
19 it happen or is going to slow it up.

20 MS. SIPES: Okay, thank you. Thank you
21 very much.

22 DR. PHILLIPS: Thanks.

1 MS. SIPES: Our next speaker is Mr. Linc
2 Williams, again speaking as a private citizen.

3 MR. WILLIAMS: Good morning. My name is
4 Linc Williams. I am a documentary filmmaker, but
5 I'm here talking today about my experience with
6 NRTs. So I'm going to briefly run you through my
7 experience, what I think the future of NRTs are, and
8 then my recommendations for what I think actions
9 should be.

10 So a little bit of history from me. I
11 smoked for 23 years, and I'm just going to get this
12 out of the way. The only person I blame for my
13 smoking is myself, not the tobacco companies, not
14 any of that. I made the choice. I fully knew that
15 it would probably kill me, but I chose to take up
16 the habit anyway. I was young. I wasn't
17 necessarily making the wisest decisions. But I did
18 it.

19 So 17 years of that 23 years, I actually
20 was on the road of trying to quit. The last ten
21 years of that, I was a four-plus-a-day smoker of
22 cigarette packs. I went through multiple cartons in

1 a week. I tried patches. I tried the gum. I tried
2 lozenges. I even tried hypnotherapy, which lasted I
3 think about somewhere around seven minutes. Very
4 effective.

5 (Laughter.)

6 MR. WILLIAMS: I bought magnets to put
7 along my wrists and on my ears, but none of that
8 helped. I tried Wellbutrin, and didn't affect it at
9 all. And I had a severe reaction to Chantix. After
10 about three to four days of taking Chantix, I
11 started having uncontrollable rage and suicidal
12 thoughts. Luckily, my family was keen enough to
13 recognize it, to get me to a doctor, and to get
14 treatment to be able get off of the Chantix.

15 Within two weeks of being off the Chantix,
16 I was back to my normal self. But I was one of
17 those few, where you hear the stories of Chantix's
18 side effects. I got to see it firsthand, and it was
19 not a pleasant experience.

20 I've also done support groups -- Smokers
21 Anonymous -- and guided help lines, where you would
22 call, and daily they would call you and remind you

1 of why you were quitting and all of that.

2 My longest quit period was actually using a
3 combination of wearing 24-milligram patches, and
4 then when the urge really came along, using nicotine
5 lozenges to get me through those urges. And that
6 lasted nine months, until I revealed to my doctor
7 that I was doing that, and I was told that it was
8 extremely bad for my health and I had to stop.
9 Within stopping of using the nicotine lozenges with
10 the patches, within three weeks I was back to
11 smoking again.

12 My average quit time was about one month,
13 some of them a little less. The hypnotherapy was, I
14 said, about seven minutes. My wife and I estimate
15 that I've literally spent close to \$17,000 on
16 cessation gimmicks, products, et cetera over the
17 course of that 17 years. So it's been a significant
18 investment for it.

19 So three years ago, I was 342 pounds.
20 Massively overweight. I was a type 2 diabetic; I
21 still am a type 2 diabetic. I was taking 180 units
22 of Humalog a day. I was also taking eight oral

1 medications to be able to get through it. I could
2 barely climb and walk a set of stairs, and I had
3 resigned myself to the fact that I was never going
4 to quit smoking.

5 Today, I've now been 28 months smokefree.
6 I'm now at 240 pounds, not exactly a fit and thin
7 what I would consider model of health, but it is a
8 dramatic improvement, just in my life and that. I'm
9 still diabetic because you're never really diabetic,
10 but no longer take insulin. I no longer have to
11 take any oral medication. I just have to control my
12 diet and exercise.

13 There's a little typo on this. I
14 apologize. In October 2012, which is just a couple
15 months ago, I ran my first 5K, which, if you had
16 asked me three years ago if I was even going to run
17 a block, I would have laughed and said that time of
18 my life had gone by. And today I'm resigned to
19 never smoke another cigarette again. But I still
20 use nicotine. I use nicotine in multiple formats.

21 So how did I get to here today? I wasn't
22 trying to quit. That was the first thing that came

1 out. I didn't want to quit. My goal is to try and
2 save some money and cut back on my consumption, and
3 try not to smell like cigarettes around my wife and
4 daughter because they were the biggest naggers in my
5 life, and I love them. But every day, it was, come
6 home, go take a shower, just because of the smoke.

7 I used cigarettes with my choices of
8 nicotine for three months. Dual user. But a lot of
9 people talk about this dual user thing. I smoked
10 four packs a day. When I was dual using, I was
11 smoking less than a pack a day. So there was a
12 benefit to that.

13 Now, after three months, it turned out I
14 liked the alternatives better than actual smoking.
15 My taste started to return, those type of things.
16 And also, by not smoking and using the nicotine
17 alternatives, my entire diet changed. The
18 McDonald's greasy hamburger didn't taste as good as
19 it used to. Simple things like salad and bleu
20 cheese; the taste returned.

21 Oh, and I forgot to mention. My choice of
22 nicotine today is electronic cigarettes and snus.

1 And I would include nicotine lozenges on that, but
2 when I compare the price of nicotine lozenges to the
3 other alternatives, it just doesn't make sense for
4 me. I think if there were a lower-price
5 alternative, then potentially that would be
6 something that would be included.

7 I am resigned to I will never give up
8 nicotine. I'm a nicer person with nicotine. I
9 enjoy my life with nicotine. And I don't have the
10 serious health benefits (sic) that I had with
11 smoking.

12 So the future -- so the things I would like
13 to encourage you to do is, one, I want to see NRTs
14 encouraged for people to use for long term. This 8
15 to 12 weeks is not enough to really break a cycle of
16 smoking.

17 I'd also like to see it encouraged for
18 temporary use. I got into it because I wanted to
19 temporarily not smoke, to be able to go out and,
20 say, wear a patch when you're on a plane so that you
21 can get through the flight. Those type of things,
22 I'd like to see that happen.

1 Because of my experience was unsuccessful,
2 I don't think that NRT products should be a tobacco
3 dependence product. I think they should be a
4 tobacco harm-reduction product because I think they
5 fail significantly when they're used just as a
6 tobacco dependence product.

7 My personal experience with Chantix, I
8 would encourage you -- I would like to see it
9 removed from the market completely, especially since
10 the reactions that I had to it, and no kind of real
11 warning other than little small printed text at the
12 bottom. It wasn't sufficient, so I think the public
13 needs to be informed about that.

14 I'd like to see the government invest in
15 harm-reduction strategies as opposed to
16 abstinence-only strategies. And I'd like to see
17 them promote a multivector program for tackling
18 harm reduction as well as lifestyle improvement.
19 And when I say multivector, I think it's about
20 finding that not everybody is the same. And right
21 now, when you've gotten down to smokers, they
22 are -- I'm running out of time -- they are

1 different, very different. The ones that were going
2 to quit have quit. The tough cases are really
3 what's left.

4 Final recommendations: Include
5 stakeholders. This is the first opportunity I've
6 seen for, as a smoker, to be able to come in and
7 talk. I want to see more smokers, ex-smokers, NRT
8 users, participating in panels and providing
9 feedback and making that information available. And
10 I'd also encourage you to invite groups like CASAA
11 and AEMSA and SAFTA, who are interested in the
12 industry and who are trying to improve things and
13 bring them to the table and have discussions with
14 them.

15 I know my time ran out. I apologize. Yes,
16 ma'am?

17 MS. SIPES: Thank you very much.

18 DR. LEONARD-SEGAL: Thank you for sharing
19 your personal story with us.

20 So we have data that supports that NRTs and
21 Chantix help some people quit, not everybody, not
22 even necessarily the majority of people that are

1 seeking to quit. But we have data that support that
2 the products help some people quit, and do it safely
3 and effectively, which is why they're approved.

4 So I want to be sure I'm understanding that
5 you're -- are you approaching this as an either/or?
6 Are you suggesting by unapproving that we not be
7 thinking about those people that can benefit from
8 those drugs, as they are currently approved, and
9 remove all that and just be looking towards long-
10 term use or --

11 MR. WILLIAMS: Not towards long-term use.

12 DR. LEONARD-SEGAL: But what do you --

13 MR. WILLIAMS: My personal belief is that
14 through tobacco harm-reduction strategies, those
15 people, that 5 percent that would successfully quit,
16 would still quit using the THR route as opposed to
17 just going and promoting.

18 I think you get much greater public
19 benefit -- by encouraging the harm-reduction
20 strategies, you will find more who are able to
21 successfully quit over the long run than just the
22 3 to 5 to even 10 percent that use those to quit.

1 I'm not saying don't use it as a cessation.
2 Ultimately, cessation should be the ideal golden
3 path. But I'm saying if you only pursue the ideal
4 golden path, you lose 90 percent.

5 DR. LEONARD-SEGAL: May I follow-up, then?
6 So when you're saying unapprove, you're not really
7 meaning that. You're meaning that there could be
8 multiple paths to a goal to improve the public
9 health. Is that what you're saying?

10 MR. WILLIAMS: The only one I say
11 unapprove, really, for is Chantix. And that is my
12 personal experience and not being educated on the
13 real risks of using Chantix. Now, I understand I'm
14 a small percentage that reacted in that way. But
15 there's still a significant amount that there are
16 actually deaths associated with it.

17 My personal belief is because it was fast-
18 tracked and that there wasn't actually enough
19 studies on it. And when you start to mess with the
20 chemistry of the brain, I don't think any type of
21 non-nicotine-based product should be fast tracked
22 through. That's my personal opinion.

1 DR. LEONARD-SEGAL: And one more follow-up
2 question. I see that in your personal story, you
3 were able to stop smoking for nine months
4 completely, with nothing else. Right?

5 MR. WILLIAMS: Well, with using the
6 combination of a patch and nicotine lozenges.

7 DR. LEONARD-SEGAL: Okay.

8 MR. WILLIAMS: My best cold turkey attempt
9 was less than a month.

10 DR. LEONARD-SEGAL: Thank you.

11 DR. RAPPAPORT: Sort of a two-step
12 question. It seems that you finally were able to
13 stop when you added in the electronic cigarette. Is
14 that correct?

15 MR. WILLIAMS: That's correct.

16 DR. RAPPAPORT: So what do you think about
17 that made the difference compared to using other
18 nicotine replacement systems?

19 MR. WILLIAMS: It brought the pleasure back
20 into it. No offense. A patch and a lozenge, you
21 get no real pleasure from it. The act of smoking ex
22 of all the bad things about it -- the inhaling, the

1 exhaling -- it's very pleasurable. And all those
2 times when I really struggled for a cigarette after
3 a meal, driving on long car drives, patches and
4 lozenges just do not do that. And they happen to
5 catch us in our weakest moment.

6 When I ended up quitting, it was ranging
7 from items of, I had a death in the family to, oh,
8 somebody just ran a red light. Those were all
9 things that would trigger me to go back to smoking.
10 Because, really, living day by day thinking about
11 smoking, anything can trigger you to come back to
12 it. With the electronic cigarette, I still feel
13 like I'm smoking. I get that social interaction of
14 it. It's really that breathing in and breathing
15 out.

16 I didn't list it on there, but I tried the
17 Nicotrol inhaler, and it was one of the most
18 horrible, unpleasant experiences I have had. It had
19 no kind of -- it was more like trying to punish
20 myself for not having a cigarette as opposed to
21 doing it.

22 So the electronic cigarette really brings

1 that social aspect, really, the hand-eye-mouth, all
2 of those things that I found pleasurable about
3 smoking back into the equation. And it literally
4 was relatively easy once I had that.

5 Yes, ma'am?

6 DR. HUSTEN: So would you recommend that
7 manufacturers of the e-cigarettes do the studies and
8 come in for a cessation indication?

9 MR. WILLIAMS: To be honest, no, because
10 all the manufacturers of the e-cigarettes don't play
11 on the same level that the FDA plays. Most
12 manufacturers and vendors that I know make less than
13 \$1 million a year. That's not even really enough to
14 fill out the paperwork. The industry is not there.

15 Now, you have large players like Lorillard
16 and Njoy and those, but those don't really represent
17 the core of this industry. The core of this
18 industry is the small shops that have gone out and
19 spread the word and put those things out there.

20 So to go and become a cessation product is
21 just too expensive. You don't make it realistic for
22 this industry, a new industry emerging, for them to

1 be able to practically do that. I'll say the same
2 thing with making it a modified risk tobacco
3 product. The research requirements based on that
4 basically say, don't try.

5 Yes, ma'am?

6 DR. NGUYEN: Hi there. Thank you for your
7 story. It was very informative.

8 I actually have two questions. You had
9 mentioned that 12 weeks is not long-term. What
10 would be a reasonable long-term period? Should it
11 be indefinite, or should there be a goal that we're
12 looking for?

13 MR. WILLIAMS: Sure. I think there is no
14 set limit on it. I know I had a professor in
15 college that managed to quit smoking for four years,
16 but used the patch for the entire four years. I
17 think it's individual-based.

18 But I think by saying that you're only
19 supposed to use this product for 8 to 12 weeks, even
20 though I know plenty of people who used them well
21 beyond that, you put a stigma on them. There's
22 something wrong. People should only use this for

1 12 weeks, and now I've been using this for 9 months.
2 There must be something wrong with me.

3 Demoralizing and demonizing a person who's
4 trying to go through and quit and change their life,
5 unfortunately, it just doesn't work. It makes them
6 go back to being closet smokers.

7 DR. NGUYEN: And my second question is,
8 what I'm hearing a lot is short of tobacco
9 cessation, meaning not using any tobacco product, we
10 should be offering routes where the goal should be
11 smoking cessation. Am I correct?

12 MR. WILLIAMS: Hundred percent.

13 DR. NGUYEN: So that should be a goal, or
14 perhaps a new efficacy measure, so to speak, that we
15 should be looking at. And what you're proposing in
16 terms of using the nicotine replacement, various
17 products, perhaps indefinitely, then should that be
18 looked at as nicotine or tobacco maintenance? That
19 would be an acceptable public health goal?

20 MR. WILLIAMS: It's a very good question.
21 One, I think nicotine and tobacco, when we look at
22 the actual lower-harm alternatives to it -- so I'm

1 going to say the Swedish snus, which is low in
2 nitrosamines, or the lozenge -- I think those are
3 perfectly acceptable lifestyle habits, especially
4 when we compare it to people who drink a pot of
5 coffee a day.

6 I don't think the goal should be
7 maintenance. I think the goal should be quitting
8 smoking, removing the primary harm agent, and then
9 letting people live their lives after that.

10 If I had my way, I would say all NRT
11 products were over the counter, low cost, and
12 available to everybody at any time to use however
13 they want. One of the biggest barriers that I think
14 you have in the NRT world is the patches are
15 ridiculously expensive. When I look at the lozenge,
16 I would pay \$24 to \$40 for a box of lozenges, but I
17 can pay \$3 for a can of snus.

18 DR. NGUYEN: Thank you.

19 MR. LINDBLOM: Sort of following up on
20 that, yes. I think what you said is that when
21 you're doing the nicotine patch and the lozenges,
22 your doctor then said that you shouldn't be doing

1 that for such a long time.

2 MR. WILLIAMS: That's correct.

3 MR. LINDBLOM: What if your doctor had
4 said, "Great, that's working for you, keep it up"?
5 What do you think would have happened?

6 MR. WILLIAMS: I think I'd still be on that
7 today, hopefully at a lower nicotine level. But I
8 think I would still be doing it because the patch,
9 while it gives me a baseline nicotine level, you
10 need something -- at least I need something -- for
11 those high-stress spike type of environments. And
12 often that would be around another smoker.

13 MS. SIPES: Thank you very much. Much
14 appreciated.

15 MR. WILLIAMS: Thank you.

16 MS. SIPES: All right. Our next speaker is
17 Ms. Elaine Keller. She is with the Consumer
18 Advocates for Smoke-free Alternatives Association.

19 MS. KELLER: Good morning. My name is
20 Elaine Keller, and I'm president of the Consumer
21 Advocates for Smoke-free Alternatives Association,
22 which is a very long name, so we abbreviate it to

1 CASAA. I have no financial conflicts of interest.

2 I plan to address these six questions from
3 my point of view as a consumer as well as a former
4 smoker who is well-experienced in the use of many
5 different kinds of cessation products and methods.

6 I can see some of you squinting. Don't worry. I'm
7 going to present these in larger font onscreen.

8 Some of you probably forgot to bring your opera
9 glasses with you. See? No opera glasses required.

10 The most critical unmet need is to provide
11 smokers with effective ways to stop inhaling smoke.

12 Population growth has reduced smoking prevalence
13 when viewed as a percent of the adult population,
14 but absolute numbers tell a different story.

15 In 1990, there were 43.8 million smokers,
16 adult smokers, that is. The numbers went up and
17 down, but not by very much. Twenty-one years later,
18 we're right back to 43.8 million smokers.

19 During the past 21 years, the places where
20 people can't smoke have expanded even to the great
21 outdoors. Now it has reached a point where people
22 are being kicked out of their homes and barred from

1 employment.

2 Despite all these vigorous applications of
3 the metaphorical stick, there are just as many
4 smokers now as there were 21 years ago. Maybe it's
5 time to start thinking about carrots instead of
6 sticks.

7 Over the past 21 years, many medications
8 have been developed that the public health community
9 refers to as "safe" and "effective." Well, NRTs are
10 safe, but 7 percent is not what most folks would
11 call effective.

12 Okay. A breakthrough therapy would be
13 anything that helps more than 7 percent of its users
14 to escape from smoking. In the absence of studies
15 on long-term user of NRTs, as an earlier speaker
16 pointed out, Dr. Neal Benowitz presented evidence on
17 the safety of long-term use of snus type of tobacco
18 used in Sweden, and said if people are not going to
19 be developing cancer or having heart attacks or
20 strokes because of snus use, there's no reason why
21 that wouldn't be the same for NRTs as well.

22 There's no excuse for ignoring this very

1 powerful evidence since it is based on population-
2 level research. After-market surveillance can
3 determine the true success rates, and often reveal
4 problems that weren't identified during clinical
5 trials, such as the deaths from Chantix.

6 Now, these statistics speak for themselves.
7 Also, research shows that switching to smokeless
8 tobacco reduces cardiovascular, cancer, and lung
9 disease risks and lowers mortality rates.

10 Now, if CDER can implement a fast-track
11 process for previously unknown, unproven, innovative
12 smoking cessation pharmaceutical products, the
13 Center for Tobacco Products should be implementing a
14 fast-track, modified, risk tobacco product approval
15 process for the smokeless tobacco products that have
16 a proven beneficial effect at the population level.

17 Instead, the CTP has issued guidance for
18 the MRTP approval process that will cost millions
19 and take years. If cutting lung cancer mortality in
20 half isn't considered modifying risk, I'd like to
21 know what is.

22 Research should not be forced to start at

1 the most basic level on products that are proven to
2 be less hazardous at the population level. How many
3 lives will be lost before HHS tells smokers the
4 truth?

5 Excuse me a minute. I've got a case of
6 cotton mouth.

7 Those who switch from smoking continue to
8 use smokeless tobacco for years and years with no
9 ill effects, and they don't relapse to smoking. The
10 same should be true for indefinite use of NRTs.

11 Quitting nicotine triggers relapse. Since
12 we know long-term use of smokeless tobacco greatly
13 reduces health risks, we can deduce that any non-
14 smoked source of nicotine is safer than continuing
15 to smoke. Reducing smoking-related morbidity and
16 mortality is much more important than moralistic
17 concerns about addiction.

18 In certain populations, the health benefits
19 from smoking cessation are offset by impaired
20 cognitive and emotional health caused by nicotine
21 abstinence. The Royal College of Physicians' 2007
22 report pointed out that nicotine abstinence is

1 unworkable for some smokers, especially those who
2 are self-medicating underlying conditions that
3 impair their cognitive and/or emotional health. The
4 practice of tobacco harm reduction, offering less
5 hazardous alternatives to smoking, could save
6 millions of lives.

7 In every age group, ever-smokers with
8 depression are more likely to be smokers and less
9 likely to have quit smoking than ever-smokers
10 without depression. And this is true of other
11 diseases as well, such as attention deficits.

12 I can hear some of you thinking, very
13 loudly, if a smoker is depressed or has some other
14 mental or cognitive illness, they should treat it
15 with FDA-approved medications. But consider these
16 facts.

17 The FDA-approved medications don't work for
18 everyone. Many smokers might not be able to afford
19 these medications, especially if they don't have
20 health insurance. Smokers who do have health
21 insurance might lose it if they cannot afford the
22 50 percent premium surcharge permitted under

1 Obamacare. If nicotine works to keep the smoker's
2 cognitive and emotional problems under control, why
3 not encourage a safer delivery mechanism?

4 Let's talk about innovative products that
5 reduce or eliminate smoking. CASAA supports three
6 classes of alternatives: smokeless tobacco
7 products; electronic nicotine vaporizers, e.g. the
8 electronic cigarette; and pharmaceutical nicotine
9 products for long-term use, with nicotine dosages
10 that more closely approximate dosages from smoking,
11 and without unwarranted warnings.

12 A meta-analysis found that when used as
13 directed to wean down and off nicotine, cessation
14 rates were 7 percent at six months and less than
15 2 percent at the one-year mark. Long-term use of
16 nicotine gum results in better smoking cessation
17 rates, or abstinence rates, than weaning off
18 nicotine.

19 London colleagues looked at seven studies
20 that compared smoking quit rates of snus users to
21 never-users of snus. In every case, a higher
22 percentage of snus users had quit smoking. Out of

1 eight population surveys, success rates for smokers
2 who switched to electronic cigarettes were highest
3 among participants in an online forum who used a
4 variety of products and who received advice and
5 support from more experienced users.

6 The success rate of NRTs could be improved
7 greatly if higher doses were available and if
8 consumers were not instructed to stop using them.
9 In effect, this page tells smokers, nothing is any
10 safer, so you might as well smoke. In my book, that
11 constitutes the real health fraud. The government
12 needs to stop encouraging people to stick with
13 smoking.

14 Why are consumers shut out of the
15 regulatory process? The worst that could happen to
16 any other stakeholder group pales in comparison with
17 what consumers stand to lose, their health and their
18 very lives. The public needs more accurate
19 information about nicotine. HHS needs to stop
20 misleading the public. Products that don't produce
21 smoke are less harmful than smoking.

22 It's reprehensible to continue promoting a

1 lie that is a barrier to smokers improving their
2 health and saving their lives. It's time to start
3 educating smokers about the health benefits realized
4 by switching to low-risk alternatives.

5 This should not be about politics or
6 profits. Peoples' lives depend on a change in
7 attitude, education, and product availability.
8 Thank you.

9 MS. SIPES: Thank you.

10 MS. KELLER: Yes?

11 DR. HUSTEN: I was just curious of the
12 source of the statistic about 62 percent of smokers
13 earn less than \$36,000 a year.

14 MS. KELLER: I'm sorry. I can't hear you.

15 DR. HUSTEN: I was just wondering what the
16 source for the data that 62 percent of smokers earn
17 less than \$36,000 a year. It's on slide 14, I guess
18 that is.

19 MS. KELLER: Sixty-two percent of smokers
20 are what?

21 DR. HUSTEN: Earn less than --

22 MS. KELLER: Oh, oh, yes. Got it on the

1 Internet. They're not allowed to lie on the
2 Internet. Right?

3 DR. HUSTEN: Well, I'm just -- it just
4 seems different than some other statistics I was
5 aware of, so I was just curious what the source was.

6 MS. KELLER: Yes. Well, if you think about
7 depression and attention deficits being common in
8 smokers, maybe that's why they're earning much less
9 money.

10 DR. HUSTEN: I'm just saying that that
11 statistic seems different than other statistics I've
12 seen. It seemed a much higher percent than other
13 statistics. So I was just curious of the source
14 because I wanted to check it out.

15 MS. KELLER: I'm not sure that I documented
16 where I got that from.

17 DR. HUSTEN: Okay. Thank you.

18 MS. KELLER: Anything else?

19 DR. LEONARD-SEGAL: FDA does not control
20 costs of the medications that are approved. But
21 there's been a lot of conversation so far this
22 morning about the cost of some of these products,

1 both in your talk and in previous talks.

2 Do you have a sense that if all of
3 these -- is there a threshold that you can imagine
4 where costs could actually help people to stop
5 smoking one way or the other?

6 MS. KELLER: You me if they lowered the
7 prices of some of the medications?

8 DR. LEONARD-SEGAL: Is there a threshold
9 and -- yes.

10 MS. KELLER: Couldn't hurt.

11 DR. LEONARD-SEGAL: You think?

12 MS. KELLER: That's my sense of it. I know
13 that when NRTs first came out, they cost more than
14 smoking. They cost about three times more than
15 smoking. And it was like, uh, I'm not sure I can
16 afford this.

17 DR. LEONARD-SEGAL: Because the states keep
18 raising taxes on cigarettes. I mean, I just
19 wonder -- we don't control this, but I'm just
20 wondering.

21 Another question I have is you talk about
22 the safety of these products, and lung cancer deaths

1 certainly are higher in inhaled smoke tobacco
2 products than in products that are not inhaled.

3 I've seen data and read about the fact that
4 pancreatic cancer is higher in people who use
5 Swedish snus and maybe other kinds of snus. And
6 pancreatic cancer is a cancer that seems to be
7 increasing in rate in this country now. I don't
8 know why, but I've read that it is.

9 So I'm wondering how you would -- if we
10 were going to go in those directions, how would you
11 suggest that these products be labeled? Should we
12 be informing people of other risks, such as
13 pancreatic cancer, that have been shown to be
14 associated with some of these other kinds
15 of nicotine ingestion products?

16 MS. KELLER: Well, I think you'd better
17 take another look at that pancreatic cancer issue.
18 The person who noticed that increase had done two
19 studies. One of them showed an increase; the other
20 one didn't. And he cherry-picked the one that
21 showed an increase and included that across the
22 board.

1 But even so, when you look at absolute
2 numbers, even if that were true, I think we would be
3 looking at an extra four cases per 100,000 or
4 something. So I think what we need is more research
5 to tie that down more precisely, and then try to
6 give accurate information to the public.

7 DR. LEONARD-SEGAL: Thank you.

8 MS. KELLER: Any others?

9 MS. SIPES: Thank you very much.

10 All right. Our next speaker was to have
11 been Mr. Phil Daman, but I do not believe he's here
12 yet. Mr. Daman, if you're here?

13 (No response.)

14 MS. SIPES: Okay. In that case, I'll ask
15 Mr. Jonathan Foulds to come up. Are you here,
16 Dr. Foulds? Thank you very much. Dr. Foulds is
17 here for the Society for Research on Nicotine and
18 Tobacco.

19 DR. FOULDS: Good morning. My name is
20 Jonathan Foulds. I'm a professor at Penn State
21 College of Medicine. I've been doing research
22 on nicotine, tobacco, and smoking cessation for over

1 20 years. And I'm here this morning to speak on
2 behalf of the Society for Research on Nicotine
3 and Tobacco, which is the largest research
4 organization in the world, focusing on nicotine
5 and tobacco. It's got over a threshold members
6 worldwide.

7 By way of disclosure, SRNT does not accept
8 tobacco industry funding. But some SRNT members,
9 including myself, have done consulting work for
10 pharmaceutical companies.

11 So I'm going to speak about most of the
12 questions that were mentioned in the Federal
13 Register publication by FDA. And I'm going to
14 summarize the main points that we wish to make in
15 the time allowed this morning.

16 So regarding fast-track and breakthrough
17 therapies, SRNT regards dependence on smoked tobacco
18 products as a serious and life-threatening condition
19 based on a very high likelihood -- it's about 50
20 percent -- that continued smoking will cause
21 somebody to die prematurely.

22 As we all know, it's probably the only

1 legal product that will kill you as used as
2 intended. And so we believe that tobacco dependence
3 should be considered a life-threatening condition.

4 Continued smoking, with all of its risks,
5 should be considered the comparator for safety
6 questions. So given that so many people will
7 continue to smoke, even when they try and quit,
8 as we've heard from people this morning, then the
9 comparator when you're evaluating a treatment or
10 a medicine to help you to stop smoking shouldn't be
11 that if you didn't take the medicine, you'd quit and
12 have no other drugs in your system. The comparator
13 should be continued smoking.

14 The safety standard should be that the
15 treatment is therefore much safer than continued
16 smoking, not that it needs to be completely free of
17 risk. Okay? All medicines, all treatments, will
18 have some risk. As we know, nicotine withdrawal
19 itself has some risks.

20 But it's about the relative risks. And
21 products or indications that have advantages over
22 existing products or indications, we believe, should

1 therefore be fast-tracked because of the magnitude
2 and the likelihood of the serious health effects
3 suffered by continuing smokers.

4 On the subject of extended use of nicotine
5 replacement therapies, there have already been
6 authoritative reviews published. And the scientific
7 evidence on longer-term use of nicotine replacement
8 therapy, which includes the U.S. Public Health
9 Service guideline published by the federal
10 government, concludes that the risk of relapse to
11 smoking is less if you have continued use of NRT,
12 and it's certainly preferable to continued smoking.

13 I've cited some studies here, and will
14 provide the evidence and the citations in writing to
15 FDA. But the evidence on this is really very clear,
16 and it's been part of the U.S. Public Health Service
17 guideline since 2000.

18 So clinicians in this country have been
19 faced with this challenge of evidence suggesting
20 that one kind of treatment, long-term treatment and
21 combination pharmacotherapy, is helpful, and yet the
22 labeling suggests against it.

1 So NRT may be used safely and effectively
2 beyond the recommended 8- to 12-week cycle. Package
3 labeling should reflect the safe and effective use
4 of nicotine replacement therapy.

5 We're not recommending this for all; all
6 smokers don't need to use nicotine replacement
7 therapy long term. And one of the speakers -- one
8 of the panel asked before, "Well, how long is long
9 term?" And everybody is different.

10 So we feel to recommend to patients that
11 they should use the medicine for as long as it takes
12 for them to have no cravings or withdrawal symptoms
13 or near-slips or near-smoking for 14 consecutive
14 days, at that point, after they've gone 14
15 consecutive days without cravings or smoking, or
16 nearly smoking, that may be a point to start
17 thinking about reducing the medication. And the
18 point when that comes will vary for the individual,
19 depending on how addicted or how dependent they have
20 been.

21 On the question of indications for craving,
22 there's a question about do we have valid and

1 reliable measures. And we do have valid, reliable,
2 and brief measures of craving and nicotine
3 withdrawal. They already exist. They've previously
4 been accepted by FDA as evidence of the effect of
5 medicines in relieving craving and withdrawal.

6 So we think we already have these, and
7 we've cited some studies that have looked at it more
8 carefully. And we don't think that we need to
9 invent complicated new ones. The ones that have
10 been used already seem to do a reasonably good job.

11 The majority of ex-smokers still report
12 urges to smoke after six months. Although the
13 magnitude of the craving relief that's provided by
14 the medications is actually quite small on these
15 standardized measures, it is associated with an
16 increased risk of sustained abstinence.

17 So we believe that studies that show that a
18 medication reduces craving significantly, that
19 should be taken as a valid sign that the product is
20 likely to help people quit smoking.

21 Many smokers benefit from longer-term use
22 of nicotine replacement, partly because these

1 cravings don't just go away within 8 to 12 weeks. A
2 significant proportion of smokers still report
3 cravings after six months.

4 On the topic of indications for relapse
5 prevention, there was a question about what should
6 the outcome measures be? What's the definition of
7 relapse? And we're recommending that the outcome
8 measures should distinguish between a slip or a
9 lapse, which is any use of cigarettes or smoking
10 after a quit attempt, and a relapse, which in many
11 studies has been recommended to be defined as
12 occurring on the first of seven consecutive days of
13 smoking.

14 We think there are advantages of
15 distinguishing between a slip and a lapse, which is
16 an isolated incident of smoking, and a longer-term
17 sustained period of smoking, we think seven days of
18 consecutive smoking is a reasonable way to define a
19 relapse.

20 Distinguishing between those things also
21 enables one to examine whether a medicine, continued
22 use of the medicine, actually helps somebody recover

1 from a lapse to not go on to a full-blown relapse.

2 Of course, currently we have the problems
3 I'm sure you've had before, that the labeling on the
4 nicotine replacement therapies, says you must not
5 smoke and use the product at the same time. And so
6 we have many patients that if they have a lapse,
7 they smoke a cigarette while wearing the patch, they
8 think that the first thing they must do is take the
9 patch off. Rather, the first thing they must do is
10 get rid of their cigarettes. They have a fear,
11 partly based on what it says on the labeling, that
12 something terrible will happen, and they give up the
13 medication rather than their cigarettes at that
14 point.

15 MS. SIPES: Dr. Foulds, I'm sorry to
16 interrupt you. I would like to have you finish, but
17 you're getting pretty much to the end of your time.
18 I just want to make you aware of that.

19 DR. FOULDS: Okay. So I'm going to
20 summarize briefly that we recommend additional
21 indications that include smoking reduction,
22 treatment of nicotine withdrawal symptoms and

1 craving, and combination nicotine replacement
2 therapy. We'd encourage you to look at how that's
3 going in the United Kingdom and other countries that
4 have liberalized the labeling on medicines, and
5 reduced the barriers to wider use of these
6 medicines.

7 I'm going to stop with trying to summarize
8 what I believe is the appropriate analogy here, is
9 that we have a massive shipwreck with thousands of
10 people in the water at risk, at risk of death,
11 premature death. And while some of these people may
12 make it to shore on their own without any help, many
13 will die if we don't provide them with help.

14 We shouldn't hesitate to throw them a
15 flotation device out of concern that it could give
16 them a bump on the head. And that's what current
17 regulation does. It's too cautious, and there's an
18 urgent need to provide smokers with more treatment
19 options. And when weighing the risks and the
20 benefits, the comparator is continued smoking and
21 its massive health effects. Thank you.

22 MS. SIPES: Thank you.

1 DR. WINCHELL: Thank you very much. I have
2 a number of questions, and I hope and expect that
3 SRNT will be providing a submission to the docket
4 that will answer some of these.

5 DR. FOULDS: Yes.

6 DR. WINCHELL: I'm sure that's something
7 you're working on.

8 But to begin with, I want to ask whether
9 there's any help you can give us on one of the
10 specific questions that you didn't address, which is
11 3.1a, about whether the concept of craving, that
12 word, "craving," has been adequately characterized,
13 well-defined, well-understood.

14 The statute requires us to consider that
15 word verbatim as a potential indication. But I
16 noticed that in your talk as well as in your slides,
17 you interchange different words for that such as
18 strong urges or cravings. And my understanding of
19 the literature across addictions is that it doesn't
20 seem that people have agreement on whether that word
21 is a word that all patients understand the same way.
22 So I'm hoping you might be able to provide us with

1 some information on that.

2 DR. FOULDS: Well, if you want just my
3 opinion, my opinion is that there is not a whole lot
4 of difference. We're talking, really, about fine
5 semantics.

6 Smokers understand when they have a strong
7 desire to smoke. And whether you call it a craving
8 or an urge -- we measure, and we have medicines
9 that, and whether you call it a craving or an urge,
10 that the medicines reduce the severity of that, as
11 rated by people on active or placebo in double-blind
12 trials.

13 So my opinion is there's not a very
14 meaningful difference between those two. And many
15 of the studies find that one simple question is
16 enough, and is maybe not any less effective in
17 measuring this than 20 questions.

18 So it wouldn't be a problem to ask it both
19 ways. Have a question about craving; have a
20 question about urges. My expectation would be that
21 they'd correlate extremely highly.

22 DR. WINCHELL: Then my next question has to

1 do with the two very distinct settings in which this
2 word is used, which we also spoke to in the
3 questions that we put out there. And I'm also
4 hoping for some help with this.

5 One is that craving or urge to smoke is
6 observed in the context of withdrawal. When people
7 are in the state of nicotine withdrawal, they
8 experience a desire to smoke or to use nicotine.

9 Then the other is this concept of cue-
10 induced or provoked craving in someone who may have
11 been an ex-smoker for a period of time. And my
12 understanding of the literature is that medications
13 that are effective in one are not necessarily
14 effective in the other, that findings in laboratory
15 settings in which craving is provoked are not
16 necessarily predictive of relapse.

17 So we're looking for some help about the
18 study designs that would support claims, whether
19 there would need to be distinct and separate study
20 designs for these two separate types of craving, and
21 whether the use of the same term in both contexts
22 could promote some confusion.

1 DR. FOULDS: Yes. Well, I actually don't
2 agree with the way these things were characterized
3 in the original document. Smokers don't just have
4 cue-induced cravings when they've been abstinent for
5 significant periods of time. Smokers have cue-
6 induced cravings every single day while they're
7 smoking. Smokers actually rate -- they have
8 stronger urges to smoke while smoking than shortly
9 after abstinence.

10 So cue-induced cravings primarily refers to
11 the situation that the person's in or the thing that
12 triggered it. Now, when we are doing studies, we
13 typically use the best cues we can think of, like
14 making the person abstinent for a period of
15 time -- it could be only 24 hours -- and then
16 presenting them with their own brand and letting
17 them handle it, because we know that's a really good
18 way to study cue-induced craving in the lab.

19 But everybody will have -- all smokers will
20 have a craving triggered in response to that. But
21 many smokers will have a craving induced by things
22 within themselves: boredom, sitting listening to me

1 speak. There could be somebody in the audience that
2 I would be a cue to want to go and smoke. They
3 would find my voice boring and monotonous, and they
4 would want something to pep them up.

5 So I think it would be an unfortunate thing
6 if FDA decided that this craving business is really
7 complicated, and it's fine-grained, and we need to
8 have really subtle and sophisticated measures,
9 really, to understand this and all its complicated
10 dimensions before we do anything about it. That
11 would be a mistake. We have measures now that can
12 measure these things just fine.

13 MS. SIPES: Did you have --

14 DR. WINCHELL: I have others, but it's
15 okay. Go ahead. Well, maybe we'll come back around
16 at the end.

17 DR. HUSTEN: Yes. I just had a question
18 about one of the slides that you didn't have a
19 chance to get to. And they aren't numbered, but I
20 think it's maybe slide 12. But it says, "In
21 addition, any regulatory barriers to decreasing unit
22 pack size should be removed." I was just interested

1 in hearing your thoughts on that and your
2 recommendations.

3 DR. FOULDS: On pack sizes? Yes. Well,
4 it's based on a simple point that I think one of the
5 speakers already brought up this morning, that if
6 you can pop into a gas station and buy a pack of
7 cigarettes for five bucks, or a packet of smokeless
8 tobacco for a buck 80, which you can in Pennsylvania
9 where I live, and you're feeling that craving for
10 nicotine and you know that's what you're craving
11 for, and you have to travel a longer distance and
12 buy a larger volume, and maybe shell out 25 or \$50
13 to get the smallest pack size they have, then that
14 becomes a barrier.

15 When it's giving the smoker the choice of
16 what form of nicotine am I going to take, the safer
17 form -- or the much more harmful form is kind of
18 pointing them in the direction we don't want them to
19 go in. So I feel that you should be allowed to sell
20 NRT products in small and less expensive pack sizes
21 that would compete with like a \$3 pack.

22 DR. HUSTEN: So you're suggesting something

1 like that you could get a day's worth in a package,
2 or individual --

3 DR. FOULDS: I personally wouldn't put a
4 minimum limit. But a day's worth would be good,
5 yes. But you could -- a strip of nicotine gum, with
6 even five or six pieces.

7 Right now, you can go to one of our larger
8 vendor stores that begins with W that we're all
9 familiar with, and you can buy a pack of nicotine
10 gum for ten bucks. But you've got to drive to that,
11 out of your way, to find a place where you can get
12 it. Most pharmacies are selling nicotine
13 replacement products in packs that are more like
14 \$50.

15 DR. RAPPAPORT: This is a follow-up to
16 Dr. Winchell's last question. Is craving, the term
17 "craving," specific enough that you feel that that
18 is really the word that needs to be used? Or would
19 a description, any other term describing that urge,
20 that immediate need to have a cigarette, be adequate
21 in labeling for whatever this concept is?

22 DR. FOULDS: Well, I think either of them

1 is fine. There's an item on one of the most widely-
2 used withdrawal questionnaires, the Minnesota
3 Nicotine Withdrawal Scale, that refers to urges.
4 You can cut it into frequency and strength.

5 I also think that part of the difference
6 between the background craving and the cue-induced
7 craving relates more to the time frame that you're
8 referring to. So, very often, the Minnesota
9 Nicotine Withdrawal Scale is administered once a day
10 or less, and usually it's referring to the last
11 24 hours.

12 So when you're referring to how you've been
13 feeling, whether you've been depressed or irritable
14 or had a strength of urges in the last 24 hours,
15 you're taking like an average. And when you're
16 answering the question, you may think back to, oh,
17 yeah, there was a few times that I really had a
18 strong urge, and you can average it out.

19 Whereas when you're doing a laboratory
20 study or a study where you have people onsite for a
21 research study, then you typically will be asking
22 them, "Oh, in the last ten minutes or right now, how

1 have you been feeling?"

2 Of course, we don't tend to do studies
3 where we're asking them, how have you been feeling
4 in the last ten minutes, when nothing was happening,
5 unless we're comparing it to when we give them the
6 cigarette or we show them the video that presents
7 the cues.

8 So how we measure and define these things
9 is partly defined by the time frame that we're
10 focusing on, and that's one difference.

11 Also, it partly depends on the product,
12 because things like the patch, for example, you put
13 it on and it's not designed to and there's no reason
14 to believe it's going to be particularly effective
15 in reducing an acute cue-induced craving.

16 What you hope is that by reducing the
17 background level of nicotine withdrawal, that the
18 severity or the frequency of those cravings coming
19 on will be less; whereas you've got things like the
20 gum or the nasal spray that you take acutely, they
21 are partly designed that when you have an acute
22 craving come on, then you use that product in that

1 time frame to get rid of it. And you do it instead
2 of smoking a cigarette.

3 That's part of the reason these medicines,
4 although they're both nicotine replacement products,
5 they work in a slightly different way. And one of
6 them has got something to do, and the other one
7 doesn't. And that's part of the reason why the
8 evidence is clear that combining the two gives you a
9 higher quit rate. And that's why it's so
10 unfortunate that the labeling currently on nicotine
11 replacement products tells smokers not to do that,
12 that very thing that is more effective.

13 DR. WINCHELL: This relates to your
14 recommendations on how to define a lapse or a
15 relapse in studies of relapse prevention. I'm
16 hoping you can give us some concrete suggestions on
17 how day-to-day smoking behavior at that level of
18 granularity can best be measured in a clinical trial
19 in a way that doesn't increase the cost
20 prohibitively of conducting the trial.

21 Customarily, we rely on people's
22 recollection because we think people remember pretty

1 clearly whether they did or didn't smoke in the
2 context of being someone who's trying to quit
3 smoking. But as far as exactly when or how many, we
4 have some uncertainty about the best ways to measure
5 those accurately.

6 DR. FOULDS: Do you mean uncertainty about
7 whether people can remember accurately how much they
8 smoked that day?

9 DR. WINCHELL: Well, if we see people, say,
10 once every two weeks or once every month, and you're
11 going to ask them how much they smoked or whether
12 they smoked on every single day since the last
13 visit, there just doesn't seem to be a lot of
14 confidence in the use of timeline follow-back, which
15 is a reconstructed self-report method that's used in
16 some other addictive disorders. There may be other
17 ways to collect this data, but there's some concern
18 about the cost of incorporating those things in
19 clinical trials.

20 So I don't know if you have an answer right
21 now, but that might be something you could --

22 DR. FOULDS: Well, I'll give you my two

1 cents' worth right now. But I think we could
2 probably give you a better answer in writing, with
3 other people's input.

4 If it's the cost issue, then if you're
5 doing a well-designed, randomized, double-blind
6 control trial, then there's no reason to think that
7 the people in one arm of the trial, I don't think,
8 would have any less accurate memory than the people
9 in the other arm of the trial.

10 So I think you have to accept there's a
11 little bit of variability and lack of accuracy in
12 people's memories. But assuming they both equally
13 have fallible memories, then what you're really
14 looking for is a significant difference between the
15 two.

16 If you really want to get at a more
17 meaningful measurement, then you do have to spend a
18 little bit more. And there I would think you need
19 to go to -- it's ideal to go to biochemical
20 measures. We can measure some of the things that
21 people absorb from their smoke. And CO, for
22 example, is not at all expensive. But it depends

1 very much on time of day and things like that.

2 But again, as long as these are equalized
3 between the two comparison groups, that can give you
4 more confidence that your consumption measure, as
5 self-reported, is reasonably accurate.

6 MS. SIPES: Thank you. I had a question
7 for you, and there may be others, too.

8 This is going back to a point that you made
9 early on in your presentation, when you were talking
10 about fast-track and breakthrough therapies.

11 Although it's not directly related to that -- and
12 forgive me if you already spoke to this, but I still
13 had a question -- your bullet says, "A smoking
14 cessation product candidate that shows potential to
15 have advantages over existing products should be
16 considered as eligible for fast-track status. This
17 could be based on improved craving relief for use by
18 a broader population of smokers, e.g., reduce to
19 quit."

20 I'm curious about how you see "reduce to
21 quit" fitting in there. Do you see that as linked
22 to use by a broader population? What is the

1 connection there?

2 DR. FOULDS: Yes. The indication of reduce
3 to quit brings in the potential group of people who
4 would try and use a med to reduce their smoking, a
5 much larger segment of the smoking population.

6 Right now it's primarily -- not exclusively
7 but primarily -- for and is used by people who are
8 making a decision, I'm ready to quit right now, and
9 I'm ready to quit suddenly, because that's what the
10 labeling -- that's how it tells me I must do it.
11 And it actually implies to me that it will be
12 dangerous for me to do it gradually with this
13 product.

14 So the market would be expanded of people
15 who -- if they could be included, people who are
16 interested in reducing gradually. And we have
17 evidence that that doesn't seem to be harmful to use
18 the products while you're reducing your smoking at
19 the same time. There's some evidence that it could
20 actually improve the long-term efficacy and
21 outcomes.

22 But I think the key point here is that a

1 new indication that could bring into the behavior
2 change field, using medicines that are shown to be
3 effective, a larger segment of the smoking
4 population, that could have a big public health
5 impact on its own.

6 So we didn't want to specify, oh, this is
7 the definition or that's the definition. It's a
8 complicated question to answer in a bullet point.
9 But we think that new indications that are supported
10 by evidence, that would assist a larger group of
11 smokers than are using the products with current
12 indications, could produce a big benefit.

13 DR. NGUYEN: Just following up on the
14 clinical trial concepts for an indication of craving
15 relief, you had mentioned that there are instruments
16 out there that can capture treatment differences,
17 perhaps, in this benefit.

18 I was just curious if you think it's
19 important to also have an objective outcome, such as
20 the number of cigarettes smoked, when one of these
21 cravings hit, and compare that between the treatment
22 groups, either placebo versus new treatment or two

1 different treatments.

2 DR. FOULDS: When you say an objective
3 outcome, like number of cigarettes smoked?

4 DR. NGUYEN: Something like that, because
5 I'm not familiar with these instruments, but I
6 suspect it's probably just -- it is subjectively
7 reported.

8 DR. FOULDS: Most of the trials that are
9 being carried out today have not been really
10 focusing on reduced smoking because they have not
11 been designed to get that indication. It has been a
12 requirement that the product helps people to quit
13 smoking.

14 So many studies, including the ones that I
15 do, we do ask people, first of all, have you smoked
16 in the last seven days? And if they say yes, we
17 say, how many have you smoked in the last seven
18 days? Because we have interest in it.

19 But most of the clinical trials that have
20 been designed for FDA purposes, because they're
21 trying to meet the current indication of helping
22 people to quit smoking, haven't gone into the "how

1 many cigarettes have you smoked" aspect in a whole
2 lot of detail.

3 But, as you know, there have been trials on
4 this other indication of reduce to quit. And
5 they've generally simply used the person's summary
6 of how many they've smoked, and biochemical
7 verification is used. So you generally find that
8 the people who say they've reduced have got a lower
9 exhaled carbon monoxide, for example.

10 If you wanted to go further, you can
11 measure other substances in people's body fluids
12 that can provide more verification that they are
13 reducing their exposure to toxins in a way that
14 would be meaningful. And if you're worried about
15 cost, that's more expensive.

16 But if you want to be reassured that people
17 really are not just reducing their number of
18 cigarettes but reducing their intake of toxins,
19 which is probably more important, then you're best
20 to go for biochemical measures.

21 There's one thing that is worth noting.
22 It's not just the number of cigarettes reduced that

1 we're aiming for. We're aiming for a real reduction
2 in harm, and that comes from a reduced exposure to
3 the harmful toxins in cigarette smoke.

4 People are inhaling cigarette smoke
5 primarily to get nicotine. And so there's reason to
6 think that by giving them nicotine in a cleaner and
7 safer way, they will be less likely to inhale as
8 much smoke from each cigarette that they do smoke
9 because they're getting some of their nicotine from
10 another source, and that drive to get nicotine is
11 less.

12 MS. SIPES: Could you speak a little bit
13 more to the post-approval surveillance data and the
14 evidence from other countries? I know that was part
15 of what you wanted to get to.

16 DR. FOULDS: Yes. The point here was a
17 simple one, that we live in a big, wide world, and
18 there are other countries that use these medicines
19 in addition to the United States. And some of them
20 have pretty good surveillance mechanisms, and they
21 do a good job, the regulators in those countries, as
22 well as the regulators in this country.

1 So we think it would be a good idea, where
2 other countries have gone -- maybe have been a bit
3 more adventurous than we have in this country and
4 have an experience of having these products on the
5 market for broader indications, or that the data has
6 been collected in a different way in another
7 country, that that should be considered just as much
8 as the data collected prospectively in the United
9 States.

10 Some things we don't need to do another
11 study in this country. If something's already
12 happened in another country and really no harm has
13 resulted, maybe good has resulted, that should
14 influence our decision making as to whether we
15 should go that way in this country.

16 MS. SIPES: All right. In that case, thank
17 you very much.

18 DR. FOULDS: Thank you.

19 MS. SIPES: I think that rather than trying
20 to cram another speaker in before 10:00, I think
21 maybe we will take our break now.

22 Why don't we break until five minutes after

1 10:00. And our next speaker after that will be
2 Dr. Steinberg. Thank you very much.

3 (Whereupon, a brief recess was taken.)

4 MS. SIPES: All right, everyone. We're
5 going to get started with our next speaker.

6 Our next speaker is Dr. Michael Steinberg.
7 He's here for the Association for the Treatment of
8 Tobacco Use and Dependence.

9 DR. STEINBERG: Good morning. Always good
10 to come after a break, where everybody's rejuvenated
11 and awake, hopefully. My name is Mike Steinberg.
12 I'm a primary care physician currently practicing in
13 New Jersey. I'm also representing the Association
14 for the Treatment of Tobacco Use and Dependence, or
15 ATTUD, as its current president.

16 As a primary care physician and tobacco
17 treatment specialist, I treat both smokers who are
18 trying to quit as well as the unfortunate
19 consequences of smokers who are unable to quit. I
20 see young and vibrant people every day suffering a
21 horrible illness from their smoking.

22 I thought it was critical that this panel

1 not only hear from those who market smoking
2 cessation products and other tobacco products, but
3 also from those of us who use these medicines to
4 save lives and help people actually stop smoking
5 every day.

6 As a matter of disclosure, I have in the
7 past received funds from companies that make
8 cessation medications in order to fund research and
9 provide educational programs. In addition, ATTUD
10 has received some sponsorship in the past from these
11 companies.

12 The goals of the FDA Center for Drug
13 Evaluation and Research and ATTUD are entirely
14 aligned regarding tobacco treatment. CDER's goal is
15 to improve the health of people by making safe and
16 effective drugs available, clearly with the
17 intention that these drugs will be utilized, thus
18 improving health.

19 ATTUD is an international, not-for-profit,
20 volunteer organization of health care and other
21 public health professionals who use evidence-based
22 methods to help tobacco users quit. These are

1 clinicians on the front lines of treatment, seeing
2 the benefit of success and consequences of failure
3 for smokers trying to stop. These clinicians base
4 their treatment on the latest scientific evidence
5 available, not simply anecdotes, tales, or opinions.
6 The importance of evidence-based decisions is at the
7 core of our practices, and the access to evidence-
8 based treatment is our mission.

9 Thus, the goals of FDA and ATTUD are
10 unified, improving the health of our communities.
11 And we all understand that policies such as the ones
12 we're discussing today impact real people, in this
13 case not only consumers but also clinicians.

14 Now, speaking from the trenches, a major
15 issue is how the current product labeling for
16 smoking cessation treatments relates to the current
17 scientific evidence. We have vast amounts of data
18 that these medications have been proven safe and
19 effective. However, only a very small proportion of
20 smokers who make an attempt to quit take advantage
21 of these effective treatments.

22 There are many factors that impact the

1 situation, with one of the most ones being the fact
2 that current labeling directly contradicts the
3 evidence-based scientific data.

4 In the case of smoking cessation
5 medications, product labeling is of vital
6 significance for several reasons: First, these
7 products are largely over-the-counter; therefore,
8 consumers will be purchasing them on their own and
9 will rely heavily on information they read on the
10 box.

11 Second, treatment providers for tobacco
12 often do not have the authority to overrule the
13 product labeling in an off-label manner, and
14 therefore are forced to follow the directions
15 precisely.

16 Finally, most providers, even physicians,
17 are not well-trained in cessation therapy, as we
18 heard from Mr. Williams' experience in his physician
19 telling him to stop using the combination of
20 medications immediately and how dangerous it was.

21 Medical students at my medical school
22 receive only one hour of tobacco treatment education

1 out of their entire four-year medical education
2 experience. One hour. These physicians and other
3 providers will also rely heavily on the package
4 labeling for their prescribing information.

5 In addition, there are some other practical
6 implications of the product labeling. Tobacco
7 treatment specialists often find themselves in the
8 awkward position of having to explain to their
9 patients why they want them to disregard what it
10 says on the package. This puts us immediately on
11 the defensive with our patients.

12 After providing patients with the clinical
13 trial evidence that combinations of, say, patch and
14 gum work very well together, these highly dependent
15 smokers will often express a renewed confidence in
16 their success, having failed numerous times with
17 lower-dose single nicotine replacement medicines.

18 The product labeling also scares potential
19 consumers. The long list of petition side effects,
20 warnings, and cautions is enough to frighten anyone.
21 This is particularly ironic in contrast to the
22 minimal volume of warnings found on cigarette packs.

1 It is not surprising that a significant
2 number of smokers believe that nicotine replacement
3 medicines are just as dangerous as their cigarettes,
4 and thus the utilization of these safe and effective
5 medicines is less than optimal.

6 Finally, a possible unintended consequence
7 of the current labeling is the impact it has on the
8 determination of insurance coverage for these
9 medicines. We know that smoking preferentially
10 impacts lower-income members of our society, folks
11 who can least afford unnecessary medication costs.
12 Labeling that demarcates set durations of treatment
13 and prohibits combinations of products leads to
14 insurance denials for these effective approaches.

15 We have evidence based on thousands of
16 studies and hundreds of thousands of smokers from
17 over nearly 30 years of experience that these
18 medications are safe and effective. This is what
19 distinguishes this discussion from that of some of
20 the other products that you're going to hear about
21 today.

22 From the U.S. Public Health Service

1 Clinical Practice Guidelines, we know that
2 combinations of NRTs are more effective than single
3 NRTs alone. We know that for some smokers, who are
4 more dependent, the labeling regarding dose can
5 deter appropriate amounts.

6 For other over-the-counter medications such
7 as common analgesics, directions for these products
8 are based on symptoms and are left to the consumer's
9 discretion, not spelled out in such a limiting
10 fashion. We need similar flexibility for NRT
11 dosing.

12 Finally, studies indicate that current
13 labeling duration may be inadequate for some
14 smokers. Therefore, for those people, extended
15 duration may be beneficial.

16 In the evidence-based literature, as well
17 as in our clinical experiences, which were published
18 in the Annals of Internal Medicine, it is rare that
19 smokers will need to use these medications for
20 longer than the standard treatment duration.
21 However, for those few smokers who do need to use
22 them for longer, this extension of treatment should

1 not be prohibited. Again, we need flexibility to
2 tailor our treatment to the individual person.

3 The key clinical points I want to leave you
4 with are these.

5 The latest evidence and clinical experience
6 clearly illustrate the benefit of extending the use
7 of NRT medications. This extended use includes the
8 combination of NRTs, since they have been proven
9 more effective; the flexibility of dose and
10 duration, so that consumers can use as much of the
11 medications as they need to, to maximize their
12 treatment; and to increase the indications for these
13 safe and effective products so that their
14 utilization can be expanded.

15 As more and more smokefree policies and
16 laws come into effect, there will be an increasing
17 number of settings where smokers will not be able to
18 smoke, such as the setting we're talking in today.
19 There is no reason that these people should need to
20 suffer the symptoms of nicotine withdrawal when safe
21 and effective products can reduce their cravings.

22 The use of these medications should be

1 encouraged in all settings where people are not able
2 to smoke. The positive experiences towards these
3 medicines, even in temporary abstinence settings,
4 can only help in their future attempts to quit
5 completely.

6 The current labeling on smoking cessation
7 medications is a clear barrier to FDA's goal of
8 making these medicines available to people of the
9 U.S. The labeling, as it stands, contradicts the
10 scientific evidence, leads to unrealistic fears, and
11 results in denied coverage and thus less
12 availability.

13 When consumers have the evidence-based data
14 available to them and are allowed to use these
15 medicines tailored to their needs, they feel more
16 confident in their chances of success and have
17 higher utilization of these products.

18 Changes to the current product labeling
19 will be a huge step forward in helping both the FDA
20 and ATTUD reach their mutual goal of reducing the
21 harm caused by tobacco use through increasing
22 availability of these effective treatments.

1 Thank you very much.

2 MS. SIPES: Thank you very much. I have
3 one quick question for you.

4 One of the things thank you discussed was
5 an indication for temporary use, for use of craving
6 and maybe other withdrawal symptoms. Can you talk a
7 little bit more about whether it's your own views,
8 state of the evidence, or a combination about
9 whether use for that purpose, during periods of
10 temporary abstinence, can be a spur to quitting or
11 not?

12 DR. STEINBERG: One of the settings where
13 we've done a lot of work recently, our clinical
14 experience includes both outpatients in primary care
15 practice as well as inpatients in hospital settings.
16 So a lot of the examples of data from temporary use
17 of medications and what happens to people after that
18 setting we find in the hospital setting.

19 So just as that as an example, I can tell
20 you that there's a lot of evidence from multiple
21 studies that show that people who use medications
22 during hospitalization for the sole purpose of

1 reducing withdrawal systems and cravings during that
2 forced abstinence, a higher proportion of people end
3 up using these medications after hospitalization. A
4 higher proportion of these people end up making quit
5 attempts after they leave the hospital, as opposed
6 to people who don't use those medications.

7 So not only in settings where these
8 medications are used for reducing cravings and
9 withdrawal symptoms on a temporary basis, not only
10 do people feel more comfortable, they have a
11 positive experience with these medications and
12 they're more likely to use them for subsequent quit
13 attempts after that period.

14 MS. SIPES: Are those studies you're
15 talking about specifically with smokers, or
16 different types of addiction?

17 DR. STEINBERG: Different types of
18 addiction, you mean, beyond tobacco? To be honest
19 with you, I don't have a lot of experience with
20 addiction outside of tobacco. So this is
21 predominately in smokers who are hospitalized.

22 MS. SIPES: All right. Thank you very

1 much.

2 DR. STEINBERG: Thank you.

3 MS. SIPES: Appreciate it.

4 Our next speaker is Danny McGoldrick, who's
5 here from the Campaign for Tobacco-Free Kids.

6 MR. MCGOLDRICK: Good morning. Thanks for
7 the opportunity to speak this morning, and also for
8 addressing a very unmet need, and that is more
9 effective ways to get smokers to quit.

10 I'm with the Campaign for Tobacco-Free
11 Kids. As a matter of disclosure, we do get a small
12 portion of our funding from manufacturers of smoking
13 cessation products and operators of quit lines.

14 I think people have said it already. It's
15 very clear, and the reason for all of this is
16 because too many people are dying and not enough
17 people are quitting. While 70 percent of smokers
18 say they want to quit and about half try every year,
19 only about 4 to 7 percent succeed. And that's
20 really what we're all about here.

21 A few of those who try to quit, only about
22 one in five, use the evidence-based medications that

1 are available. And while the evidence is clear that
2 these medications work when used appropriately, even
3 the best quit rates and the clinical work is less
4 than optimal.

5 This is, of course, part of the reason why
6 we still lose more than 400,000 Americans every year
7 to tobacco use, 1200 every day. And that really is
8 what needs to drive our thinking here in terms of
9 making more and better smoking cessation approaches
10 and products available.

11 So we need more and better ways to help
12 smokers quit, and FDA has the authority to make that
13 happen. With the passage of the Family Smoking
14 Prevention and Tobacco Control Act, the FDA now has
15 the authority, or at least the potential authority,
16 to regulate tobacco and nicotine in all its forms:
17 cigarettes, smokeless, gum, patch, inhaler, cigars,
18 e-cigarettes, toothpicks, strips, or whatever
19 form nicotine or tobacco may come in.

20 So it can now address addiction from both
21 sides. It gives the FDA the opportunity to address
22 both the addictive nature of tobacco products and

1 the availability and efficacy of the products that
2 help smokers quit.

3 We think FDA must use this authority and
4 coordinate across centers -- it's great to see both
5 of you represented here today -- to establish a
6 regulatory scheme that could potentially remove
7 addiction to the products that kill, and increase
8 availability in the use of products that can help
9 break that addiction and save lives.

10 These complimentary approaches can maximize
11 the number of smokers who successfully quit, and of
12 course have the added benefit of keeping kids from
13 becoming addicted as well.

14 Quickly, on the tobacco side, the Center
15 for Tobacco Products should, and I hope is already,
16 fund and foster research on the best ways to reduce
17 or eliminate the addictive nature of tobacco
18 products. This approach should take into account
19 the ways that tobacco companies make the products
20 more addictive -- because you can forbid them from
21 doing that -- and also examine whether and how to
22 reduce, or if possible, eliminate the ability of

1 tobacco products that cause harm and kill people to
2 also addict.

3 Now, this process is obviously going to
4 take some time and a lot of investment in research.
5 So at the same time, the FDA must also move
6 immediately to improve smoking cessation outcomes.
7 Even as we work to make sure that all of the current
8 evidence-based smoking cessation therapies are
9 available and encouraged for all tobacco users, we
10 must develop new interventions that more smokers
11 will use and that will help more of them quit, as
12 you've been hearing already.

13 Congress clearly recognized this in the
14 Tobacco Act in its instruction to FDA, to look at
15 ways to generate greater consumer acceptance and use
16 of existing smoking cessation products while also
17 fostering innovation of new smoking cessation
18 products that are more effective than products
19 currently on the market.

20 To do this, FDA must work collaboratively
21 with the private sector and industry to encourage
22 innovation in developing new uses for NRT, including

1 changes and labeling and indications, as you've
2 heard about; but also new products that tobacco
3 users will be more likely to use and to use more
4 effectively to quit.

5 We believe it's very important that FDA
6 preserve the safety and efficacy standard, while
7 encouraging innovation and ensuring that wider
8 availability of nicotine does not simply serve to
9 keep smokers smoking conventional products by
10 serving as a bridge product in providing nicotine in
11 times and places where smokers can't smoke, or
12 convincing them that they're taking a step toward
13 quitting when in fact they are not. And I know this
14 is many of the questions you were raising already
15 this morning.

16 We strongly encourage FDA to work with
17 responsible companies genuinely interested in
18 improving public health to develop a process that
19 will bring more innovative and effective NRT and
20 other products to market without compromising safety
21 and efficacy standards such that the public health
22 is harmed.

1 As others have said, though, in evaluating
2 the safety and efficacy of new approaches and
3 products, FDA must compare the risk of the use of
4 these products to the risk of continuing smoking,
5 rather than just doing nothing.

6 We support the FDA exploring with industry
7 the possibility of the fast-tracked process for
8 tobacco cessation products. With tobacco continuing
9 to kill more than 430,000 Americans every year and
10 smoking declining at way too slow a rate, a strong
11 case can be made that the serious diseases caused by
12 smoking -- cancer, heart disease, COPD -- represent
13 an unmet medical need.

14 This fast-track process should facilitate
15 more engagement between FDA and manufacturers to
16 design a process for evaluating innovative products
17 that is faster and brings more products to market,
18 but also ensures that standards are not compromised.

19 This will include a commitment from
20 manufacturers to conduct postmarket surveillance to
21 ensure that the desired outcomes are met. This
22 postmarket surveillance is not a substitute for the

1 clinical component, but a compliment. And we've
2 heard both sides of that over the past months.

3 We also support FDA working with industry
4 to determine if indications for extended use of NRT,
5 craving relief or relapse prevention, can lead to
6 more smokers quitting successfully. Again, though,
7 the key question is to determine whether these
8 indications don't just facilitate continued smoking
9 of conventional cigarettes to the degree that the
10 overall public health is harmed.

11 Obviously, for all of us, the goal in this
12 is less death and disease from tobacco use. It's
13 not just a matter of having this meeting and us
14 submitting our comments and putting out a report.
15 We really believe strongly that the FDA should take
16 proactive steps to collaborate with the private
17 sector to encourage the use of these existing
18 evidence-based therapies and bringing new ones to
19 market, and that that commitment by the FDA must be
20 matched by industry and manufacturers of these
21 products to that very same goal.

22 Thank you, and I'm happy to take any

1 questions.

2 MS. SIPES: Thank you very much.

3 MR. MCGOLDRICK: Thank you.

4 MS. SIPES: Our next speaker is Angela
5 Jones from the American Cancer Society Cancer Action
6 Network.

7 MS. JONES: Good morning. I am Angela
8 Jones, presenting testimony on behalf of the
9 American Cancer Society and its affiliate, the
10 American Cancer Society Cancer Action Network, or
11 ACS CAN.

12 First, the Society and ACS CAN support the
13 use of fast-track approval authorities for smoking
14 cessation products, including NRTs. Accelerated
15 approval processes that are used for certain cancer
16 medications have been successful, and a similar
17 approach for cessation medications and therapies
18 should be implemented.

19 While it's encouraging that there are now
20 five FDA-approved NRT products currently on the
21 market that have proven effective, there are still
22 nearly 44 million people in the U.S. who smoke.

1 Sixty-nine percent of smokers indicate they want to
2 quit, and about 52 percent attempt to quit each
3 year, but fewer than 7 percent succeed.

4 This clearly represents an unmet medical
5 need and a need for new products or new variations
6 on existing therapies that address smokers' quitting
7 needs. It is vital that these issues be addressed
8 in a very timely manner to reach smokers as quickly
9 and effectively as possible to stop the devastating
10 health consequences of tobacco use.

11 As noted by the U.S. Public Health Service
12 in its 2008 guidelines update, the volume of
13 evidence surrounding NRT is large and would help
14 pave the way for fast-track approval of other NRTs
15 and related therapies. NRTs fulfill FDA's fast-
16 track criteria in a number of ways.

17 Tobacco dependence is a serious disease,
18 and its health consequences are highly fatal. In
19 2012, 216,000 new cases of lung cancer alone are
20 expected, and the disease will have claimed the
21 lives of more than 160,000 people, mostly smoking-
22 related.

1 The NRT clearly impacts day-to-day
2 functioning as well as risk of developing chronic
3 disease or death. If smokers do not quit, they have
4 at least a 30 percent chance, and in some cases
5 closer to a 50 percent chance, of dying prematurely
6 from a smoking-related disease.

7 Quitting earlier in life with evidence-
8 based treatment, such as NRT, significantly elevates
9 a smoker's chances of a healthier and longer life.
10 Not only will risk of cancers and other chronic
11 diseases decrease, but respiratory and heart
12 functioning and quality of life will improve almost
13 immediately.

14 There is clearly a demand for potential new
15 products or new variations of existing therapies
16 that address smokers' quit needs, and these can be
17 addressed in a very timely manner to reach smokers
18 as quickly and effectively as possible to help stop
19 the devastating health consequences of tobacco use.

20 Unmet population needs, including those
21 among pregnant smokers, adolescents, certain ethnic
22 groups, light smokers, those with comorbidities, and

1 mental health issues, would be very well served by a
2 fast-track process to address these critical groups
3 as quickly as possible.

4 While currently approved NRTs have proven
5 effective when used as directed, the effectiveness
6 of these products remains limited and there are
7 clearly opportunities to find even more effective
8 NRT delivery systems and formulas.

9 Secondly, we support the potential for NRTs
10 to be used for extended periods of use beyond
11 current indications. The U.S. Public Health Service
12 Clinical Practice Guidelines on Treating Tobacco Use
13 and Dependence, the U.K.'s National Institute for
14 Health and Clinical Excellence, and others, have
15 provided evidence to support the efficacy of
16 extended use of NRTs in reducing tobacco dependence.

17 Thirdly, with regard to regulation of
18 innovative products and treatment, ACS and ACS CAN
19 urge FDA to maintain its well-established science-
20 based standards of drug safety and efficacy with
21 regard to all cessation medications, including NRTs.

22 As it does with other drugs, FDA must

1 carefully investigate the product characteristics
2 such as composition and manufacturing quality and
3 its efficacy in permanently quitting tobacco use, as
4 well as its clinical effects, including dose-
5 response profiles, likely-used topography, harm
6 profile, interactive effects, and potential for
7 acute and long-term adverse effects. FDA should
8 also consider population effects such as impact on
9 tobacco use generally, secondhand effects, and
10 impact on cessation population-wide.

11 The FDA also needs to investigate the
12 continuum of risk presented by all products related
13 to the reduction of tobacco dependence, or which
14 purport to do so. This would involve considering
15 what the public health and agency-wide implications
16 for regulatory policy would be of recognizing a
17 continuum of risk, and the surrogate endpoints
18 and markers, such as reduction in the number of
19 cigarettes smoked per day, which could accompany
20 that recognition.

21 Thank you for this opportunity to provide
22 input on the critical issue of treatment for

1 millions in the U.S. facing tobacco dependence and
2 its deadly health consequences. I'll take any
3 questions.

4 Yes?

5 DR. LEONARD-SEGAL: Thank you. Regarding
6 the use of fast-track, can I have a better
7 understanding of when you talk about -- you framed
8 it within the context of smoking cessation.

9 What does that mean to you? Does that mean
10 giving up cigarettes, but if there were long-term
11 use of NRT, that would be the consequence of giving
12 up cigarettes? Would that be a fast-track? Like
13 indefinite use of NRT, would that be a fast-track
14 kind of indication for you? Or are you talking
15 about people that are off nicotine? What is
16 your -- please clarify.

17 MS. JONES: Okay. I'll try to clarify, and
18 I will certainly address that in our written
19 comments as well more specifically.

20 Right now we're talking about cessation
21 from smoking and nicotine use. I think we'd be open
22 to the possibility of learning more about what

1 happens with extended use of nicotine or continuing
2 to use nicotine long-term. We're not prepared to
3 give our final position on whether that is -- I
4 think we need more research and one big
5 investigation on the potential health consequences
6 of that.

7 DR. LEONARD-SEGAL: Thank you.

8 MS. SIPES: Thank you. Our next speaker is
9 David Abrams, who's with the Schroeder Institute for
10 Tobacco Research and Policy Studies at Legacy.

11 DR. ABRAMS: Thank you for the opportunity.
12 My name is David Abrams. I'm executive director of
13 the Schroeder Institute at Legacy, and a professor
14 at Johns Hopkins School of Public Health and
15 Georgetown Medical Center. I'm speaking today on
16 behalf of Legacy. I have over 35 years of
17 experience in tobacco control, research, and
18 practice.

19 Legacy is a 501(c)(3) whose mission is to
20 help all young people reject tobacco and help adults
21 to quit. The Schroeder Institute conducts
22 intervention and policy research at Legacy. By way

1 of disclosure, Legacy has received financial support
2 from several pharmaceutical companies that make
3 cessation therapies.

4 Today I'll address questions mainly from
5 Sections 1 to 3 of the hearing. We ask FDA to adopt
6 more flexible standards to reach more smokers and
7 help them quit and stay quit. To do so, FDA needs
8 to level the playing field with the tobacco
9 industry.

10 By leveling the playing field, I mean
11 making therapeutic cessation products more consumer-
12 friendly, effective, and more widely available so
13 they can reach many more smokers and stand side by
14 side with the marketing and widespread distribution
15 of cigarettes and other tobacco-derived nicotine
16 products.

17 FDA must also keep pace with the latest
18 research evidence. Most critically, when
19 considering any therapeutic product, it's imperative
20 that the comparison for safety and risk be continued
21 smoking. Smoking kills over 1200 people daily.
22 That's equivalent to three fully-loaded jumbo jets

1 crashing with no survivors every single day of the
2 year, holidays included. The risk of a therapeutic
3 nicotine product compared to placebo drug or no
4 treatment pales by comparison with the risk of
5 continued smoking.

6 With respect to Section 1 questions, it
7 is not enough to limit the therapeutic nicotine
8 replacement for abrupt cessation, as is currently
9 indicated. This indication has not kept pace with
10 the PHS clinical guidelines.

11 Legacy recommends greater use of fast-track
12 and breakthrough therapy mechanisms. The safety of
13 medicinal nicotine is well-known. The product does
14 not need to be risk-free when compared to the known
15 risks of continued combustible tobacco use.

16 We recommend FDA consider less burdensome
17 premarket requirements for approval of medicinal
18 nicotine products, and that postmarket surveillance
19 is adequate and can be used to track outcomes.

20 Under Section 2 of your questions, we
21 concur that evidence presented by Dr. Foulds and
22 others on behalf of SRNT is sufficient for approval

1 of extended use of NRT, both to achieve cessation
2 and to maintain abstinence following cessation.

3 This is consistent with evidence from the
4 2008 PHS clinical guidelines, and also there's a
5 wealth of backup evidence in the cosigned petitions
6 submitted to FDA in February and in August of 2010.
7 Thus, NRT can be used for as long as is needed, and
8 also can be used in preparation to quit or when
9 experiencing a lapse or relapse.

10 PHS guidelines also support the use of
11 combination NRTs. The indications, labeling, and
12 packaging should be adjusted accordingly.

13 With respect to Section 3, we support new
14 indications, including the five listed here: use of
15 NRT as a reduce-to-quit strategy among current
16 smokers has the potential to reach much larger
17 segments of the smoking population. For craving
18 relief, we note that validated craving scales and
19 also laboratory cue-reactivity paradigms do exist
20 and are well characterized. In fact, our lab our
21 Brown University developed some of these
22 standardized measures over 25 years ago.

1 NRT use during lapses and relapses is also
2 indicated, as is combination use, and they also
3 improve treatment outcomes and likelihood of relapse
4 prevention.

5 Also, to make NRT products more convenient,
6 accessible, and consumer-friendly, smaller pack
7 sizes would enhance convenience, and widespread
8 distribution in retail outlets would help to reach
9 many more smokers, as was recently approved in the
10 Nicovum application for Zonnic.

11 These new indications and others
12 recommended under Sections 1 and 2 can dramatically
13 reach many more smokers and increase, one, the
14 number of smokers that make a quit attempt each
15 year; two, the number of smokers that succeed in
16 their quit attempts; three, that use nicotine
17 replacement therapies to make these quit attempts;
18 and improves the likelihood that they will stay quit
19 and prevent relapse.

20 To illustrate the dramatic lifesaving
21 effects, let me show you a publication in the
22 American Journal of Public Health using David Levy's

1 SimSmoke simulation modeling. By 2020,
2 the projections here will be that if we do nothing,
3 the status quo would remain, and smoking prevalence
4 will be well above the Healthy People 2010 goal,
5 which was 12 percent.

6 Our model also shows that simply increasing
7 treatment use and treatment effectiveness alone has
8 very minimal impact on reducing population,
9 prevalence, and health impact. However, by
10 contrast, note that if we could increase the vast
11 number of smokers who make quit attempts, this will
12 significantly begin to reduce prevalence to
13 13 percent by 2020.

14 In addition, if we add to that increased
15 access to use and improvement in treatment
16 effectiveness, both short-term and long-term
17 benefits could be absolutely dramatic in reducing
18 the number of smokers who are using dangerous
19 combustible products, saving potentially millions of
20 lives and millions of dollars in a relatively short
21 time frame.

22 In summary, Legacy recommends that FDA does

1 adopt more flexible and consumer-friendly approaches
2 to level the playing field. Mindful that the
3 comparison for therapeutic products is the lethality
4 of continued smoking, FDA should make more timely
5 use of the research; use fast-track status with less
6 burdensome premarket testing; approve changes in NRT
7 labeling for extended and combination use; and
8 consider new indications like reduce to quit,
9 craving relief, and relapse and lapse prevention.

10 As my simulation model shows, small changes
11 in reach, access, and effectiveness can have a very
12 large population impact on the population prevalence
13 of smoking, saving thousands more lives sooner
14 rather than later. With over 430,000 lives lost
15 each year, this is a medical and public health
16 emergency moving forward.

17 Finally, in conclusion, in concurrence with
18 others, I want to note that FDA now has full
19 authority to regulate all tobacco-derived nicotine
20 delivery products to protect individual and public
21 health.

22 With the passage of the Tobacco Control Act

1 and since this hearing is more focused on
2 Section 918, our comments did not address the
3 different standards and processes regarding
4 non-therapeutic problems under the Center for
5 Tobacco Products.

6 Both CTP and CDER regulate tobacco-derived
7 nicotine products either for recreational use or for
8 therapeutic-intended use. It is critical that FDA
9 coordinate agency-wide the standards to ensure that
10 optimal protection of individual and public health
11 is achieved.

12 There is a pressing need for FDA CTP to
13 exercise its regulatory authority and extend its
14 jurisdiction to tobacco-derived nicotine-delivering
15 products that are intended for non-therapeutic use.
16 And it is critical for agency-wide coordination of
17 the regulation of all tobacco- and nicotine-derived
18 products.

19 Despite 50 years of progress since the
20 first Surgeon General's report on the health-
21 damaging effects of smoking, we must not be
22 complacent in facing this continued medical and real

1 public health emergency. Immediate action is needed
2 to save up to 1200 lives every day and 430,000 lives
3 every year.

4 Thank you for your attention.

5 DR. LEONARD-SEGAL: Thank you. A couple of
6 questions for you.

7 Do you have any specific suggestions as to
8 how we would best decrease the premarketing burden
9 to get products out faster? And then as a second
10 question, what would be the appropriate types of
11 postmarketing surveillance that you have in mind?

12 Let me just throw out there that in the
13 over-the-counter drug world, which is where I spend
14 my time, we have postmarketing commitments for this
15 kind of thing, but we don't have postmarketing
16 requirements. Those are prescription authorities.

17 So there would be a thought process
18 involved as to whether these postmarketing
19 surveillances ought to be requirements and whether
20 these products ought to be OTC first and based upon
21 what we could do and not do related to that kind of
22 regulatory authority.

1 DR. ABRAMS: Okay. Your first question
2 around premarket burden, there are a couple of
3 things that I can think of off the top of my head,
4 and we're happy to submit more specific
5 recommendations in our written comments.

6 But one thing is that the characteristics
7 of current nicotine replacement therapies are
8 extremely well-known. And both short-term and long-
9 term use is certainly safe and effective, again
10 especially if we keep in mind that the comparator is
11 combusted cigarette tobacco use and not necessarily
12 modest or minor risks compared to placebo or no
13 treatment.

14 So relative to the health-damaging effects
15 of tobacco, I think one could take into account the
16 prior history and 20-plus years of experience with
17 nicotine replacement products; so that with
18 a modification of a substantially equivalent
19 existing product, or even a new product that
20 primarily delivers nicotine in a noncombustible
21 manner, those precedents could be used to reduce
22 premarket requirements and premarket burden and

1 negotiate appropriately with the manufacturers for
2 more flexible and faster-track indications for
3 market.

4 If I could stop there. Does that answer
5 your question?

6 DR. LEONARD-SEGAL: Are you suggesting that
7 depending on the delivery system and what have you,
8 that we don't look at as many issues related to like
9 leachables and extractables coming from a particular
10 delivery system, if there were some kind of a
11 device-type entity involved with the drug?

12 Are you talking about fewer requirements
13 for the number of clinical trials, or the number of
14 patients in the clinical trials, or the duration of
15 the clinical trials? Anything that you can provide
16 to us with those kinds of thoughts I think in your
17 written comments might be helpful to us.

18 DR. ABRAMS: Sure. I mean, one of the
19 quick answers is, it depends on the product and the
20 indications that are being fast-tracked. I could
21 certainly imagine, again, products with known
22 characteristics that are substantially equivalent to

1 existing products could be fast-tracked with almost
2 minimal other requirements.

3 Clearly, if it was a new product like a new
4 combustible delivery mechanism -- I mean, a new
5 noncombustible delivery mechanism, there certainly
6 should be appropriate negotiations for safety and
7 efficacy testing; but again, keeping in mind that
8 nicotine exposure and long-term nicotine use is
9 known to be far safer when compared to nicotine
10 delivered in a combustible cigarette.

11 So again, I think you could have
12 substantial reductions in burden on any one off the
13 usual requirements, depending on the specific
14 application, which, as I understand it, is generally
15 negotiated in discussions with the manufacturers,
16 obviously keeping in mind safety and efficacy, but
17 also the standards and the prior history of delivery
18 and use of nicotine products, which, as I would call
19 them, are more clean nicotine delivery as opposed to
20 dirty nicotine delivery that is found in the
21 delivery in a combustible cigarette.

22 With respect to postmarket surveillance, I

1 think here's where some discussion and agency-wide
2 collaboration between the two branches, CTP and
3 CDER, might be warranted, as well as considering
4 what might be the kinds of outcomes that one would
5 be looking for.

6 But certainly I think some obvious criteria
7 would be that, for example, if one were to fast-
8 track approval of, say, current NRTs for craving
9 relief or reduce to quit dual use, along the way, to
10 reducing substantially or eliminating combustible
11 cigarettes, one could envisage very specific
12 criteria and thresholds for what we mean by reduced
13 harm or reduced amount of exposure of combustible
14 cigarettes, again as the standard, in order to
15 reduce the harms that primarily come from the
16 combustible cigarette.

17 So I could see that being necessary for
18 some postmarket surveillance to ensure, for example,
19 that an unintended population consequence doesn't
20 occur where dual use leads to continued dual use,
21 without substantial reduction in harm exposure and
22 reduction in amount of combustible cigarettes used.

1 So those would be some of the parameters to
2 consider. But again, given the enormous amount of
3 death, disease, and dollar costs of continuing
4 combustible cigarette use, one could argue, as
5 Dr. Foulds did, that we'd far rather see some of
6 these things tested and evaluated in postmarket
7 surveillance than have unnecessary delays and huge
8 excessive burdens in premarket testing.

9 Yes?

10 DR. RAPPAPORT: To probe the fast-track
11 issue just a little bit more, on slide 4, you say
12 products with promising signs of effectiveness and
13 relatively safety versus smoking should be
14 considered for fast track. We've also heard from
15 people today that perhaps the fast-track approval of
16 Chantix is somewhat responsible for the serious
17 adverse events that have been associated with it.

18 Could you comment on whether you see a
19 difference between NRT products, new molecular
20 entities, or other types of treatment in terms of
21 fast track?

22 DR. ABRAMS: Yes. As I said before, this

1 needs to be done on a case-by-case basis. I think
2 certainly a new entity with relatively less known
3 about its mechanisms, and what molecular structure,
4 and whether it's truly a well-characterized nicotine
5 replacement product or derived from another well-
6 characterized drug, would make a difference and
7 would require much more careful premarket
8 evaluation, probably of the type that's already
9 being done, in a more conservative manner to protect
10 the individual and public health.

11 With respect to the example of Chantix,
12 though, again, while there are clearly some warnings
13 and side effects that have been of concern that
14 resulted in black label warnings, I think I would
15 also still want to point out -- it actually has been
16 even demonstrated recently, in the last two weeks,
17 with respect to population-based meta-analysis and
18 characteristics of Chantix -- the excess risks
19 involved are relatively small, certainly very small
20 compared to continued smoking.

21 So the benefits of Chantix, which doubles
22 to quadruples the likelihood of cessation, far

1 outweigh, at a population level, some of the side
2 effects and concerns that have been raised, some of
3 which are borderline or not even statistically
4 significant, although they are arithmetically of
5 concern.

6 So when you go from individual to
7 population-level benefits, keep in mind that the
8 comparator is the 400,000 deaths from combustible
9 cigarettes. And while some untoward side effects of
10 Chantix, which I believe are still largely overblown
11 when you look at the full population studies, are
12 certainly of concern. They are of much less concern
13 in the overall population benefit versus risk of
14 having that drug on the market and available for
15 some of the people who can use it successfully.

16 Yes?

17 DR. HUSTEN: I wanted to explore a theme
18 that we've been talking about a little bit further.
19 When you were talking about the fast track and the
20 evidence that would be needed, some of your remarks
21 seemed to be talking about things that are the same
22 as -- the current NRTs on the market are very

1 similar to that. And then you talked about the more
2 that it's a completely new product, the more it
3 would need more of the premarket.

4 I'm just curious where you see
5 e-cigarettes, if they were to come in as a cessation
6 indication, about the level of evidence needed. We
7 heard one speaker saying, these are small
8 manufacturers. They shouldn't have to do any kind
9 of studies.

10 So I was just curious what you would see as
11 the level of evidence for a cessation indication for
12 those types of products.

13 DR. ABRAMS: That's putting me on the spot
14 and a good question. There's certainly accumulating
15 evidence, although I do not believe it's sufficient,
16 that e-cigarettes -- certainly logically, because
17 they're noncombustible -- are likely to be quite a
18 lot less harmful than combustible cigarettes.

19 But they're not without risks, and there
20 have been some concerns about non-standardized use
21 of the cartridges. The limited studies that have
22 been done raised concerns about quality control of

1 what is produced and the derived nicotine that's in
2 an aerosolized e-cigarette, certainly among some
3 manufacturers, and some may be more responsible than
4 others.

5 But overall, I don't think enough research
6 has been done to establish that the quality control
7 is adequate and that the standards of what is put on
8 the market and exposed to consumers are safe at this
9 stage.

10 So I would one would want to require -- and
11 I don't think e-cigarettes, as good as their
12 potential may be, should be exempt from the same
13 requirements as any other people in terms of
14 demonstrating safety and efficacy. So that's a
15 quick answer.

16 On the other hand, I think e-cigarettes
17 have a great potential. Some of the presentations
18 this morning were extremely convincing that this is
19 an innovative product that has several potential
20 advantages if its potential can be realized.

21 So I think one has to weigh the balance
22 of some additional premarket testing and

1 requirements, which I think are necessary to
2 establish safety, product standards, and so on,
3 against the fact that we also would like to see more
4 appropriate randomized clinical trials of
5 e-cigarettes as an effective cessation device.

6 I think the studies that have been done
7 thus far are generally samples of convenience, very
8 small sample sizes, and do not meet the kinds of
9 requirements that would allow us to say, A, that
10 e-cigarettes are an effective cessation treatment;
11 B, that they are as good as or perhaps better than
12 some NRTs; and C, that they can be used short-term
13 and long-term, the way we're asking for NRTs.

14 But I see no reason why that shouldn't be
15 an urgent and important and very -- a process that
16 ought to be very seriously looked at on a fast track
17 because of the potential lifesaving benefits of new,
18 innovative nicotine replacement products like
19 e-cigarettes, perhaps.

20 DR. WINCHELL: You and several other
21 speakers have alluded to the concept that the risk
22 of the product should be weighed against the risk of

1 continued smoking rather than against the risk of
2 placebo.

3 I have been confused by that because when
4 we -- we compare to placebo in order to understand
5 the risks of the product, but we wouldn't say, this
6 product is unacceptably risky because it has risks
7 that are different from placebo.

8 So help me understand how comparing to the
9 risk of continued smoking differs from comparing to
10 the benefits of quitting smoking, which is what we
11 currently do.

12 DR. ABRAMS: I'm not sure I follow you in
13 terms of the benefit.

14 DR. WINCHELL: So we characterize what is
15 the adverse effect profile of the product. And then
16 we say, well, those are the risks of the product,
17 and the benefits are that this many people will quit
18 smoking. And you could say that the converse of
19 that is that all the rest of the people will
20 continue smoking.

21 DR. ABRAMS: Right.

22 DR. WINCHELL: We say, well, we know that

1 quitting smoking is good. So then we compare the
2 risks of the product to the likelihood of not
3 smoking any more.

4 Help me understand how what you're asking
5 us to do is different from that.

6 DR. ABRAMS: Well, I think, as has been
7 alluded to, both in consumer perceptions and in
8 fact, the very narrow and restrictive warnings and
9 the way that current NRTs are restricted by the
10 current guidelines of FDA seem to me to way overly
11 weight the minor side effect and concerns against no
12 use of NRT or placebo, when compared to the
13 overwhelming, health damaging consequences of
14 current smoking.

15 DR. WINCHELL: So are you speaking to how
16 we should communicate the risks as opposed to on
17 what basis we would approve the products?

18 DR. ABRAMS: Well, it could be both. But
19 at this point we're talking about communicating the
20 risk of the existing products. But it could also
21 interfere with how you develop your criteria for
22 fast track of what I would regard as substantially

1 equivalent but new indications for products; for
2 example, for craving relief, for reduce-to-quit
3 strategies prior to quitting.

4 One could also begin to worry, I think way
5 too much, about potential minor risks of using these
6 products in these new ways, compared again with the
7 huge advantage of them being used by very many more
8 consumers, potentially, as I showed in my simulation
9 model, leading to massive numbers of public health
10 benefit on a large scale.

11 I don't know. Does that answer your
12 question?

13 DR. WINCHELL: Somewhat, although some of
14 the uses that you're alluding to would have people
15 continuing to smoke. So that might be hard to
16 implement. But I think I understand where you're
17 going.

18 DR. ABRAMS: Yes?

19 DR. KWEDER: This has been on my mind a
20 little bit for the past few speakers, and you're
21 going to get the question because it's time now.
22 It's come to my thinking in a few of the

1 presentations.

2 Most of the organizations that are here,
3 they have spoken about what the purpose of their
4 organization is. What continues to come up, and
5 we've not had any conversation about -- perhaps
6 because of the narrow questions posed in the Federal
7 Register notice -- is preventing young people from
8 beginning to smoke.

9 Most of our discussion has assumed
10 that -- or at least I have interpreted it as
11 assuming -- that the products that are being
12 proposed to be more widely available would be used
13 by people who are attempting to decrease their
14 actual cigarette use.

15 I'd like to know what your thoughts are
16 about -- and you used the word -- "unintended
17 consequences" of more widespread availability of
18 nicotine-containing products, and what we ought to
19 be thinking about were that to occur, and what the
20 consequences of that might be for young people.

21 The studies that have been done have
22 compared, again, smoking to stopping smoking,

1 continued smoking to stopping smoking. They
2 have not looked at -- and they have looked at
3 assumptions based on comparing the effects of
4 combusted tobacco to just nicotine in patients.

5 But what have you considered in terms of
6 consequences for the public, the broad public
7 health, over a longer period of time, to the
8 population of simply replacing the use of tobacco
9 plants with widespread recreational use of pure
10 nicotine-containing products?

11 DR. ABRAMS: That's the \$64,000 question on
12 some level.

13 DR. KWEDER: You may not be able to answer
14 that today, and I understand that. But I do think
15 that it's something as a public health need we need
16 to consider.

17 DR. ABRAMS: No. It's a good point, and I
18 think I allude to that in my final comment, which is
19 that there is complexity here with regard to whether
20 you're using an individual safe and effective
21 standard, which is important, or whether you're
22 elevating that to what is really in the Tobacco

1 Control Act's new statement, which is somewhat
2 untested in regulations in general, which is a
3 "public health standard" to determine whether the
4 overall public health benefit versus harms are more
5 for users and non-users, which would include youth.

6 So I think this is another area where we
7 would like to see perhaps a lot more discussion, a
8 lot more thought, about what are the vectors and
9 dynamics that alter population prevalence rates of
10 uptake, particularly transitions from starter
11 products and seductive starter products that
12 ultimately would lead to use of combustible
13 cigarettes as a final outcome.

14 So that's, I think, a very complex
15 question. And on some level, it might be that very,
16 very close surveillance of the marketplace as these
17 things play out, as they are now -- because, absent
18 of deeming regulations, we have e-cigarettes, snus,
19 and many other noncombustibles on the market. So if
20 you will, like it or not, we're in a natural
21 experiment. So I think something like the FDA,
22 funded through NIDA, PATH study, which is on over

1 50,000 people, including 20,000 or so adolescents
2 and young adults, can begin to give us the kind of
3 tracking and surveillance that will give us a little
4 bit of a sense of what's going on.

5 Although you can't generalize culturally,
6 the Swedish experience is also perhaps interesting
7 to both contrast and look at how America is
8 different and similar. But, for example, in Sweden
9 we know there's largely a lot less people who
10 transition from, say, Swedish snus to combustible
11 cigarettes.

12 Now, that could be cultural and
13 intergenerational, so that could be a very dangerous
14 generalization. But it's not out of the realm of
15 possibility that because a generally buccal
16 absorption and these other forms of noncombustible
17 delivery are not nearly as -- don't have nearly the
18 presumed immediate addiction liability that
19 combusted cigarette has, that there could be complex
20 benefits or unintended harms here.

21 So I don't think any of us can answer that
22 question at the moment. It's clearly something that

1 requires some careful measurement in the real world
2 in real time, which is happening.

3 Then I think there's only -- in order to
4 deal with the complexity, we need much better
5 simulation models of the entire vectors of the
6 system that influence both the pro- and the
7 anti-harm forces and vectors as they impinge on not
8 only individuals but groups and the overall pattern.

9 So I don't think we have an easy answer to
10 that question now. But I think, certainly, current
11 restrictions on sales to minors can and should be
12 enforced for all nicotine products. So we shouldn't
13 relax any of that.

14 But I also think the huge urgency of
15 helping adults to stop smoking -- and regardless of
16 whether they then use safer forms of nicotine
17 delivery even for their lifetime -- or whether it's
18 self-medication in the sense of people with comorbid
19 mental illness where nicotine could be a very
20 valuable and positive drug, absent the dirtiness of
21 its delivery in a combusted cigarette, I think we
22 haven't fully explored anywhere near enough the

1 ability to do that and reduce the harm death and
2 disease.

3 That's a long answer. I'm sorry.

4 DR. KWEDER: No. That's okay.

5 DR. ABRAMS: Yes?

6 MR. LINDBLOM: I was interested in the
7 simulation model that you referred to with a chart.
8 And it seems like the main driver there is increased
9 quit attempts. That's where you get the big act.

10 DR. ABRAMS: Yes.

11 MR. LINDBLOM: And I was wondering whether
12 you think that the proposals in your presentation
13 relating to NRTs and nicotine products would produce
14 that kind of doubling of the quit attempts by
15 itself, and if so, how that would work.

16 DR. ABRAMS: Yes. Frankly, I don't think
17 we have good population-level estimates of exactly
18 how much it would help. But I think the take-home
19 message is that that curve begins to go down with
20 various scenarios, a sort of sensitivity analysis.
21 But, clearly, it would be quite dramatically
22 advantageous to the degree that we can get closer to

1 the assumptions in this model.

2 It is also a combination. If you're
3 getting way more people to become involved in
4 thinking about reducing, as in the reduce-to-quit
5 strategy, and if some of those then start making
6 quit attempts, and if they then use effective
7 nicotine replacements at double the rate they are
8 now -- which, frankly, isn't asking for much because
9 less than 20 percent of current people, when they
10 make a quit attempt, are using any evidence-based
11 treatment.

12 So getting 40 percent of them to use an NRT
13 because they're not more flexible, there are less
14 scary warnings, and they're readily available in
15 mom-and-pop grocery stores throughout the country in
16 small pack sizes, I think could well get us close to
17 some of the better curves in these what-if
18 scenarios.

19 So we don't have the data at the moment,
20 but it certainly could do no harm. And since so
21 many people are dying, why not go for it, and then
22 measure it and see whether we're right?

1 Yes?

2 DR. LEONARD-SEGAL: I have one population
3 I'd like to talk about that no one has talked about
4 today and didn't make it into our questions.

5 But in terms of the postmarketing
6 surveillance that you spoke about earlier, do you
7 have thoughts about what to do with the pregnant
8 population? We don't know how to label these
9 products -- well, the NRT products, certainly -- for
10 use in pregnancy for quitting. Do you have thoughts
11 about where we might be exploring there?

12 DR. ABRAMS: I think I'd rather not comment
13 on that here, but do written comments. My
14 recollection is, from Neal Benowitz and other data,
15 that, again, the harms of a mom smoking during
16 pregnancy far outweigh the risks of maintenance
17 doses of nicotine replacement therapy.

18 But clearly not using any nicotine in the
19 case of pregnancy would be the most prudent because
20 there is evidence, for example, that nicotine
21 clearly crosses the placental barrier. And there is
22 some evidence, but it's really from combusted

1 tobacco use in the moms, that it may well influence
2 and change structure and function of the brain,
3 leading to even mild ADHD and other disorders in the
4 developmental trajectory.

5 So I think here, when you're talking about
6 in utero exposure, the sensitivities and
7 vulnerabilities of the infant are much more blown
8 up, and we have to be more careful. But again, if
9 my recollection is correct, the studies that have
10 been done very clearly show that combustible
11 cigarette use is also very dangerous.

12 But the issue there is, I think, much more
13 tricky, and one probably should be more cautious.
14 But we'd be happy to respond to that in writing
15 because I can't remember all the studies off the top
16 of my head at the moment.

17 DR. LEONARD-SEGAL: Thank you. I know it's
18 a curve ball, but it's something I just --

19 DR. ABRAMS: That's okay. No, it's a good
20 question.

21 DR. LEONARD-SEGAL: Thank you.

22 DR. ABRAMS: It's a critically important

1 question.

2 MS. SIPES: I think there was at least one
3 study about a year and a half ago showing that use
4 of NRT in pregnant women didn't quite accrue the
5 benefit that was expected, which gets away from the
6 harm question. And I know you want to answer
7 further in another context, but do you have any
8 comment on that?

9 DR. ABRAMS: No. I wouldn't want to
10 comment at the moment. Actually, one follow-up
11 comment. It raises another issue, which we haven't
12 discussed, and that is the use of NRT in adolescents
13 and young adults who might sincerely be wanting to
14 quit. And, again, I wish there were more data on
15 that. But I would also think that there are
16 probably reasons to at least try it and do more
17 research on it.

18 But, again, you're in the slippery slope
19 where if a kid is just beginning to use combusted
20 tobacco products, one worries that if they start
21 using NRT very early, you might be promoting the
22 addiction rather than eliminating it. But, again, I

1 think that that's not relevant if the restrictions
2 on availability and sale of NRTs are largely to
3 adults, where you could get the biggest life saving
4 in the shortest amount of time.

5 MS. SIPES: I have one other question.
6 This goes back to a little bit of what Dr. Kweder
7 was talking about, or at least gets to one small
8 piece of it. You and others have talked about
9 reduce to quit as a strategy, as a way to reach more
10 smokers and to move things forward. I have a couple
11 questions about that.

12 The first is, do you envision that type of
13 use pattern as a self-directed, self-titrated one,
14 or something that needs to be put into a
15 programmatic context?

16 DR. ABRAMS: That's a good question. I'm
17 not sure we have enough evidence to answer that
18 question. I think the studies that have been done
19 are done under somewhat ideal conditions, with
20 volunteers, generally more higher SES volunteers and
21 so forth.

22 So as you generalize from the study

1 populations to the broader population, I think it's
2 a little more difficult. However, I would imagine,
3 and I think some of the studies do speak to this,
4 that self-directed is generally okay, and it
5 generally does lead to more people then making quit
6 attempts and succeeding in their quit attempts than
7 anything else. And, secondly, that even if it leads
8 to dual use but with some substantial reduced use of
9 combustibles, that should be considered as a
10 reasonable, intermediate outcome.

11 I think a lot of the evidence is, though,
12 that once people are on that path, they're much more
13 likely to eventually stop using combustibles or stop
14 using all products. So I think the advantages
15 outweigh the concerns.

16 MS. SIPES: That was going to be my next
17 question, is do you have any concerns about the way
18 dual use plays into that scenario.

19 DR. ABRAMS: Yes. Again, that's a little
20 bit of a tricky systems issue. I think in general,
21 one could make the statement that dual use, as long
22 as there's significant reduction in combustible use,

1 could have advantageous benefits, obviously because
2 there's less exposure to the harmful products that
3 are in combusted cigarettes.

4 But there are two things that I think
5 simulation modeling can help with here. One is when
6 you do it on a population level, you have to look at
7 what proportion of the population are dual using but
8 not reducing their combustible use, using it, let's
9 say, as a bridge product when they can't smoke at
10 the workplace.

11 That could, in fact, on a population level
12 begin to undermine indoor air smoking laws and
13 demotivate them or make them decide, hey, this
14 is cool. I think I'm smoking slightly less
15 cigarettes, so this is harm reducing for me. And I
16 now don't have to quit because I'm not that
17 uncomfortable at the workplace or in my home when I
18 don't want to smoke around my kids.

19 So in that situation, the proportion of the
20 population that goes that route might lead to
21 unintended consequences of delayed quitting and not
22 much harm reduction from reduced amount or exposure

1 of combustibles. So that's something we'd have to
2 look at and worry about.

3 However, the other side of the coin is,
4 you've got a lot of people that might actually try
5 reducing harm that otherwise wouldn't have, and
6 that's going to be a public health benefit. Of
7 those that do it, it's more likely that some of them
8 will substantially reduce their combustible use, and
9 there's some evidence that most of them go on to
10 quit.

11 So a simulation model could begin to put
12 those things together with reasonable input
13 parameters and reasonable transitional assumptions
14 based on data. So it wouldn't be as speculative a
15 model because all models are wrong and some models
16 are useful. But this could be a useful one,
17 provided you have those caveats, number one.

18 Number two, I think the bigger concern is
19 with longer-term users that have had more than 15 to
20 20 pack years of exposure -- if you look, for
21 example, at the lung cancer risk curve, it
22 exponentially takes off somewhere between 18 and

1 22 years of cumulative exposure. And when that
2 takes off, almost any, even minimal, combustible use
3 is life-threatening and bad for you.

4 So you can't make the generalization
5 between younger and older smokers because it's more
6 risky for dual use with some combustible use in an
7 older smoker with more than 20 pack-years of
8 exposure.

9 Again, maybe those are things that we need
10 to educate the public about in terms of things like,
11 if you're going to reduce to quit, don't be seduced
12 completely into, I can still smoke 5 cigarettes a
13 day, and especially not if I've already smoked for
14 20 or more years. And the data on that are clear,
15 and you could make very clear statements about that.

16 So again, not all the answers are here, but
17 I think we know a lot, and we could do a lot more
18 than we're doing now to move more of the population
19 towards reducing the health-damaging consequences.

20 So again, delaying cessation or dual use
21 has some risks, but it also has some benefits. And
22 overall, probably the benefits will outweigh the

1 risks, although, again, that could be postmarket
2 surveillance needs to track that. Because, again,
3 some of these experiments can't be done in a lab. I
4 don't think you could set up a study to look at this
5 that would be generalizable enough for us to know
6 what would happen in the real world. So some of
7 this has to be done with postmarket surveillance.
8 But, again, worth the risks, because there are
9 430,000 people dying every year, and we've got to do
10 more than we're doing.

11 MS. SIPES: All right. It looks like that
12 at last concludes our questions. Thank you very
13 much, Dr. Abrams.

14 All right. Our next speaker is Bill
15 Godshall, who's here from Smokefree Pennsylvania.

16 MR. GODSHALL: Hello. I'm Bill Godshall,
17 founder and executive director of Smokefree
18 Pennsylvania, a nonprofit organization that since
19 1990 has been advocating local, state, and federal
20 policies to ban smoking in workplaces; reduce
21 tobacco marketing to youth; hold cigarette companies
22 accountable in civil litigation; increase cigarette

1 tax rates; fund tobacco education and smoking
2 cessation services; inform smokers that smokefree
3 tobacco and nicotine products are far less hazardous
4 alternatives to cigarettes; and to ensure that
5 smokefree alternatives remain legal and affordable
6 to smokers.

7 In 2007, I convinced Senator Mike Enzi to
8 amend the Tobacco Control Act in the Senate to
9 require colored graphic warnings on all cigarette
10 packs; and two decades ago, we urged the FDA to
11 approve NRT for over-the-counter sales.

12 For disclosure, neither I nor Smokefree
13 Pennsylvania has ever received any funding from any
14 tobacco, drug, or electronic cigarette company or
15 trade association.

16 I'm here to once again urge the FDA to stop
17 protecting cigarettes from market competition by far
18 less hazardous smokefree alternatives, to correct or
19 clarify FDA's many inaccurate and misleading claims
20 about low-risk smokefree tobacco and nicotine
21 alternatives, and to keep all smokefree alternatives
22 legal and affordable for smokers.

1 More than 99 percent of all tobacco-
2 attributable mortality and health care costs in the
3 United States are caused by repeated inhalation of
4 tobacco smoke, while less than 1 percent of
5 mortality and health care costs are caused by the
6 use of noncombustible tobacco and nicotine products.

7 Epidemiologic evidence indicates that
8 cigarettes are at least 100 times more hazardous
9 than smokefree nicotine and tobacco products
10 marketed in the U.S., including smokeless tobacco,
11 electronic cigarettes, and NRT products.

12 While quitting all tobacco and nicotine
13 is an effective way for smokers to improve their
14 health, switching to smokefree alternatives reduces
15 smokers' risks nearly as much as quitting all
16 tobacco and all nicotine use.

17 Survey and sales data indicate that more
18 than a million smokers have quit smoking by
19 switching to smokeless tobacco products, that
20 several million smokers have switched to smokefree
21 electronic cigarettes in just the past several
22 years, and that many smokers use NRT products as

1 temporary or long-term alternatives to cigarettes.

2 Since there have been many reports of
3 suicide, suicidal thoughts, and adverse
4 cardiovascular events associated with Chantix, I
5 urge the FDA to consider removing Chantix from the
6 market, or to at least require additional warnings
7 to better inform consumers of its risks.

8 I also urge the FDA to not fast-track the
9 approval process for any new drug for treating
10 dependence. After seeing what the FDA has not done
11 on Chantix, I would not want to see another drug
12 like that approved.

13 Although FDA has approved many NRT products
14 to treat tobacco dependence, NRT products have a
15 95 percent-plus failure rate for treating tobacco
16 dependence and for smoking cessation. Therefore, I
17 urge the FDA to disapprove all NRT products as
18 treatment for tobacco dependence, and to not approve
19 products as smoking cessation aids unless clinical
20 trials find a 20 percent or higher success rate; or
21 to at least require manufacturers to notify
22 consumers of the 6-month and 12-month success rates

1 the product was found to have for both smoking
2 cessation and for achieving nicotine abstinence.

3 But since NRT products are far less
4 hazardous alternatives to cigarettes, and since most
5 NRT products are consumed for off-label use as
6 either temporary or long-term substitutes for
7 cigarettes, the FDA should approve all NRT products
8 as temporary and long-term harm-reduction
9 alternatives to cigarettes.

10 The FDA should adopt R.J. Reynolds'
11 citizens petition to replace the intentionally
12 deceptive "not a safe alternative" warning on all
13 smokeless tobacco products with one that informs
14 consumers that cigarettes are far more hazardous.
15 And the FDA should propose a similar warning for
16 cigarette packs, since smokers are at greatest risk.

17 Warning labels on NRT products should also
18 state that the product is a far less hazardous
19 alternative to cigarettes, and should encourage,
20 instead of discourage, smokers to continue using NRT
21 as long as they continue to smoke.

22 If FDA implements these regulatory changes,

1 manufacturers of electronic cigarettes,
2 dissolvables, and even smokeless tobacco products
3 may consider applying to the FDA to market these
4 product as nicotine replacement therapy/tobacco
5 harm-reduction alternatives. NRT manufacturers
6 should consider more aggressively marketing their
7 products to smokers as well.

8 In contrast to most NRT products that have
9 been marketed in the last 20 years in \$40-plus
10 packages at pharmacies only, R.J. Reynolds Nicovum
11 is test-marketing Zonnic nicotine gum in \$3 ten-
12 packs -- that's 30 cents per piece of gum -- at
13 convenience stores throughout Des Moines, Iowa.
14 These kind of marketing changes are necessary, and
15 I'm glad the FDA has approved that for that
16 marketing.

17 Regardless of regulatory changes for NRT
18 products, the FDA should never again ban or oppose
19 unwarranted or unreasonable regulations on
20 electronic cigarettes, dissolvables, or smokeless
21 tobacco products because these products have nearly
22 identical health, safety, risk/benefit profiles as

1 do NRT products.

2 In 2009, in an attempt to justify its
3 unwarranted and unlawful import ban on electronic
4 cigarettes, then-FDA Deputy Commissioner Josh
5 Sharfstein misrepresented the agency's laboratory
6 test findings on e-cigarettes to scare the public
7 and to falsely claim that the products were target-
8 marketed to children.

9 But even after FDA concurred with Judge
10 Leon's ruling prohibiting FDA from banning
11 e-cigarettes as unapproved drugs, the FDA has still
12 refused to correct or clarify any of its inaccurate
13 and misleading claims about e-cigarettes. Even
14 worse, the agency has issued additional misleading
15 claims since then about e-cigarettes. And yet
16 e-cigarette sales continue to skyrocket and should
17 surpass NRT sales next year, whose sales have
18 remained stagnant, about \$1 billion annually for the
19 past decade.

20 The FDA has repeatedly stated its intent to
21 propose a deeming regulation to apply Chapter 9 of
22 the Tobacco Control Act to e-cigarettes, but

1 Sections 905 and 910 would ban all e-cigarettes, and
2 other provisions of Chapter 9 would also decimate
3 the e-cigarette industry, protect cigarette markets,
4 and otherwise threaten public health. The FDA
5 should not propose or approve any regulation that
6 would deny cigarette smokers legal or affordable
7 access to less hazardous alternatives.

8 The FDA has also denied the growing body of
9 scientific evidence and consensus among experts by
10 falsely stating on a webpage entitled "Health
11 Fraud" -- it says, "To date, no tobacco products
12 have been scientifically proven to reduce risk of
13 tobacco-related disease, improve safety, or cause
14 less harm than other tobacco products."

15 Is there anybody in this room that truly
16 believes that smokeless tobacco and e-cigarettes are
17 just as hazardous as cigarettes? I don't think so.
18 The FDA should immediately take that webpage off.

19 Many other FDA and DHHS websites also
20 contain false and misleading fear-mongering claims
21 that exaggerate the risk and deny the benefits
22 of smokeless tobacco products for smokers.

1 One week after FDA's TPSAC issued a report
2 that acknowledged dissolvable tobacco products are
3 less hazardous than cigarettes and can reduce risk
4 of smoking, the FDA issued a draft guidance for MRTTP
5 applications that denied the scientific evidence and
6 would require smokeless tobacco companies to spend
7 tens of millions of dollars on unnecessary studies
8 just so that FDA might consider allowing the company
9 to truthfully inform smokers that smokeless tobacco
10 is less hazardous than cigarettes.

11 Smokers have a human right to truthful
12 health information and legal access to less
13 hazardous alternatives, and the FDA has an ethical
14 duty to inform smokers that all smokefree tobacco
15 and nicotine products are far less hazardous
16 alternatives to cigarettes, and to keep all less
17 hazardous alternatives legal and affordable for
18 smokers.

19 Instead of wasting public dollars
20 defrauding the public and abusing its authority and
21 the rights of tobacco consumers by demonizing and
22 campaigning against all tobacco use, the FDA, CDC,

1 Surgeon General's office, and other DHHS agencies
2 should focus on reducing the leading cause of
3 disease, disability, and death, which is cigarette
4 consumption and daily smoking, not tobacco or
5 nicotine use. Abstinence-only, prohibition
6 policies, and propaganda didn't work for alcohol,
7 marijuana, or sex, and they don't work for tobacco,
8 either.

9 I think it's important to point out that
10 the four previous speakers before me all oppose all
11 tobacco use and all urge the FDA to ban
12 e-cigarettes, and yet they're here today -- and I
13 applaud them for saying we should judge these NRTs
14 based on compared to continued smoking, but when it
15 comes to judging e-cigarettes and smokeless tobacco,
16 they want to judge it against quitting everything.
17 And that's the problem. You can't have different
18 rules apply.

19 What's the difference between a dissolvable
20 tobacco lozenge and a dissolvable nicotine lozenge?
21 Nothing. You can market it right now as either/or.
22 Under the law, if I have a company and I want to

1 sell its product, I say, well, should we sell it as
2 a tobacco product or should we sell it as an NRT?
3 And the problem is, there are two routes right now.
4 And the one, it's good nicotine that's lifesaving
5 medicine, and the other is an addictive, deadly,
6 evil tobacco product. And it's the same product.
7 It's just a matter of how you're marketing it.

8 So we need to really look at the bigger,
9 broader issues of public health instead of just the
10 minutia of each subsection of this law.

11 I'd be happy to answer any questions on any
12 of these issues. Yes?

13 DR. RAPPAPORT: Just to tease out one
14 section of this, I think there's substantial
15 evidence -- or at least we've heard from a lot of
16 groups and heard a lot of people speak about the
17 serious health consequences of chewing tobacco. Do
18 you include that in your calling noncombustible
19 cigarettes as relatively safe?

20 MR. GODSHALL: The epidemiologic studies on
21 chewing tobacco found that it's about 99 percent
22 less hazardous than cigarettes. And the 1986

1 Comprehensive Smokeless Tobacco Education Act
2 mandated the warning on all smokeless tobacco
3 products that says, "This is not a safe alternative
4 to cigarettes." No, it's not a safe alternative,
5 just 99 percent less hazardous.

6 That's a deceitful warning. It's
7 intentionally deceptive to -- and I know because I
8 was around when that discussion occurred 25 years
9 ago. And the people behind that were smokeless
10 tobacco prohibitionists. They didn't want smokers
11 to switch to smokeless tobacco. And I'd say, well,
12 why? And they'd say, we want them to quit. And
13 besides, if they switch to smokeless, that won't
14 achieve our goal of destroying the tobacco industry.

15 That's really the problem you have here. A
16 lot of people that claim to be public health
17 advocates are tobacco prohibitionists, and their
18 goal is to wipe out the industry. And they don't
19 want smokers to switch to any product that the
20 industry profits from.

21 Right now, R.J. Reynolds, their statements
22 recently, they're having higher profit margins from

1 their sales of Grizzly smokeless tobacco than they
2 are from their Camel cigarettes. And that's good,
3 because as long as tobacco companies can make more
4 profits selling a smokefree alternative than they
5 can selling a cigarette, they have a vested
6 financial interest. And the FDA should encourage
7 these kinds of products to be marketed.

8 DR. RAPPAPORT: So with these images I have
9 in my head of these young men who have lost pieces
10 of their jaw and such from chewing tobacco, can you
11 include the references to those epidemiologic
12 studies in your submission to the docket?

13 MR. GODSHALL: I'd be happy to. And I've
14 already sent them to the FDA at least seven or eight
15 different times in previous dockets, and all that
16 information has been ignored, including the MRTTP
17 panel. They just totally ignored it.

18 In fact, the FDA told the MRT panel to
19 ignore these harm-reduction issues, the risk of
20 smokeless. And the IOM, when they contracted with
21 the Institute of Medicine, they instructed them not
22 to talk about the comparable risk of different

1 tobacco products because -- this is unfortunate.

2 The FDA has this prohibitionist mentality.

3 Why do we tell tobacco companies they're
4 not allowed to tell smokers that smokeless is less
5 hazardous? That just keeps people smoking. And
6 even the tobacco companies say, we'd be happy to
7 tell them the truth about these less hazardous
8 products, and the FDA is saying, no, you can't.
9 You've got to keep selling them cigarettes instead.

10 Back to your question about chewing tobacco
11 risk. Most mouth cancer, oral cancer
12 deaths -- 75 percent of all oral cancer deaths in
13 America, according to the CDC and according to the
14 American Cancer Society, among men are caused by
15 cigarette smoking. The risk of mouth cancer from
16 smokeless tobacco is about one-tenth of the risk of
17 smoking causing mouth cancer. And most mouth
18 cancers that do occur in smokeless users occur in
19 people over the age of 65.

20 Those few cases -- and yes, everybody
21 that's ever used a smokeless tobacco product and got
22 mouth cancer under the age of 30 is now being hired

1 by some anti-tobacco group to run around the country
2 and show their jaws. That's not science. That's
3 fear-mongering and propaganda.

4 MS. SIPES: I had one quick question for
5 you. Could you explain a little bit about your
6 statement that Sections 905 and 910 of the Tobacco
7 Control Act -- or the Food, Drug & Cosmetic Act, as
8 amended by the Tobacco Control Act, would ban
9 e-cigarettes?

10 MR. GODSHALL: Yes. Section 910, when it
11 was enacted in 2009, any product -- currently,
12 cigarettes and smokeless tobacco are regulated by
13 Chapter 9.

14 It said that any product that wasn't on the
15 market before February 15, 2007 would either have to
16 apply for a substantial equivalence application,
17 that it was substantially equivalent to a product
18 already on the market before 2007, or they'd have to
19 submit a new tobacco product application.

20 Then Section 905 said anybody that's
21 marketing one of these products in 2010/2011 could
22 still market the product, but they had to get their

1 substantial equivalent applications in -- I think it
2 was May 2011 was the deadline.

3 Well, if you deem -- so it's too late. The
4 deadline's already passed for any products that
5 weren't on the market by 2007 to get them
6 grandfathered in. And so now, if you take a new
7 product like electronic cigarettes or some of these
8 dissolvables and say, okay, now we're going to apply
9 you to all Chapter 9 regulations, well, they missed
10 the deadline.

11 At the time, FDA back in 2009 was telling
12 the federal courts, e-cigarettes are not tobacco
13 products; they're drug devices. But now, if you'd
14 pass the deeming regulation, you'd be saying, okay,
15 all you e-cigarette companies should have known we
16 were going to deem you as a tobacco product in 2013,
17 and you should have known that back in 2009 to get
18 your substantial equivalence applications in on
19 time.

20 So you'd have to amend those sections. And
21 there's many more. I mean, Section 911, the
22 modified risk tobacco products section, would make

1 it a crime for any e-cigarette company to market
2 their product as not emitting any smoke. Just
3 making a claim that it's smokefree is a federal
4 felony under Chapter 9.

5 So you really need to look through. And
6 I've presented this many times to many people at the
7 FDA, all these problems with Chapter 9 and how they
8 actually threaten public health instead of benefit
9 public health. And to just say, let's take all this
10 new category and apply to them the rules that we
11 applied to cigarettes and smokeless three years ago,
12 it just doesn't work.

13 I don't think that regulations for these
14 new products should be appropriate for protecting
15 public health. And if you go through Chapter 9,
16 you'll see many of these regulations were
17 not -- they have no benefit for public health. They
18 were just in there, I think, to demonize
19 this -- releasing the list of potentially hazardous
20 and hazardous chemicals? What's that going to do
21 to -- how's that going to benefit public health?

22 That's off-subject, but I could go on for

1 an hour of all the problems with Chapter 9 and how
2 it doesn't benefit public health. But you guys are
3 now required to uphold the law, so you're required
4 to threaten public health. So you've got a quandary
5 that you've got to deal with.

6 MS. SIPES: Thank you. Thank you very
7 much.

8 MR. GODSHALL: Thank you.

9 MS. SIPES: Appreciate it.

10 All right. I would like to take one more
11 speaker before we break for lunch. Great. I'm glad
12 that you were here.

13 Our next speaker is Kathleen Dachille -- I
14 apologize if I'm pronouncing that wrong -- from the
15 Legal Resource Center for Tobacco Regulation and
16 Litigation Advocacy at the University of Maryland
17 School of Law.

18 MS. DACHILLE: Thank you. And I'm keenly
19 aware that I'm what's between everyone here and
20 lunch, so I will attempt to --

21 MS. SIPES: No. Not at all. We have
22 plenty of time. Do not consider yourself --

1 MS. DACHILLE: Well, the last name is
2 Dachille. I'm actually -- well, that's the title.
3 I am the director of the Legal Resource Center.

4 I'm here speaking today on behalf of the
5 Tobacco Control Legal Consortium, which is a
6 consortium of legal centers that work to assist
7 state and local public health officials, policy-
8 makers, and advocates to devise and develop and
9 implement sound tobacco control policy.

10 Of course, the work of the consortium
11 expanded in 2009 when Congress passed the Tobacco
12 Control Act. And since that time, TCLC, the
13 consortium, has worked to develop products designed
14 to help state and local health officials understand
15 the Act and the role that they can play.

16 Probably the most important role that they
17 can play is providing evidence and input to the FDA
18 on how you can use the powers that you have under
19 the Tobacco Control Act, and to avoid the regulatory
20 gaps that do exist, particularly with respect to
21 nicotine-containing products.

22 As the FDA contemplates regulating

1 innovative products and treatments for tobacco
2 dependence, the consortium urges the FDA to do so as
3 part of a comprehensive approach to the regulation
4 of nicotine across the centers.

5 What's most important is that CDER and
6 the CTP work together to prevent any of those
7 regulatory gaps with respect to these innovative
8 nicotine products. The failure to have a
9 comprehensive plan for regulating tobacco and
10 nicotine products will result in these gaps that
11 will be exploited by the tobacco industry,
12 undermining the FDA's public health objectives.

13 To be frank, for 50 years, for more than
14 five decades, the tobacco industry has manipulated
15 their products in order to enhance the effect of
16 nicotine. They have attempted to achieve the
17 optimal delivery of nicotine for the sole purpose of
18 addicting and sustaining that addiction in its
19 users. So we must be mindful of that role that
20 nicotine has played in tobacco products over the
21 years.

22 Of course, in response to the Master

1 Settlement Agreement and the Tobacco Control Act, we
2 have seen a change in the industry in developing
3 innovative products such as snus and dissolvable
4 tobacco products.

5 In fact, while not particularly engaged in
6 the development of the e-cigarettes, now tobacco
7 companies have purchased some of the leading
8 e-cigarette products. And this should give us pause
9 because this is the industry that designed the
10 manipulation of tobacco products to addict and
11 sustain addiction. And now these innovative
12 products, whether tobacco-containing or simply
13 nicotine-containing, are a threat to the public
14 health because of this controlling of the nicotine
15 delivery in a variety of forms.

16 So with such a wide range of novel tobacco
17 and nicotine-containing products available, it's
18 important that CDER and CTP work together to avoid
19 creating these gaps, or we will see the continuation
20 of smoking as a result instead of the diminution in
21 smoking.

22 Obviously, e-cigarettes plays the best

1 example for us here. And I want to comment
2 particularly on the question about the youth access
3 issues that haven't been addressed today because
4 e-cigarettes helps us with answering that question.

5 So right now, you're in the state of
6 Maryland. And just last year, the Maryland
7 legislature passed a provision prohibiting the sale
8 of e-cigarettes to minors. But before then and in
9 most states across the country, that's not the case.

10 So while the Sottera court determined that
11 the CTP can regulate e-cigarettes as tobacco
12 products, and CDER can regulate e-cigarettes if
13 therapeutic claims are made, at this time CTP, while
14 demonstrating an intention to take action, has not
15 done so.

16 So none of the provisions in the Tobacco
17 Control Act apply to e-cigarettes, and CDER has yet
18 to issue any guidance about what constitutes
19 a therapeutic claim with respect to electronic
20 cigarettes. And so we don't know whether any of
21 them should be subject to CDER regulation.

22 What falls in the middle is children's

1 access. So while there may be viable and safe uses
2 for electronic cigarettes, none of us want to see
3 them in the hands of children. Perhaps if CTP were
4 able to deem jurisdiction over electronic cigarettes
5 and the sales and distribution regulations could
6 then applied to electronic cigarettes, we could
7 address that problem. But this is one of the
8 regulatory gaps that exists right now, in part
9 because CDER and CTP have not worked collaboratively
10 in response to this particular innovative problem.

11 Just as troubling, the response to Sottera
12 is that if there are products that contain nicotine
13 that are not tobacco products and are not marketed
14 for therapeutic purposes, who regulates them? Where
15 do they fall?

16 It's incredibly important that CDER and CTP
17 work together to make sure there aren't any products
18 that fall through that gap; and if there are, that
19 we go back and we see which agency should be
20 taking -- or which entity should be taking
21 responsibility for these products.

22 So the bottom line is that the tobacco

1 industry has been exploring expansion into the
2 NRT market themselves. As was indicated previously,
3 R.J. Reynolds is now marketing nicotine replacement
4 therapy products; particularly Zonnic gum is in test
5 launching. Other products in the works for Reynolds
6 include an electronic cigarette, nicotine extract
7 products such as lozenges, and smokeless pouches and
8 pellets.

9 The involvement of the tobacco industry
10 in the NRT market is particularly concerning in
11 light of Judge Kessler's 2006 opinion in U.S. versus
12 Philip Morris, in which she found that the tobacco
13 industry for decades knew about nicotine's
14 pharmacological properties and addictive nature;
15 incorporated design techniques into their products
16 to assure delivery of precise levels of nicotine
17 that were necessary to maintain addiction; and took
18 public positions, suppressed and concealed research,
19 and destroyed documents so that the information
20 would not be available to federal regulatory
21 agencies.

22 In light of Judge Kessler's ruling that the

1 tobacco industry conspired to defraud the American
2 public about the dangers of tobacco products,
3 including that it can and does control nicotine
4 levels to sustain addiction, it seems unlikely that
5 Reynolds American is investing in NRT products to
6 help reduce addiction to nicotine and encourage
7 cessation.

8 Instead, it seems quite likely that
9 Reynolds and other tobacco companies are expanding
10 into the NRT market to further their business of
11 keeping consumers addicted to tobacco products. For
12 this reason, it is essential that the FDA's centers
13 work together to regulate nicotine products in a
14 comprehensive manner. Thank you.

15 MS. SIPES: I have one question for you, a
16 little bit of an abstract question. Do you feel
17 that there can ever be addiction without harm, or is
18 addiction itself always harmful?

19 MS. DACHILLE: Sure. I'm not a lawyer -- I
20 mean, a doctor. I'm a lawyer. So I get to play
21 that card here. But I obviously work with a lot of
22 physicians and PhDs who study these issues.

1 I think that where we are on the spectrum
2 right now is nowhere near where you're talking
3 about. And if we can work on policy that works us
4 till where that question really is not abstract but
5 is real, I'd like to get us there. And I think
6 working to reduce the likelihood of increased uptake
7 of any nicotine-containing products will help us to
8 get to that question.

9 So it didn't answer your question, but I
10 want to get to where we have to answer that
11 question, and our research is more focused on
12 whether allowing the sustaining of an addiction
13 to nicotine really isn't really a public health
14 problem any more. But we're nowhere close to there,
15 and that's what CDER and CTP need to get us to.

16 MS. SIPES: In that case, thank you very
17 much.

18 MS. DACHILLE: Thank you.

19 MS. SIPES: I think what we should do,
20 because Mr. Hughes is not going to be able to attend
21 today, let's start the lunch break now and come back
22 at ten to 1:00. Ten to 1:00. Our next speaker will

1 be Dr. Gilbert Ross.

2 Thank you very much. I'll see you at ten
3 minutes to 1:00.

4 (Whereupon, at 11:47 a.m., a luncheon
5 recess was taken.)

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

2 (12:55 p.m.)

3 MS. SIPES: All right, everyone. I'm sorry
4 for the delay. I think we're going to get started.

5 Our first speaker this afternoon is going
6 to be Dr. Gilbert Ross. He's here from the American
7 Council on Science and Health.

8 DR. ROSS: Thank you very much. And thank
9 you folks at the FDA for having this public hearing
10 on this most crucially important topic.

11 The most reliable estimates are that one
12 billion people will die from cigarette smoking over
13 the course of this century. That's cigarette
14 smoking, that is, not tobacco use. Even in our
15 country, with its stringent regulations and
16 longstanding absence of mass marketing, over
17 45 million Americans still smoke. Over 400,000,
18 perhaps 450,000, die each year to the effects of
19 cigarette smoke.

20 This is a massive public health problem
21 that we face. We have to address this today and
22 moving forward in order to reduce the frightful toll

1 of smoking. Creative approaches are needed, not
2 blind adherence to the failed approaches of the
3 past.

4 Fear and mistrust of the tobacco companies,
5 which was well-earned during the deceptive,
6 manipulative, and fraudulent practices of the
7 previous century, should not be allowed to trigger
8 hyper-precautionary regulation on far safer
9 noncombustible products, whether tobacco-based or
10 not. Such an approach will hamstring effective
11 approaches to reducing the toll of cigarette
12 smoking. Strict compliance, for example, with the
13 recommendations of the most recent IOM report will
14 eliminate any possibility of reduced-risk tobacco or
15 nicotine delivery products getting onto the market.

16 We cannot await decades of data from gold
17 standard, random-controlled trials that can never be
18 done to pharmaceutical-level standards. While
19 waiting for such data to accumulate, millions will
20 die.

21 The deep-seated antipathy of governmental
22 agencies, NGOs, and academics toward the tobacco

1 industry is something we should never forget. But
2 erecting impenetrable obstacles to truthful
3 communication about the relative risks of different
4 tobacco products and other modified-risk products is
5 counterproductive. Those who will be penalized are
6 not the tobacco companies, but addicted smokers.

7 The current regulatory environment, as well
8 as the stated goals of leadership of the tobacco
9 industry, bear no relationship to those of the last
10 century. I implore you not to ignore reliable
11 epidemiological evidence of the low relative risks
12 of noncombustible tobacco and nicotine delivery
13 products.

14 Sticking to the tired mantra, there is
15 no safe tobacco product, is not informative nor
16 helpful. While technically true, it is equally true
17 that there is no safe automobile or medication. But
18 we allow them on the market and accept the down side
19 for the greater good.

20 Let me talk about the greater good for a
21 moment. The sad state of affairs of millions of
22 addicted smokers who want to quit, and tried to quit

1 and failed, clear evidence collected over decades of
2 use, is those for which -- to see
3 it (indiscernible).

4 Moderate smokeless products such as snus,
5 low in measurable carcinogens and low clinical
6 adverse outcomes, are about two orders of magnitude
7 safer than smoking; not safe, it's true, but safer.
8 None of the official FDA sites, nor those of the CDC
9 or other public health agencies, come to terms with
10 these simple facts.

11 Among the 45 million addicted adult smokers
12 in our country, 70 percent say they want to quit,
13 40 percent try each year, but only 10 percent or
14 less succeed. Current approved cessation aids fail
15 90 percent or more of the time, an unacceptable rate
16 by any reasonable standard.

17 Epidemiological studies over the past
18 decade-plus, documented by E.U. health authorities,
19 show that the rate of smoking and smoking-related
20 disease and death in Sweden among men is the lowest
21 in the E.U., directly correlated -- inversely, I
22 should say -- with the amount of smokeless tobacco

1 use. Ignoring these facts restricts smokers seeking
2 guidance to the same dogma: There is no safe
3 tobacco product.

4 Other official sites warn of the dangers,
5 the ephemeral dangers, the hypothetical dangers, of
6 e-cigarettes. Smokers will just get the message:
7 If these advisories don't help you to quit, just
8 keep on smoking.

9 The sad and inconvenient truth is that the
10 approved products -- I won't go through them
11 all -- succeed infrequently, over a one-year period
12 of time, less than 10 percent. And the article
13 acknowledging this fact was published not by Big
14 Tobacco but by anti-tobacco spokespeople well known
15 to you, Drs. Greg Connolly, Hillel Alpert, and Lois
16 Biener in January of this year.

17 The abstract says, "This study finds that
18 persons who have quit smoking relapsed at equivalent
19 rates whether or not they used NRT to help them in
20 their quit attempts." So why brother? And they
21 have their own side effects, which are rarely
22 mentioned.

1 The driver of ongoing smoking, despite the
2 well-known risks, is nicotine addiction, which takes
3 hold after only a brief experience with inhaling
4 cigarette smoke. The addiction to nicotine,
5 strongly enhanced by the rituals of smoking, keeps
6 millions of smokers hooked.

7 Smokers quit all the time, it's very true.
8 There are more ex-smokers than smokers now. And yet
9 it takes five, eight, ten attempts to quit, and over
10 that period of time deadly, insidious damage is
11 accumulating. And lethal diseases such as
12 cancer -- especially cancer -- develop years after
13 quitting has occurred.

14 Smoking-related COPD, which starts during
15 smoking years, continues to progress relentlessly,
16 even after quitting. Secondhand smoke sickens and
17 kills how many? We don't know exactly. But none of
18 those problems occur in smokeless products or with
19 e-cigarettes.

20 So why bother with the facts about relative
21 risks and chance confusing smokers with possibly
22 reduced-risk products? Here's why: Because

1 millions of nicotine addicts will keep on craving,
2 seeking, and getting their drug. It is not the
3 nicotine that kills, although many consumers, and
4 even some physicians, believe otherwise. Even if we
5 could make all the cigarettes in the world disappear
6 with a snap of the fingers, their replacements
7 arrive very quickly. It's not that simple.

8 If smokers are discouraged from access to
9 or information about alternative reduced-risk
10 products, some will quit; but sad experience shows
11 that the overwhelming majority will just keep on
12 smoking. And the most lethal, dangerous nicotine
13 delivery system is also the one that's readily
14 available everywhere.

15 Other governments in the World Health
16 Organization are trying to address this devastating
17 problem by banning smokeless products and
18 e-cigarettes, conflating tobacco and smoking. I
19 would urge you not to do the same thing.

20 Let me devote a few moments to
21 e-cigarettes. Electronic cigarettes, of course, are
22 not cigarettes. They're nicotine delivery devices.

1 Despite the lack of statistically significant
2 information collected on them, millions of smokers
3 have taken up this technology.

4 The substances that are being provided in
5 e-cigarettes -- water, glycerin or propylene glycol,
6 and vaporized nicotine at various dosages -- are
7 quite benign and, at worst, far less harmful than
8 the products of tobacco combustion.

9 Common sense is not something that I as a
10 public health person usually resort to. However,
11 the stakes here are higher than in any other
12 situation, given that smoking is the most
13 devastating public health problem we can deal with,
14 and it is preventable.

15 We can't wait for decades of trial data to
16 accumulate and ignore the simple truth by adhering
17 to warnings of illusory dangers while waiting that
18 will cost millions of lives. Some have expressed
19 concerns that reduced-risk products will lead young
20 people toward smoking, toward nicotine addiction and
21 eventually smoking. There is no valid evidence that
22 smokeless products or e-cigarettes function in such

1 a gateway capacity.

2 The issue I ask you now to confront is
3 crucially important: the formidable barrier to
4 truthful communication erected by the FDA and other
5 agencies about the relative risks of various tobacco
6 and nicotine delivery products. Of course, when we
7 attempt to broach that problem, we run into the
8 Family Smoking Prevention and Tobacco Control Act,
9 which erects barriers to truthful communication,
10 certainly, by the tobacco companies.

11 So who can tell the truth to the public, to
12 the desperate smoker? I ask you to do so. I'm not
13 asking you to flout the law, nor even to lobby for
14 its revision. But nothing in the law or regulations
15 requires your consumer-oriented websites to continue
16 to promulgate false or misleading information about
17 these products and their risks.

18 FDA websites uniformly warn smokers away
19 from much safer products in what seems to be an
20 intentionally misleading campaign to keep smokers
21 getting their nicotine from cigarettes, the most
22 lethal delivery system. This is counterproductive

1 and in fact dangerous.

2 These advisories should be removed or,
3 better still, modified to reflect the accumulating
4 scientific reality, mostly from Scandinavia. These
5 data clearly show the inverse correlation of
6 smokeless tobacco consumption with cigarette-related
7 mortality. Further, the warning labels on low-risk
8 tobacco products should be amended to reflect the
9 new scientific evidence.

10 The inexcusable, fraudulent behavior of the
11 cigarette makers is on record. I became well-versed
12 in it in my tenure at the American Council on
13 Science and Health, where anti-tobacco and anti-
14 smoking efforts and mistrust of Big Tobacco was part
15 of our marrow.

16 We at the American Council recognize that
17 times have changed, thanks to the devoted efforts of
18 many in the anti-tobacco, anti-smoking movement.
19 Smoking rates have plummeted, although over the past
20 few years it seems to have plateaued; quit rates
21 also, despite the addition of several newer
22 cessation products. But some of those methods, as I

1 mentioned, have their own risks, and that's really
2 downplayed on the FDA sites as well.

3 In order to save the lives and health
4 of millions of addicted smokers, the time for
5 decades-old mistrust and recriminations has passed.
6 The current leaders of the tobacco industry will
7 continue to sell tobacco products, but they also
8 state their aim is to harm and kill fewer of their
9 customers than they used to.

10 The recent statistics showing reduced
11 cigarette sales, along with increased smokeless
12 sales, is exactly what we should be striving for,
13 but even those data bring forth attacks from those
14 who wish that tobacco would just disappear. But it
15 won't.

16 I believe that one day -- I don't know
17 when -- public health authorities who now mislead,
18 and continue to mislead, smokers by ignoring
19 scientific evidence about the relative risks of
20 various tobacco products will be held to account,
21 like the tobacco company executives who are now
22 required to confess and accept responsibility for

1 their actions of the past.

2 The current public health authorities may
3 have to explain why they stubbornly adhere to a
4 dogma based on belief or agenda despite clear
5 evidence to the contrary, maintaining with straight
6 faces that there is no safe form of tobacco;
7 smokeless products are not a safe alternative to
8 smoking. Such a position is not based on science,
9 has caused and will cause many smokers their lives
10 if nothing changes. Thank you very much.

11 Questions?

12 (No response.)

13 DR. ROSS: No questions? Thank you again.

14 MS. SIPES: Thank you very much.

15 Our next speaker is Scott Ballin, who's a
16 health policy consultant.

17 One quick housekeeping announcement I meant
18 to mention right after the break. If any of you are
19 interested in speaking during the public comment
20 period, please remember to put your name on the list
21 outside the room. Thank you very much.

22 Mr. Ballin?

1 MR. BALLIN: Thank you very much. I
2 appreciate the opportunity to make a few comments on
3 what is really a discussion about not only NRT
4 products and how they should be regulated, but more
5 importantly, about how the spectrum of tobacco,
6 nicotine, and alternative products should be
7 regulated in a more rational and consistent manner.

8 I think everybody knows that up until about
9 three years ago, traditional tobacco products were
10 for the most part unregulated by any governmental
11 agency, and what regulation there was, was pretty
12 much piecemeal.

13 Products that were attempted to be put
14 on the market that were somewhat different or
15 innovative were often prohibited because of the
16 tobacco in them or because they made adulterated
17 claims.

18 The topic of this hearing, the topics of
19 this hearing, are obviously intertwined, and I think
20 really serve as a catalyst for a more civil
21 discussion and transparent discussion on the need
22 for the development of a more uniform nicotine and

1 tobacco policy. And I heard that sprinkled
2 throughout many of the presentations this morning.

3 It's strange that in some ways we've come
4 full circle since the time when FDA Commissioner
5 David Kessler sought to level the regulatory playing
6 field by seeking to bring tobacco products under the
7 FDA's drug and device authorities back in the '90s.
8 That was a time when there was obviously no Center
9 for Tobacco Products, and today there is, and that's
10 a big distinction.

11 It seems appropriate, therefore, to discuss
12 how a more consistent regulatory scheme might be put
13 in place to deal with what is a very dynamically
14 changing tobacco, nicotine, and alternative products
15 environment.

16 That includes a growing spectrum of
17 products, and you've heard some of those mentioned
18 this morning. This includes discussing not just now
19 we should regulate NRT, but other -- and I've coined
20 a new phrase -- smoking replacement products,
21 whether tobacco-based or nicotine-based or something
22 else. It may be a dietary supplement type product.

1 Much has changed since the statute was
2 enacted just some three years ago. And while
3 Section 19 hits on a number of important issues, it
4 also raises many more questions.

5 I was recently reminded that the language
6 of Section 918 didn't just come into being three
7 years ago, but was actually a product of a
8 discussion and debate that was inserted into the
9 legislation in the early part of 2003.

10 So much has changed -- with respect to the
11 science, the technology, and the innovation, and who
12 the manufacturers are in both of these tobacco and
13 nicotine areas.

14 Section 918, like many provisions in the
15 statute -- including Section 911, which also needs
16 to be discussed -- were well-intentioned, but
17 outdated and really stimulates the need for the
18 discussion I'm talking about.

19 When one considers the continuum of risk
20 associated with the wide spectrum of nicotine and
21 tobacco, it's very clear to everyone that it's the
22 smoking that causes the overwhelming number of

1 deaths. While we use the word tobacco, it really is
2 the toxic cigarette and the chemicals in the smoke
3 that cause that harm, with over 400,000 deaths each
4 year in this country.

5 When you stop the combustion, you drop the
6 risks considerably, not all of them. In other
7 words, however, if one can change the product, and
8 technology allows us to change the product, we
9 can reduce risk substantially. And I see both
10 tobacco- and nicotine-based products playing a role
11 in doing that, as long as it's done in a carefully
12 regulated environment.

13 There's another area I'd like to just
14 raise, is we use a lot of different terms in talking
15 about tobacco and nicotine. And I think we need to
16 step back and look at those terms and redefine them.
17 I see it in government. I see it in the NGOs. I
18 see it in the media. And we need to sit down and
19 talk about what it is we actually are talking about
20 in this new era of tobacco and nicotine regulation.

21 I mean, what is an NRT product, really?
22 What's a tobacco product? And there's discussions

1 about that. What is a smokeless product? Are NRT
2 products and very low-risk tobacco-based products in
3 fact part and parcel of the same category, which I
4 refer to, as I said before, as smoking replacement
5 products? What's an innovative product? Where do
6 you draw those lines?

7 What is relapse? What is risk? How do you
8 define risk and relative risk? What is cessation?
9 Is it smoking cessation? Tobacco cessation? And
10 there are even some people out there talking about
11 total nicotine cessation.

12 I say all this because we've got to get our
13 terms straight when we're talking about legislation
14 and regulation so that we can develop the most
15 appropriate policy possible.

16 Consumers are also left out of the
17 discussions on a regular basis. I find it very
18 distressing that in many of the surveys and reports
19 that I see, the average consumer out there or user
20 of tobacco products thinks it's the nicotine -- I
21 mean -- yes, the nicotine that causes the cancer,
22 and that all tobacco products are equally harmful.

1 It's not the case.

2 So consumers need to have more consumer-
3 friendly information on all these products, from NRT
4 all the way through. And I think the FDA has a
5 major responsibility and role to play in seeing that
6 that gets accomplished.

7 I've also suggested that there's a formula
8 that we should be looking at, and that is that now
9 that we have regulation of both nicotine and
10 tobacco, and growing levels of science, and the CTP
11 is going to be doing even more science, we've got
12 innovative happening across the board, not with just
13 tobacco and pharmaceutical companies, but others.

14 We're talking about, even in this notice,
15 what incentives should be out there, and we're
16 talking about competition. And I think those things
17 combined can actually change the marketplace very
18 dramatically, that it'll promote public health as
19 well as change the behaviors of the various
20 companies that we want to see behaviors changed.

21 So what can we do to bring tobacco and
22 nicotine into the 21st century? That's really what

1 I've been talking about for several years now. I
2 think that one of the things to seriously consider
3 is not only these two centers working together, but
4 actually restructuring the statute to have a new
5 center.

6 Since we now have the Center for Tobacco
7 Products, which has nicotine issues related to
8 it, that we establish the Center for Tobacco,
9 Nicotine, and Alternative Products, where we can
10 deal with all of these various things under one
11 umbrella, and maybe set up some advisory committees,
12 one to deal with the combustible products, one to
13 deal noncombustible alternative products, and one to
14 deal with those kinds of products that actually have
15 the level of science necessary to make therapeutic
16 claims.

17 I think that we need to move down that road
18 and have some serious discussions about that. The
19 establishment of a more rational, balanced, science-
20 based but flexible approach to regulating all these
21 products would bring some predictability to the
22 environment, serve the interests of public health,

1 promote competition, and hopefully make FDA's work a
2 little easier.

3 All the products could be more easily
4 surveyed and monitored, and you heard some
5 discussion about keeping tabs on all these various
6 products. It could be done through better
7 coordinated mechanisms under one center.

8 So let me just close by making some
9 suggestions to you, and they're in my written
10 remarks.

11 I don't see anything that prevents CDER or
12 FDA from making additional recommendations as part
13 of its report to Congress, and I would encourage you
14 to do so because the environment has changed
15 dramatically and I think that kind of information
16 needs to be incorporated.

17 First, as I mentioned before, I think FDA
18 should suggest to Congress that all tobacco and
19 nicotine products should be brought under that same
20 umbrella and overseen by a new center.

21 Second, FDA should convey to Congress that
22 there's an urgent need to review all the various

1 terminologies of products and what we mean by that,
2 and to bring some order to the chaos that's out
3 there with respect to consumers.

4 Third, FDA should indicate to Congress that
5 the agency will continue to convene workshops like
6 this one to explore and continue to build dialogue
7 on the various issues that are going to have to be
8 addressed.

9 Also, on the fourth issue, FDA should, with
10 the private sector, talk about incentives that could
11 be put in place to move these companies in the right
12 direction to reduce disease and death.

13 One of those things that I would suggest as
14 an incentive is developing a fast-track system
15 within a new constituted center; you're relying on
16 some of the provisions of 506. But because tobacco
17 and nicotine are so unique within the FDA, it may be
18 appropriate to look at doing something very
19 independently within the reestablished center.

20 Fifth and lastly, encourage Congress to do
21 its job in holding some oversight hearings -- real
22 oversight hearings, not political oversight

1 hearings -- so that these issues could be addressed
2 in the public, and we can bring more attention to
3 what needs to be done to make this a more rational
4 process for the health and welfare of the American
5 public. Thank you.

6 MS. SIPES: Thank you very much.

7 MR. BALLIN: Thank you.

8 MS. SIPES: Our next speaker is James
9 Dillard from Altria Client Services.

10 MR. DILLARD: Madam Presiding Officer,
11 members of the panel, good afternoon, and thanks for
12 this opportunity to talk to you from one tobacco
13 industry perspective.

14 My name is Jim Dillard, and I'm senior vice
15 president of regulatory affairs for Altria Client
16 Services. And I'm here today on behalf of Philip
17 Morris USA, U.S. Smokeless Tobacco Company, and Nu
18 Mark. I'll be brief today.

19 I'd like to discuss, from a strategic
20 perspective, the role that innovative tobacco
21 products can play in reducing the harms associated
22 with tobacco use, and more specifically, cigarette

1 smoking. We intend to file comments in detail
2 before the January 16th time frame.

3 First, I'd like to discuss the range of
4 harms associated with tobacco products, in
5 particular cigarettes, then discuss why a continuum
6 of innovative, lower-risk tobacco products is needed
7 to reduce the harm from cigarette smoking. Lastly,
8 I'll discuss how FDA and other HHS agencies can
9 regulate innovative, lower-risk tobacco products in
10 a manner that best protects and promotes public
11 health.

12 Cigarette smoking is the most hazardous
13 form of tobacco consumption. The weight of
14 scientific evidence establishes that the harm caused
15 by tobacco use is primarily attributable
16 to cigarette smoking. The U.S. Surgeon General has
17 described cigarette smoking as the single greatest
18 cause of avoidable morbidity and mortality in the
19 United States.

20 Core strategies to reduce tobacco-related
21 harm are, and should be, to discourage initiation
22 and promote cessation, particularly among those not

1 legally permitted to buy tobacco products.

2 There is a growing consensus, however, that
3 public health policies based solely on prevention
4 and cessation are not sufficient in the real world.
5 Millions of adults are likely to continue using
6 tobacco products, notwithstanding efforts by
7 government, public health, and others to encourage
8 them not to use tobacco at all.

9 A harm reduction approach can compliment
10 smoking prevention and cessation strategies. This
11 approach focuses on reducing tobacco-related
12 mortality and morbidity by making available and
13 providing accurate information about consumer-
14 acceptable tobacco products that are proven to be
15 lower on the risk continuum of tobacco products.

16 This continuum can be represented on the
17 slide that you see here, that looks like it's a
18 little cut off. I apologize for that. Conventional
19 cigarettes are at one end of the spectrum,
20 presenting the highest risk due to combustion and
21 inhalation of tobacco smoke. We've heard a lot
22 about that today. And smoking cessation, of course,

1 is at the opposite end of the continuum, which is
2 completely to the right.

3 The U.S. Surgeon General and other public
4 health authorities have determined that smokeless
5 tobacco products are addictive and cause serious
6 disease. There is, however, an overwhelming
7 scientific, medical, and public health consensus
8 that moist smokeless tobacco products, including
9 those widely available in the United States and
10 Sweden, both snuff and snus, are substantially less
11 hazardous than cigarettes.

12 This consensus is based on extensive and
13 compelling scientific evidence, which has been
14 provided to the FDA on multiple occasions, including
15 epidemiological disease risk data in human
16 populations from the United States and other
17 countries.

18 As early as 2001, the Institute of Medicine
19 observed that smokeless tobacco products pose a
20 lower overall risk than cigarettes. Since that
21 time, panel after panel of experts have critically
22 and thoroughly examined the evidence and reached the

1 same conclusion: Using smokeless tobacco products
2 is undeniably far less hazardous than cigarette
3 smoking.

4 While debate continues over how publicizing
5 that information would impact public health, the
6 finding itself is now beyond any credible dispute.
7 Our research indicates that approximately 30 percent
8 of adult smokers are interested in innovative types
9 of spit-free tobacco product alternatives to
10 cigarettes. We believe marketing a variety of
11 consumer-acceptable, lower-risk tobacco products to
12 these adult smokers has the potential to encourage
13 movement away from cigarette smoking.

14 Earlier this year, we created a new entity
15 called Nu Mark, an Altria company, and we introduced
16 a product called Verve discs into commercial
17 distribution. Verve discs are a tobacco-derived
18 nicotine product. The primary ingredients in Verve
19 are tobacco-derived nicotine, non-tobacco cellulose
20 fibers, flavoring, and a polymer. Adult tobacco
21 consumers place the product in their mouth, chew on
22 it, and then dispose of it when they're done.

1 Nu Mark introduced Verve discs into a
2 limited market to learn about this innovation,
3 including whether adult smokers would find the
4 product acceptable.

5 FDA and other HHS agencies have the
6 opportunity to define a thoughtful and effective
7 public health strategy, including appropriate
8 communications regarding the continuum of risk,
9 which would reduce tobacco-related harm by
10 successfully helping move individuals who would
11 otherwise continue to smoke cigarettes to a
12 demonstrably less hazardous product, such as
13 smokeless tobacco or derived nicotine products.

14 The FSPTCA provides FDA, both CDER and CTP,
15 I believe, with a wide array of new authorities to
16 draw upon to create a coherent regulatory system
17 that encourages innovative tobacco products and
18 reflects the continuum of risk.

19 Public health strategies to reduce tobacco-
20 related disease should empower adult tobacco
21 consumers to make their own informed decisions.
22 Regulation can help ensure that information provided

1 to the adult tobacco consumer is complete, accurate,
2 and non-misleading. Concern that an adult tobacco
3 consumer may not make the right decision is not a
4 valid basis to deprive him or her of the information
5 needed to make it.

6 It bears repeating that the objective of
7 this strategy is to compliment, not compete with,
8 efforts to prevent the initiation of tobacco use and
9 encourage those who are willing and wish to quit
10 tobacco. This objective advances FDA's mission to
11 protect the public health, given that millions of
12 smokers are likely to continue using tobacco
13 products despite efforts directed towards prevention
14 and cessation.

15 A regulatory approach that does not take
16 advantage of the public health opportunity presented
17 by consumer-acceptable, demonstrably lower-risk
18 tobacco products might have the consequence of
19 preserving cigarette smoking as the dominant form of
20 tobacco use in the United States.

21 Reduction in the harm from tobacco is a
22 goal shared by many, including FDA, other regulatory

1 agencies, the public health community, and,
2 surprisingly, tobacco product manufacturers. Many
3 adult tobacco consumers express interest in lower-
4 risk, enjoyable tobacco products.

5 The critical scientific knowledge needed to
6 start down this path of harm reduction is available.
7 With sensible implementation of their authority, FDA
8 and other HHS agencies can encourage harm reduction
9 and therefore advance public health.

10 Thank you, and I'd be happy to answer any
11 questions at this point.

12 DR. HUSTEN: Earlier this morning, there
13 was some discussion about dual use of these
14 products. You might have folks who actually don't
15 switch, but are using products during the day when
16 they can't smoke or whatever, and continuing to
17 smoke.

18 So I see you have decrease in the number of
19 cigarettes per day on this timeline, showing some
20 potential reduction in harm but not a huge amount.
21 So I guess my question is, where do you see the dual
22 user on this spectrum?

1 Then the other point that had come out
2 earlier was this whole issue of the kids and would
3 they potentially start with one product but then
4 switch to other products, and in essence move up the
5 continuum the other direction.

6 I'd just be interested in your thoughts on
7 both of those issues.

8 MR. DILLARD: Sure. Thanks for the
9 question, Dr. Husten. I think we have supplied
10 comments, certainly, on this continuum on numerous
11 occasions. And I would say, to your question about
12 dual usage, if you look at the left-hand side -- and
13 I think this applies to the effort of harmful and
14 potentially harmful constituents that's going
15 on -- most of the issues associated with combustible
16 tobacco products, whether you see more or less of a
17 constituent, really exists around the exposure to
18 cigarette smoke, which is the left-hand side of
19 this.

20 So if you fundamentally believe that what
21 you're trying to do, which is what I believe, is
22 move people from the most harmful form, which is

1 combustion of tobacco, and move them to the lower
2 risk, that there's likely to be a point in
3 time -- and I think Mr. Williams talked about it in
4 his own experience, which is not unique to what our
5 experiences are -- is that adult cigarette smokers
6 don't immediately stop using one product today and
7 move to another product.

8 They need an acceptable product. They need
9 a reason to be switching, and then, with that, are
10 likely to go through a transition period as they get
11 used to the new tobacco product. And usually that
12 doesn't occur over this 10- to 12-week period of
13 time that we're talking about with the NRT labeling.

14 So in order to go down the journey with an
15 adult tobacco consumer, we have to recognize that
16 there may be a transition period of dual use, that
17 you hope everything is aligned to move people
18 ultimately to switching, because switching is really
19 where the benefit is, which is elimination of the
20 combustion aspect of using tobacco products. But
21 our experience is that adult smokers don't do that
22 automatically. They go through an individual

1 transition time, depending on the acceptability of
2 the product for them.

3 On your second question, of youth, we
4 certainly believe that underage individuals should
5 not use any form of tobacco product, just to be
6 clear, including the types of products that we're
7 talking about here today that could be tobacco-
8 derived types of products. They should not be
9 available for youth. These should be adult
10 products, and that's the way we think about them.

11 That being said, I do look at government
12 data quite frequently when it comes out, and it has
13 shown that even over this period of time as
14 innovative tobacco products have been beginning
15 to be introduced into the market, we still see
16 declines in youth cigarette smoking. We see
17 declines in youth smokeless consumption and youth
18 cigar consumption, even with new products onto the
19 market.

20 Now, it may be premature to necessarily say
21 that there is or is not a correlation because
22 they're rather new, and we know that some of these

1 large data sets take a year or two to catch up. So
2 I think that's, probably from a youth side,
3 something we're going to have to continue to take a
4 look at.

5 DR. HUSTEN: And just as a follow-up
6 question, do you have any data of people who maybe
7 start with the dual use? Do you have any data on
8 what percent continue dual use, what percent
9 actually switch, what percent maybe go back to
10 exclusively using the combusted products?

11 MR. DILLARD: We're beginning to look at
12 that for some of our newer products, certainly. And
13 I think a number of people have talked about them
14 today, the snus-type products, Verve as an example,
15 and some other products that we have in development
16 that, for competitive reasons, I certainly can't
17 talk about.

18 But I think that is a fundamental question
19 to ask consumers. I think the piece that's going to
20 be missing, and to some of the discussion earlier as
21 well between premarket and postmarket, what
22 questions are going to have to be answered in the

1 premarket period versus what are the more
2 appropriate, real population-based questions that
3 might be more appropriate in a postmarket period.

4 I think that when we're asking ourselves
5 the questions of where can we have an impact, we
6 believe that an acceptable product plus a reason to
7 believe, i.e. a claim, is going to be very important
8 for adult smokers to realize there's an opportunity,
9 and a differential opportunity, to make a switch.

10 So that's difficult in this point in time
11 where we can't make a claim as a manufacturer. We
12 can investigate a claim as a manufacturer, but you
13 may be taking a product that exists on the market,
14 putting a claim on it, and testing it in a
15 circumstance that, at the end, you tell people to
16 not believe it, because it was just a study that
17 they were part of to gather data.

18 So there are real executional
19 implementation issues on how you would do something
20 like that in a premarket period versus what might
21 you do in a postmarket period. And I'd only add one
22 other piece of, I think, useful information that I

1 think the folks from CTP understand.

2 We have a real opportunity because approval
3 for a product like that has a cliff date, which is
4 unlike a CDER situation, where if you approve
5 something, you might have to have new data to make a
6 different decision. We actually have a cliff date
7 on modified-risk tobacco products where a
8 manufacturer has to go back after five years. We
9 take a look at those various yearly, predetermined
10 postmarket study data, and approval can be
11 withdrawn.

12 So we do have a unique opportunity here, I
13 think, given the statute perspective, to maybe look
14 at this from a very different premarket/postmarket
15 perspective than the folks at CDER do.

16 MR. LINDBLOM: One thing, you've been
17 talking about getting smokers who are ongoing users
18 to switch to less risky, down the continuum,
19 products. And two concerns that are always brought
20 up is that that's going to either reduce cessation
21 or increase initiation.

22 I'm just wondering what methods your

1 company might have to reduce those risks through the
2 way the products might be marketed in that kind of
3 situation, assuming all the government clearance and
4 so on; and then whether those are things that are
5 available to the industry as a whole, not just
6 companies such as yourselves with more resources
7 than some of the smaller companies.

8 MR. DILLARD: Thanks, Dr. Lindblom. I
9 probably can't answer that question today. But what
10 I can say is we're doing a lot of thinking about how
11 we would do that, given a situation where we would,
12 as the tobacco industry, communicate about either a
13 relative risk or a differential risk of a tobacco
14 product; and then how do we minimize the unintended
15 audiences and the unintended effects associated with
16 doing that. And I can tell you today, standing
17 here, we don't have all the answers.

18 There are a number of areas that we're
19 looking at in terms of communication. We intend to
20 meet with the Center to talk about those and the
21 studies that might be done. But at this point, we
22 don't have the answer on how to do that. We just

1 know that that's an important issue, is how do we
2 minimize the unintended consequences associated with
3 any of these actions that we might take.

4 So I'm sorry I can't tell you what the
5 studies are. We're working on them. We want to
6 meet with you and talk about them. I'm not sure we
7 have the answer yet. I'm not sure, the first time
8 we study it, we'll have the right answer. But I
9 think we'll move towards it.

10 Anything else?

11 (No response.)

12 MS. SIPES: Thank you.

13 MR. DILLARD: Thank you.

14 MS. SIPES: Our next speaker will be James
15 Walmsley, who's from Johnson & Johnson Consumer
16 Services.

17 DR. WALMSLEY: Thank you. Good afternoon.
18 My name is James Walmsley. I'm the director for
19 global medical development for Johnson & Johnson,
20 and our interest here is that we market Nicorette
21 outside the United States.

22 Firstly, I'm grateful to FDA for the

1 opportunity to speak at this public hearing. I
2 believe this is a fantastic opportunity to engage
3 more smokers in quit attempts, and in doing so, help
4 reduce the considerable morbidity and mortality from
5 smoking.

6 When discussing new strategies to engage
7 smokers, it's really important to state up front
8 that the ultimate aim of any therapeutic
9 intervention should be complete cessation of
10 tobacco. Intervention should not seek to
11 necessarily prolong treatment, and smokers should
12 always aspire to end up free of nicotine from any
13 source.

14 It's vitally important that smokers who are
15 motivated to quit should be offered the most
16 efficacious treatments, and in this context, I would
17 like to begin by briefly reviewing combination
18 nicotine replacement therapy.

19 The rationale for using more than one form
20 of NRT together is twofold. Firstly, it optimizes
21 the level of nicotine substitution compared with
22 levels obtained from smoking. We know this is a key

1 consideration in proving cessation rates. Secondly,
2 combination therapy provides background levels of
3 nicotine through a slow-release format, usually a
4 patch, to manage withdrawal symptoms while enabling
5 use of a faster-acting NRT to treat breakthrough
6 cravings.

7 Data from systemic reviews confirm the
8 superior cessation rates for combination therapy
9 over single NRT, with an increase in the odds ratio
10 of around 40 percent. Combination therapy is also
11 very well-tolerated, with a safety profile
12 comparable to single nicotine replacement therapy.

13 In the U.K., combination NRT therapy is
14 very widely utilized and is also recommended within
15 existing public health guidance, particularly for
16 highly dependent smokers or those who have relapsed
17 after treatment with single NRT.

18 But not all smokers are ready or able to
19 quit abruptly, so alternative approaches are needed.
20 I will now discuss two strategies which would help
21 to engage and support many more smokers in quit
22 attempts.

1 The first alternative approach is smoking
2 reduction as a first step towards cessation. One
3 recent survey of U.K. smokers found that two-thirds
4 would like to stop smoking, but only 12 percent are
5 currently planning to quit.

6 This mismatch means that there is an
7 important opportunity to reach smokers who have no
8 immediate plans to quit or who feel unable to quit
9 abruptly. For these smokers, using NRT to
10 facilitate reduction represents a stepwise strategy,
11 which improves motivation to quit and ultimately
12 leads to successful quit attempts. And this
13 approach is well-tolerated. Smokers using NRT are
14 able to self-titrate their intake of nicotine to
15 avoid excessive use.

16 Reduction to quit with NRT has been
17 extensively studied in clinical trials. This chart
18 plots the difference in cessation rates between NRT
19 and placebo, that is, the effect size, for three
20 different groups.

21 Firstly, brief advice is an established and
22 effective intervention for smoking cessation,

1 resulting in an approximate 2 percent increase in
2 cessation rates in motivated smokers compared with
3 placebo.

4 In studies of smokers who are not motivated
5 to quit, a reduction-to-quit intervention with NRT
6 resulted in an effect size double this 2 percent.
7 This effect was broadly similar to abrupt cessation
8 studies of NRT in smokers motivated to quit. This
9 is a powerful demonstration that a reduction-to-quit
10 strategy with NRT can be almost as successful in
11 helping unmotivated smokers quit as current abrupt
12 quit interventions in motivated smokers.

13 Another way of engaging more smokers is
14 offering more choice on duration of NRT therapy.
15 Extended use of NRT recognizes that not all smokers
16 are alike. We know that tobacco dependence is a
17 chronic condition, so it follows that treatment
18 should not necessarily be given for one short
19 period.

20 Many former smokers still experience
21 cravings months or even years after they have
22 quit smoking, and some may benefit from longer

1 durations of NRT to quit or require a safer source
2 of nicotine if they are about to relapse to smoking.

3 In these circumstances, and where there is
4 a continued health benefit, NRT is many orders of
5 magnitude safer than smoking. Extended use of
6 treatments for smoking cessation is already
7 acknowledged in European and U.S. guidelines, so
8 there is an opportunity now for FDA to bring NRT
9 labeling into line with this expert guidance.

10 Current labeling in the United States
11 restricts NRT use to only three months. This is in
12 marked contrast to many of the countries presented
13 here, which allow longer durations of use for NRT,
14 from six months to 12 months. And some countries,
15 such as the U.K., allow open-ended use of NRT, with
16 no maximum duration.

17 We urge FDA to allow the American public
18 similar opportunities offered by many other
19 countries by recognizing the benefits of extended
20 NRT use during a quit attempt.

21 As well as offering new ways of using NRT,
22 we also believe there's an opportunity for FDA to

1 evaluate new NRT products pragmatically, bearing in
2 mind that the only meaningful comparator is
3 cigarette smoking. One rational approach is to base
4 evaluation on demonstration of pharmacokinetic
5 parameters within those of already approved NRT
6 products.

7 Existing NRT formats differ only in the
8 routes of application and the speed and extensive
9 nicotine delivery. With most forms of NRT, nicotine
10 intake is self-titrated by the patient and rarely
11 exceeds baseline nicotine intake from smoking.

12 Also, systemic nicotine has an established and
13 acknowledged favorable safety profile, although for
14 some formats, specific local tolerability studies
15 will be needed.

16 Taken together, this presents an
17 opportunity to bridge to the significant body
18 of clinical data on NRT by characterizing
19 pharmacokinetic parameters within the range of
20 existing NRT products.

21 This is a schematic illustration of
22 pharmacokinetic bracketing. The vertical axis shows

1 the key single-dose pharmacokinetic parameters, Cmax
2 and AUC. There is very good evidence to support the
3 efficacy of 2-milligram gum as a low-strength NRT
4 product. There is also very good evidence to
5 support the favorable efficacy and safety profile of
6 higher-strength products, illustrated here by
7 4-milligram gum.

8 Therefore, we believe that it is
9 appropriate to infer safety and efficacy of NRT
10 products whose pharmacokinetic parameters fall
11 within these two strengths. Even if they are not
12 strictly bioequivalent, pharmacokinetic bracketing
13 is already accepted as the basis for registration in
14 a number of countries. It's also relevant to
15 consider higher peak concentrations obtained from
16 smoking within the comparison.

17 We therefore urge FDA to consider the
18 evidence on combination therapy and reduction to
19 quit to ensure smokers receive the most effective
20 interventions. And we hope that FDA will be
21 encouraged by the example of other regulators to
22 allow extended use of NRT and evaluate new products

1 without requiring phase 3 studies.

2 In conclusion, based on wide international
3 experience with new strategies for smokers and
4 pragmatic evaluation of new NRT products, there
5 is an opportunity to engage more smokers in the
6 United States to move away from smoking safely and
7 effectively.

8 Thank you, and happy to take any questions.

9 DR. WINCHELL: Regarding combination
10 treatment regimens, can you comment on whether you
11 envision this as a co-packaged treatment regimen, or
12 cross-labeling, or what specific way would we be
13 able to make that available?

14 DR. WALMSLEY: I don't think there's
15 necessarily just one way of doing it. But what I
16 can do is give you the experience from the U.K.

17 So back in 2005, the Committee on Safety of
18 Medicines, which is the body that at the time
19 advised the U.K. regulator, the MHRA, on efficacy
20 and safety, a working group of the CSM conducted a
21 full review of nicotine replacement therapy, and
22 they endorsed the use of combination therapy. And

1 even though it wasn't specifically mentioned on the
2 labeling, basically they made it clear at the time
3 that all NRT labeling should not contraindicate use
4 of more than one NRT product together.

5 In response to your question about should
6 it be in the same pack, that's something that's been
7 tried in the U.K. I don't think it has to be in the
8 same pack. One of the difficulties there is how
9 many patches do you give, and how many flexible
10 formats do you give? Because everyone goes at their
11 own pace. I think it's the theme of today that all
12 smokers are different.

13 So it doesn't have to be the same pack. I
14 think flexibility is the key.

15 DR. WINCHELL: So just to clarify how it
16 was implemented in the U.K., is that any precautions
17 on the labeling that would appear to preclude a
18 professional making that recommendation were
19 removed, but there wasn't a specific marketing claim
20 granted to the pharmaceutical manufacturers around
21 that use. Is that correct?

22 DR. WALMSLEY: I'm not sure I fully

1 understand the question. In terms of the labeling,
2 the maximum allowed use is that allowed by each of
3 the individual products. So the maximum use of
4 patch --

5 DR. WINCHELL: I meant combined use.

6 DR. WALMSLEY: I'm sorry?

7 DR. WINCHELL: You said that the
8 recommendation was that the label shouldn't
9 contraindicate combined use.

10 DR. WALMSLEY: That's right.

11 DR. WINCHELL: But there wasn't necessarily
12 a new treatment regimen added to labeling based on
13 clinical trials?

14 DR. WALMSLEY: That's correct.

15 DR. WINCHELL: Okay. So it more or less
16 facilitated the ability of health care providers to
17 give that advice.

18 DR. WALMSLEY: Yes. I think it certainly
19 did that. And combination therapy is a mainstay of
20 treatments within the smoking cessation clinics.
21 But also, combination therapy is used without health
22 care professional intervention as well.

1 Yes?

2 DR. LEONARD-SEGAL: Can you speak to the
3 relative safety of the combination therapies
4 compared to single therapy in the context of
5 enhanced efficacy?

6 DR. WALMSLEY: Sure. As I've covered, the
7 data suggests from a number of clinical studies that
8 combination therapy compared with single NRT -- in
9 other words, NRT monotherapy -- is significantly
10 more effective.

11 The studies have also showed that it's very
12 well-tolerated by subjects. And that may well be
13 largely due to the phenomenon of self-titration, so
14 the idea that smokers are used to the amounts of
15 nicotine that they've been getting from smoking, and
16 they're well used to self-titrating and getting the
17 right amount of nicotine.

18 The evidence is that, both, when smokers
19 concurrently use NRT -- for example, when they're
20 reducing to quit -- or when smokers have quit and
21 are using two different forms of NRT, there is no
22 significant concern with overdose. Smokers seem to

1 self-titrate around their baseline levels.
2 Certainly very few get significantly above the
3 levels that they were having it from baseline
4 smoking.

5 So combination therapy very well-tolerated;
6 as I say, and widespread use in the U.K. And our
7 postmarketing surveillance is very reassuring that
8 we don't see problems.

9 Yes?

10 DR. HUSTEN: I had two questions. One was,
11 given that these other countries have approved
12 nicotine replacement therapy for longer durations of
13 use, are you aware, do any of them have any data,
14 either that there were studies done before the
15 indications were changed or put into effect, or if
16 they have good studies, subsequently, that could
17 provide some information about whether there's
18 improved cessation rates with the longer duration of
19 use?

20 DR. WALMSLEY: I don't have that
21 information. Obviously, the situation is different
22 in all of the countries that we showed in that

1 slide, and sometimes extended use was introduced in
2 conjunction with an additional indication, like
3 reduce to quit.

4 I don't know. I don't know, to be honest,
5 whether that specific data was submitted. It may
6 well be the case. We've heard today a lot about the
7 data to support extended use, and that that's widely
8 recommended in guidelines. It may well be that
9 authorities are responding to -- agencies are
10 responding to that.

11 DR. HUSTEN: And then my second question
12 is, you were talking about the pharmacokinetic
13 bracketing as one way of potentially bringing other
14 products to market, potentially. But what about the
15 idea of potentially having nicotine replacement
16 products that offer higher doses of nicotine and
17 maybe are a more complete substitution for the
18 tobacco products?

19 I guess I was curious about what you see as
20 the barriers to maybe trying to look at those type
21 of products or to bring those types of products to
22 market, because that seemed to be outside of that

1 bracketing idea that you were proposing.

2 DR. WALMSLEY: Yes. I think some products
3 will sit outside the bracketing area, either in
4 terms of the exposure to nicotine or maybe the
5 amounts in plasma concentrations.

6 I don't think I showed it very well on the
7 slide. But I think there's also that people have
8 talked today about the fact that cigarette smoking
9 should be the comparator. And I tried to show on
10 the pharmacokinetic bracketing argument the fact
11 that you obviously get very high peak plasma
12 concentrations from smoking, particularly, and you
13 get massive arterial levels of nicotine from smoking
14 as well.

15 So I believe that it's appropriate in that
16 context to use the plasma levels from smoking within
17 the bracketing argument, certainly, in terms of the
18 safety assessment. I think the bracketing argument
19 is all about a way of pragmatically assessing the
20 safety and efficacy of systemic NRT. NRT is
21 essentially a generic substance, and we know a lot
22 about the systemic safety and efficacy of nicotine.

1 So I think there's an opportunity to use
2 almost an extended bioequivalence approach. And, of
3 course, given that smokers self-titrate flexible
4 formats of nicotine, absolute bioequivalence often
5 isn't particularly relevant. Smokers will take as
6 many of these flexible formats as they need. So I
7 think that's the rationale behind the bracketing
8 argument.

9 DR. HUSTEN: So that's where it says, "or
10 cigarette comparisons"? Is that what you mean by
11 that?

12 DR. WALMSLEY: Absolutely. So we tried to
13 show the cigarette -- again, I don't think I showed
14 it very well. But we tried to show the level above,
15 certainly in terms of peak plasma concentration.
16 And I think that could be a comparator that is
17 appropriate, certainly when assessing, for example,
18 the maximum plasma concentrations.

19 So, yes, this slide shows that there is
20 another bracket. So there's the NRT bracketing area
21 within the low-strength and high-strength NRTs, and
22 then there is an area that sits between 4 milligrams

1 of NRT and a cigarette.

2 Yes?

3 DR. LEONARD-SEGAL: Along these same lines
4 regarding the bracketing, it's an interesting
5 comment, and it would seem to make maybe physiologic
6 sense at some level, I guess, it appears.

7 One of the things that we've always had a
8 question about is that different NRT products are
9 associated, regarding their use, with different
10 kinds of behaviors. The gums are used in a certain
11 way. The lozenges are used in a certain way. The
12 inhalers are used in a certain way. And we've
13 always wondered what the behavioral component of
14 that difference in use might be.

15 So are you suggesting that, with this
16 bracketing idea, we don't need to look at those
17 aspects to see what impact they might have on the
18 efficacy of the product?

19 DR. WALMSLEY: Yes. I think that's exactly
20 what I'm suggesting. And that doesn't mean that I
21 don't acknowledge that there may be some behavioral
22 or sensory effects specific to certain formats; for

1 example, the inhaler, a product that you hold and
2 there's a hand-to-mouth action.

3 But at the end of the day, these are
4 products intended to deliver nicotine to the
5 systemic circulation, and their adverse event
6 profile for systemic nicotine and their efficacy for
7 systemic nicotine will be characterized by their
8 pharmacokinetics.

9 There may well be some local issues that we
10 need to look at, so there may well be a need for
11 some local tolerability studies. So if someone
12 decided to develop a rectal form of NRT, it would be
13 highly appropriate to do some local tolerance
14 studies, I would have thought.

15 But in terms of the behavioral aspects, I
16 think bearing in mind what we're trying to do is to
17 deliver NRT to the systemic circulation. There may
18 well be some behavioral effects, but we know there's
19 a different effect if you take a red pill or a
20 yellow pill. But you would still use a
21 bioequivalent strategy.

22 MR. LINDBLOM: I'm interested, as Corinne

1 asked also, about the different countries where you
2 have different permissions for how long NRT can be
3 used or for what purposes.

4 In response to that, does your company or
5 the NRT industry as a whole change its marketing of
6 NRTs in the different countries?

7 DR. WALMSLEY: I'm not a marketer. I'm a
8 medic. So maybe I'm not best placed to answer that.
9 And I certainly wouldn't speak on behalf of any
10 other nicotine replacement therapy companies.

11 I think, for example, when Johnson &
12 Johnson received the reduce-to-quit indication, it's
13 certainly something that we talked about, we talked
14 to our consumers and to health care professionals
15 about. And I think different companies choose, to a
16 different extent, to speak about those new
17 indications, I guess without getting too complex a
18 message.

19 Yes?

20 DR. HUSTEN: I guess I left my microphone
21 on so I can be efficient here and not have to push
22 it. So this may be a very naive kind of question

1 since I'm not on the drug side of FDA. But it seems
2 like there's a lot of interest in indications for
3 longer-term use.

4 So I guess the question is, in my mind, is
5 the problem that for some reason the approval
6 process is problematic, or are the companies
7 actually submitting and doing studies to show the
8 safety and efficacy of longer-term use? I guess is
9 my question.

10 DR. WALMSLEY: I'm not sure I can speak to
11 that. I think the case that I'm presenting and that
12 others have presented is the intuitive case for
13 flexibility, and that all smokers are different, and
14 extended use has a number of potential positionings,
15 I guess.

16 One of them is that we know, with a
17 reduction-to-quit strategy, the evidence doesn't
18 tell us how long the reduction phase should be. We
19 know that. The evidence doesn't help us there. And
20 that was one of the questions I think FDA wanted to
21 help get some feedback on.

22 So therefore, it makes sense that we don't

1 know what the best period is to allow smokers to
2 determine, within reason, what that period should
3 be. So that's one potential for extended use. The
4 other is something like relapse prevention. So what
5 do smokers do that have quit? They have a lapse.
6 And before they have a lapse, can we prevent them
7 having a relapse?

8 So I think there are different reasons to
9 support extended NRT. I think for me the biggest
10 one is that smokers are different, and somehow
11 smokers go at their own pace. And I think giving
12 them that flexibility, where the alternative is
13 returning to smoking -- and I think others have made
14 exactly the same point today -- smokers should not
15 be prohibited through the labeling from continuing
16 to use NRT, which is many times safer.

17 DR. HUSTEN: So I think I'm hearing you
18 feel like there are some challenges in the approval
19 process to try to design a study where people could
20 use it as long as they individually felt they needed
21 to use it to remain abstinent? Am I hearing
22 correctly what you're saying?

1 DR. WALMSLEY: I'm not really talking about
2 the difficulties of designing studies to demonstrate
3 the efficacy of extended NRT use. I guess, like
4 others, I'm presenting the case for extended NRT and
5 reflecting the fact that guidance talks about this,
6 evidence supports it, and many authorities have
7 taken it on board.

8 DR. WINCHELL: I just want to return for a
9 moment to the idea of approving a product based on
10 pharmacokinetic bracketing. So, as you know,
11 certainly we haven't approved nicotine. A lot of
12 people think we have, that nicotine is an approved
13 product. But that's not true. Nicotine's a
14 molecule.

15 We have approved individual products that
16 have been shown to be safe and effective when used
17 according to a specific regimen. And while I agree
18 with you that we know a great deal about the
19 systemic toxicity of nicotine, every product has
20 specific characteristics. And you can actually
21 reverse engineer a bioequivalence study to make
22 something come out bioequivalent to something else

1 by the dose regimen, the inter-dose interval,
2 et cetera.

3 So there's a lot of devil in the details
4 here. And I would like you to say a little more
5 about why you think that we can do away with
6 demonstration of efficacy for a novel product,
7 just based on pharmacokinetic comparisons.

8 DR. WALMSLEY: Sure. The way I would see
9 it, that for a systemic-acting drug, comparisons
10 with other drugs, it's established, can be made.
11 And this is the basic, of course, of bioequivalent
12 studies. You make comparisons with other drugs by
13 using pharmacokinetic parameters as a surrogate, and
14 that's the basis of bioequivalence.

15 I think all we're suggesting is a slight
16 extension of that principle, that rather than
17 straight bioequivalence, we know that low-strength
18 NRT is effective. We know that high-strength NRT is
19 very well tolerated.

20 So I think there's an intuitive case that
21 between those two, if we can demonstrate that the
22 pharmacokinetic parameters are within that

1 bracketing area, I think there's a very strong case
2 that you have inferred enough to bridge to the
3 existing safety and efficacy data.

4 Surely, if NRT is all about delivering
5 nicotine to the systemic circulation, this is what
6 we are demonstrating here.

7 DR. WINCHELL: So would you then envision
8 that the pharmacokinetic comparisons would be done
9 under conditions of ad lib dosing? Because those
10 are the conditions under which we know they're
11 effective, ad lib dosing within certain labeled
12 parameters.

13 DR. WALMSLEY: Well, what I've talked about
14 here is basically based on single-dose
15 pharmacokinetics rather than multiple-dose. Of
16 course, AUC approximates very closely with average
17 plasma concentrations from multiple-dose PK studies.
18 But this is a model based on a single-dose
19 comparison.

20 Again, because NRT flexible formats are
21 used flexibly and self-titrated, you often see PK
22 studies with regular dosing, and that doesn't

1 reflect real life.

2 MS. SIPES: I actually had a question for
3 you as well. Could you talk a little bit more
4 about -- I want to go back to the issue of reduction
5 as potentially a step towards quitting.

6 DR. WALMSLEY: Sure.

7 MS. SIPES: Can you talk a little bit more
8 about the evidence that you have, or that you've
9 seen, that reduction increases motivation to quit?
10 You talk a lot about motivation, motivated smokers
11 versus unmotivated. Can you talk a little bit more
12 about that, please?

13 DR. WALMSLEY: Yes. Sure. Of course. So
14 a number of studies have been done, which were
15 primarily reduction studies using either gum or
16 inhalator, inhaler, and those were primarily done in
17 subjects who were not initially motivated to quit.
18 They had no immediate plans to quit. What was
19 measured was, first, the reduction; secondly, quit;
20 and thirdly, motivation to quit as well.

21 So what was demonstrated in the studies
22 that were done within my organization, and they're

1 published, is that not only does that approach
2 facilitate reduction, it also facilitates quit. And
3 you can measure improvements in motivation to quit.

4 So I don't think anyone understands the
5 mechanism of that. Maybe it's that small rewards
6 actually spur -- give smokers additional confidence
7 to say, I can do this. Maybe it's that we're
8 getting them into the game of using nicotine
9 replacement therapy, and that they are finding out
10 that NRT can be an effective way of managing their
11 withdrawal symptoms, so that when their motivation
12 does come to quit, they've got experience with NRT,
13 and they feel it's effective for them, and they can
14 make a quit attempt.

15 Because we know that motivation is -- I
16 think we used to think motivation was a very linear
17 thing, going from pre-contemplation to
18 contemplation. And I think what we believe now is
19 that motivation changes very rapidly. But if you
20 find a time when the smoker is motivated, and they
21 already have the means to quit and some motivation
22 from having reduced their smoking, it may be that

1 that's the explanation as to why we can improve
2 their motivation to quit and actually get quitters
3 from people that had no intention of quitting.

4 MS. SIPES: Yes. That's what I was trying
5 to get at. It sounds like we don't really know what
6 the connection is. There's an observation that the
7 connection might be there, but we don't really know
8 what's driving it. Is that correct?

9 DR. WALMSLEY: I think it's fair to say
10 that we don't know that, although I think maybe it
11 shouldn't be a surprise to us that people who
12 weren't motivated can become motivated. And maybe
13 it's just the randomness of people's motivation
14 to quit.

15 I think it has been called a chaos model,
16 the motivation to quit. It changes almost on a
17 second-by-second basis, and maybe it's just that
18 this is a natural variation in motivation to quit.
19 But when it happens, and when they take that time to
20 the float, if you like, they've got the means to
21 quit, and they've got the motivation from reduction.
22 But you're right. I don't think we know.

1 MS. SIPES: Thank you very much.

2 DR. WALMSLEY: Thank you.

3 MS. SIPES: Our next speaker is Mr. Howard
4 Marsh from GlaxoSmithKline Consumer Healthcare.

5 DR. MARSH: Good afternoon. My name is
6 Howard Marsh. I'm the chief medical officer for
7 GlaxoSmithKline Consumer Healthcare. I'm grateful
8 to the FDA for allowing me to present GSK's position
9 on this important matter. Today's discussions and
10 your subsequent action present a tremendous
11 opportunity to reduce the toll of unnecessary misery
12 due to tobacco-caused death and disease.

13 First and foremost, the ultimate goal of
14 any treatments or approaches discussed today should
15 be to help a smoker completely and finally quit
16 smoking. Today's greatest public health benefit
17 comes from stopping the use of cigarette smoking.

18 Smokers should be continually encouraged to
19 make quit attempts, and thereby limit their exposure
20 to the documented harmful effects of cigarette
21 smoking, even if they have tried on several
22 occasions previously. It is never too late to stop

1 smoking. It is never too late to try to stop
2 smoking.

3 There have been missed opportunities to
4 date to achieve the public health goal of smoking
5 cessation for the largest number of Americans. FDA
6 should embrace the same conclusion that the U.K.
7 regulatory authority did seven years ago, that
8 safety considerations of many new forms and options
9 in the use of NRT should be made in the context of
10 the risks associated with continued smoking.

11 The current regulatory approval process and
12 criteria for NRT products with characteristics that
13 require a more flexible and programmatic approach to
14 helping smokers stop has limited the development of
15 new options for our patients.

16 I ask that medical and clinical judgment of
17 new NRT products be applied against the real
18 comparator, the lethal cigarette, which delivers
19 nicotine in a format that poses dire health
20 consequences.

21 Traditional safety and efficacy trials may
22 no longer be the most appropriate default for the

1 evaluation of nicotine replacement therapy, whose
2 history of safety and efficacy is supported by more
3 than 100 clinical studies.

4 Smokers who find it hard to achieve or
5 maintain abstinence should be able to use nicotine
6 medications for longer than the currently permitted
7 periods. Longer-term use of nicotine replacement
8 therapy should be used as an acceptable step between
9 quitting smoking and quitting nicotine.

10 Smokers should be encouraged to use
11 nicotine replacement therapy for as long as needed,
12 but not longer, in order to avoid returning to
13 smoking. The goal is to quit smoking for good.

14 The safety of long-term NRT use has been
15 well-documented. The five-year lung health study
16 concluded that long-term use of NRT appears to be
17 safe and unrelated to any cardiovascular illnesses
18 or other serious side effects.

19 Other regulatory agencies have considered
20 this issue and acted in line with recommendations of
21 experts in the field of smoking cessation to guide
22 their policy and scientific decisions. For example,

1 the U.K.'s Royal College of Physicians Tobacco
2 Advisory Group concluded that in any circumstances,
3 the use of nicotine replacement therapy is many
4 orders of magnitude safer than smoking. This
5 conclusion has guided regulatory policy on nicotine
6 replacement products in the United Kingdom.

7 Section 918 provides FDA the opportunity to
8 open that innovative doorway through the use
9 of accelerated approval and expedited review
10 processes. It's true that most smokers require many
11 attempts at quitting before finally stopping for
12 good. The availability of other forms and various
13 flavors of oral nicotine replacement therapy can
14 lead to an increased interest in quitting, and
15 therefore has significant public health benefits.

16 Our own experience shows that almost half
17 of the use of our most recently introduced product,
18 the Nicorette mini lozenge, came from quitters who
19 had not purchased an NRT product in the previous
20 12 months.

21 The label requirement to completely cease
22 all cigarette usage on the same day as starting NRT

1 is the only currently approved option for nicotine
2 replacement therapy. Broadening treatment options
3 for medicinal nicotine would allow smokers to
4 benefit from NRT's effect in curbing cravings and
5 withdrawal symptoms in a quit attempt that does not
6 require abrupt cessation.

7 This flexibility would support more
8 spontaneous quit attempts by motivating and building
9 self-confidence in smokers, who feel unable or
10 simply overwhelmed by the prospect of quitting
11 abruptly. Studies have shown an increase in
12 motivation and intention to quit in smokers who were
13 previously unable or unwilling to quit when they
14 were using NRT simply with the intent of reducing
15 their daily smoking. And indeed, a proportion of
16 these smokers subsequently quit smoking completely.
17 Indeed, data shows that many more smokers would
18 prefer to quit gradually than abruptly.

19 Tobacco dependence directly leads to a
20 myriad of serious, life-threatening conditions.
21 Smoking cessation has been clearly proven to reduce
22 these risks, and NRT has well-established efficacy.

1 On that basis, NRT innovation to treat tobacco
2 dependence should be considered for fast-track
3 status.

4 Tobacco dependence clearly constitutes an
5 unmet medical need. Barely half of all daily
6 smokers make a serious quit attempt each year. An
7 earlier minority of these quit attempts involved
8 treatments proven to increase the likelihood of
9 success.

10 Another opportunity under fast track is the
11 use of surrogate endpoints. The basis for NRT is
12 the replacement of nicotine from cigarettes with
13 nicotine in a medicinal dosage form. The
14 pharmacological intent of nicotine replacement is
15 the reduction in nicotine cravings.

16 Minimizing these nicotine cravings helps
17 the user maintain abstinence. Using craving relief
18 as a surrogate for the standard clinical measure of
19 28 days complete abstinence at six weeks is a
20 logical surrogate, demonstrating comparable or
21 superior craving relief could be a viable surrogate
22 for innovative NRT approaches.

1 Sponsors have an important role to play in
2 proposing new indications and products. Two such
3 well-recognized innovations are using NRT to reduce
4 smoking before quitting and combination nicotine
5 replacement therapy. These approaches are already
6 approved in numerous countries and recommended by
7 the expert clinicians who are instrumental in
8 preparing the recently-published U.S. Public Health
9 Service treatment guidelines.

10 Combination NRT has been included in the
11 U.S. treatment guidelines since 2008. However, this
12 combination has not been authorized for OTC use.
13 The disconnect between current expert
14 recommendations and OTC labeling glaringly
15 highlights the missed opportunity for greater
16 availability of an effective and lifesaving
17 treatment for our patients.

18 GSK strongly recommends that FDA and other
19 health agencies adopt a comprehensive nicotine
20 regulatory policy for all nicotine-delivering
21 products. In comparison to all other regulatory
22 agencies around the world, FDA has authority for

1 regulating tobacco as well as medicines. This
2 uniquely positions FDA to develop and implement an
3 overall public health policy with regards to
4 nicotine.

5 Dr. Michael Russell's adage from the 1970s
6 has never been truer than in 2012. People smoke for
7 the nicotine, but die from the tar. The goal should
8 be to help people quit smoking for good using
9 nicotine in its cleanest and safest form, flexibly,
10 for as long as is required but no longer.

11 Tobacco remains the leading cause of
12 preventable disease and death. Taking the actions
13 we have proposed is a public health imperative.
14 GlaxoSmithKline stands ready to fulfill its
15 responsibilities to support this effort, working in
16 productive collaboration with the FDA and other
17 groups whose aim is to help people with their
18 addiction for good. Thank you.

19 DR. HUSTEN: I guess I'll ask a similar
20 question to what I had asked before. What do you
21 see as the greatest barriers to potentially
22 developing NRT products that potentially deliver

1 higher doses of nicotine or more physiologic doses
2 of nicotine, and might potentially serve as -- I
3 don't know if they'd be more effective. But in
4 terms of doing this, that could potentially show the
5 safety and effectiveness.

6 DR. MARSH: I think our immediate problem
7 is that people don't use the current products in the
8 right dose and for long enough. So I agree with you
9 that a step to develop higher-dose products would be
10 a logical step.

11 But in the meantime, what we need to do is
12 encourage people to use the current products as they
13 are indicated and for as long as they could in order
14 to prevent a relapse to smoking. For the moment,
15 people actually under-dose, even given the
16 indications that we have today.

17 DR. NGUYEN: Can you speak to the
18 quantitative correlation between the magnitude and
19 the duration of reduced use of cigarettes and the
20 ultimate cessation of smoking?

21 In your talk, you had mentioned that there
22 was a proportion of smokers who use extended NRT who

1 subsequently quit smoking completely. I was
2 wondering if there's a certain threshold we should
3 look for. Because ultimately, with the extended
4 use, what we like to see is a substantial number of
5 those people being able to quit smoking.

6 So we're talking about reduce to quit,
7 which is a very wonderful goal if we have data to
8 support that reduce to quit ultimately leads to
9 quitting of smoking. We're just talking about
10 smoking here.

11 DR. MARSH: So we did conduct a very large
12 study with nicotine gum many years ago on reduce to
13 quit, and did show that the odds of quitting were
14 much greater using a reduce to quit program for the
15 active versus placebo.

16 Smokers are individuals, and so it's
17 actually very hard -- so one of the things that
18 we're asking for is a more pragmatic and flexible
19 approach to meet individual smokers' needs. And we
20 do know that many, many smokers, more smokers than
21 half, would prefer to quit by a gradual reduction
22 rather than quitting all at once.

1 So providing a more individualized or
2 flexible approach to quitting will certainly help
3 more people make quit attempts, and that will reduce
4 the overall public health burden.

5 DR. NGUYEN: I guess what I'm trying to get
6 at is that for us to support the extended use,
7 however it will be used but certainly for an
8 extended use to reduce to quit with the ultimate
9 clinical goal of quitting smoking, we need to
10 understand the differences, so to speak, between the
11 experimental arm and the placebo arm that will be
12 clinically meaningful for us to take that regulatory
13 action.

14 So I understand. I think there's been a
15 lot of discussion how smokers need to have the
16 option of a more gradual approach, and I completely
17 agree with that. But what I'm trying to get at is,
18 are there pretty good data to support the reduce-to-
19 quit approach with the goal of ultimately quitting
20 smoking?

21 DR. MARSH: There are data where we've
22 submitted to FDA previously, some years ago, using a

1 very specific reduce-to-quit program. So the answer
2 is yes. With regard to longer-term therapy, again,
3 there have been numerous studies on nicotine
4 replacement therapy demonstrating the benefit of
5 longer-term use.

6 DR. NGUYEN: Thank you.

7 DR. LEONARD-SEGAL: Thank you, Dr. Marsh.
8 This is a slightly offbeat question, but do we have
9 knowledge, that you're aware of, as to what smokers
10 are ready to quit and which ones aren't? The
11 characteristic of the quitter versus the one who
12 can't, and the one who has to keep trying, have we
13 worked out any of that such that we could find a way
14 to better target different products or different
15 directions for quit to different people so that they
16 could help self-identify? Has anyone looked at
17 that?

18 DR. MARSH: I think there are ways of
19 assessing people's individual mitigation at one
20 point or another. The last thing I'd want you to
21 think was that pharmacotherapy was the be-all and
22 end-all.

1 You're more likely to increase your
2 likelihood of success in quitting for good if
3 pharmacotherapy is combined with a behavioral
4 support program, and that can be in the form of
5 online support programs, or interactions with a
6 telephone help line, or health care professional.

7 So that goes to tailoring the quit attempt
8 according to an individual patient's needs. And I
9 think that the psychological and social elements of
10 any quit attempt are very important.

11 DR. LEONARD-SEGAL: I guess I'm trying to
12 envision a process at some point whereby a label
13 could actually help someone understand what way of
14 using these products might be most helpful to them
15 as an individual. It's something we haven't really
16 talked about internally, particularly much or maybe
17 at all, and I'm just wondering if you envision a
18 process that way based upon what you know about this
19 issue.

20 DR. MARSH: Well, certainly the label can
21 be somewhat helpful. But it's limited in,
22 obviously, the size of the label and the amount of

1 information you can provide. But certainly the
2 support materials that we can provide -- online, for
3 example; there are many more people using online
4 support now than when NRT was made available in
5 1996.

6 So the ability to adopt our support for
7 smokers wanting to stop is much enhanced now, with
8 the availability of online help compared to what it
9 was many years ago. And I think that's key.
10 Providing support to people in addition to
11 pharmacotherapy is an important aspect of people's
12 ability to quit smoking.

13 DR. LEONARD-SEGAL: Yes. I guess my
14 question really actually goes -- I agree with all
15 that. I guess my question is going to a more
16 targeted way of helping people self-select, not
17 necessarily even for the particular medicine but for
18 the particular regimen that might help them to know
19 what might work for them.

20 I think it's an area that maybe we ought to
21 explore. I don't know if people have, but I was
22 wondering if you think that it's a silly idea or if

1 it has any merit or --

2 DR. MARSH: No. I really --

3 DR. LEONARD-SEGAL: -- exceedingly
4 complicated, what we would need to know or do, how
5 we'd find out.

6 DR. MARSH: I certainly don't think it's a
7 silly idea. I'm just not sure I'm prepared to be
8 able to give you a definitive response today. But
9 if you'll allow me, maybe I could come back to you
10 on that.

11 DR. RAPPAPORT: You talked about having
12 submitted something to us in the past. Obviously,
13 we can't talk about certain things that come to us.
14 But I'm wondering, you could talk a little bit more
15 about that data that you submitted, and what it
16 showed, and perhaps why it didn't go anywhere.

17 MS. SIPES: You're referring to the reduce
18 to quit?

19 DR. RAPPAPORT: Yes.

20 DR. MARSH: It's probably -- because it was
21 a long time, it's probably better if I submit that
22 through a written response.

1 MR. LINDBLOM: I guess I'll try another
2 marketing question even though you're a doctor and
3 with the health, medical, science, research side.
4 But I'm wondering if these sort of changes were made
5 and NRTs were allowed to be sold for different uses
6 and for extended use, multiple-use NRT, so forth.
7 If that happens, do you think that would
8 significantly change how your company markets the
9 products here in the United States?

10 DR. MARSH: Well, speaking as the medical
11 guy and not the marketing guy, it's my
12 responsibility to make sure that everything we say
13 about our products is in line with its current
14 marketing authorization. So we would always promote
15 the product in line with its marketing
16 authorization.

17 MR. LINDBLOM: I guess what I'm trying to
18 get at is if you change the label, that's great for
19 people who look at the label. The more people who
20 look at the label, the better; the more people who
21 pick up the product, the better, and so forth.

22 So I guess what I'm trying to get at is

1 whether these sorts of changes would make the market
2 more attractive to your company and that your
3 company would invest more in developing that and
4 getting those words out to the consumers.

5 DR. MARSH: Again, speaking as the medical
6 guy, the most important thing is to provide patients
7 with more opportunities to give up smoking.

8 So if we take our goal, which is to help
9 more people give up smoking permanently, then, yes,
10 I'm very much in favor of providing people with more
11 options than opportunities to give up smoking for
12 good, given that we know that people often take
13 several attempts before they're able to do that. So
14 providing more options and more flexible options is
15 an important public health goal, as the medical guy.

16 DR. WINCHELL: If I could turn to your
17 suggestion of the use of surrogate endpoints for
18 establishment of efficacy, first I just want to
19 point out that we don't ask companies to demonstrate
20 direct health benefit of nicotine replacement
21 products. We just ask them to show abstinence, and
22 then we are willing to assume that that will

1 extrapolate to health benefit, which means it's a
2 surrogate already.

3 But you're proposing a more proximal
4 surrogate than that. And I'm hoping that you can
5 help us because our reading of the literature
6 actually doesn't suggest that there's a strong
7 prediction or a consistent finding of prediction of
8 effects on craving relief and translation to smoking
9 cessation advocacy.

10 So that's an area where if we were to try
11 to move even further away from the documentation of
12 health benefit, we would really need some help in
13 understanding those predictive relationships.

14 DR. MARSH: I didn't get the question,
15 actually.

16 DR. WINCHELL: Oh, yes, you're right. I
17 didn't actually put a question mark on that.

18 So my question is whether you can comment
19 on whether there are some models or approaches to
20 measurement of craving relief that are reliably
21 predictive of smoking cessation efficacy because
22 there does not seem to be a consistent conclusion in

1 the literature about this point. There is ongoing
2 controversy about this point.

3 DR. MARSH: Well, nicotine replacement
4 therapy, as you know, is an aid to smoking
5 cessation. And it's through the relief of cravings
6 and withdrawal symptoms that it's effective.

7 So the safety and efficacy has been proven
8 again and again in numerous clinical studies. So
9 demonstrating safety and efficacy through more
10 28-day continuous abstinent studies may not be
11 necessary if you can demonstrate as a surrogate that
12 the new product is as efficacious in terms of
13 relieving cravings in a model compared to other
14 nicotine replacement therapy.

15 DR. WINCHELL: Well, I think some people
16 would say that it's the relief of withdrawal
17 symptoms overall and not specifically that one
18 symptom of withdrawal that may be the mechanism
19 of action.

20 So it does raise the question of what would
21 be the most relevant think to measure in a short-
22 term study; what would be the most predictive

1 context. Would these be quitters in a laboratory
2 setting? What tools would you use? How would you
3 measure it? What would be the quantitative
4 difference we would need to expect for us to
5 confidently predict some improvement in smoking
6 cessation?

7 Because you're suggesting that if we could
8 demonstrate an improvement over an existing product,
9 that that would certainly translate to an
10 improvement in smoking cessation. What I'm asking
11 is whether that relationship is actually as well
12 established as you suggest.

13 DR. MARSH: I wouldn't automatically make a
14 statement that improvement in craving control would
15 necessarily lead to improvement in quit rate. But I
16 would say that if you can demonstrate equivalent
17 craving control, this is going to be a safe and
18 effective product, and that there wouldn't be a need
19 to keep repeating the 28-day continuous abstinence.

20 MS. SIPES: I actually had a follow-up
21 question. This is going back to -- you've had a few
22 questions about the data around reduction to quit

1 and cessation, and we've had some questions also
2 about motivation, and how to measure that, and how
3 to sort people into those categories.

4 I have a related question, just stepping
5 back. In your comments today, like others here
6 today, you've drawn a distinction between abrupt
7 cessation and a more gradual approach, which might
8 include a reduce-to-quit scenario.

9 I guess my question is, do you envision
10 this as a situation where the whole framework should
11 simply be more flexible, so that individuals should
12 be able to choose their own method, their own ways
13 of doing things, what works best for them? Or do
14 you envision this as a situation where there are
15 going to be different indications or treatment
16 regimens that would need to be supported? There
17 could be a mix of the two, or it could be more in
18 one direction or more in the other.

19 But I'm just wondering conceptually how you
20 see it, because I think what some of the questions
21 here today have tried to get at is the connection.
22 Conceptually, people see the flexible approach, but

1 there's a question about tying that to support.

2 DR. MARSH: Yes. So inherent in
3 flexibility is the flexibility. And I would say
4 that for a particular reduce-to-quit regimen, you
5 would want to be able to allow people to have a
6 little bit of flexibility in how slowly they reduce
7 to quit. Some people may feel more comfortable
8 doing it over a period of a week; some people might
9 need longer than that to do that.

10 I think that's what's difficult to put onto
11 a label, but where we have much more opportunity now
12 in terms of providing more support and help through
13 online support systems, for example.

14 So I think the reduction, the flexibility
15 could be flexible in terms of how you approach it.

16 MS. SIPES: That's what I was going to say.
17 It sounds like, if I understand you correctly, that
18 you see it as essentially a self-directed process.
19 Is that correct?

20 DR. MARSH: Self-directed, with some
21 guidance.

22 MS. SIPES: From?

1 DR. MARSH: From us. From their health
2 care professionals, through online support programs.
3 It seems to me that individuals need to be treated
4 as individuals, and people's individual quit
5 attempts can be quite different. We know that
6 people self-titrate the amount of nicotine that they
7 need. And so we want to be able to allow that
8 flexibility in a quit attempt.

9 DR. RAPPAPORT: I just need to understand a
10 little better what it is -- I understand that
11 there's variability, and everybody should have an
12 opportunity to quit in their own time and way. But
13 is that going to be based on data? Is that going to
14 be based on clinical studies? Because I don't think
15 that's particularly feasible.

16 If not, if you can't do those clinical
17 studies, are you suggesting that we just use common
18 sense and expert opinion to make changes to the
19 labels?

20 DR. MARSH: I think that's a reasonable way
21 forward. It's certainly what the experts in the
22 area of smoking cessation have been recommending for

1 some time. It's what other regulatory agencies
2 across the world are recommending.

3 So, yes, I think the answer to that is yes,
4 that we don't need a clinical study for every
5 eventuality.

6 DR. LEONARD-SEGAL: I think I knew the
7 answer to this question, but I can't remember it
8 right now, so I'm going to ask it.

9 NRTs in the United Kingdom, are they over
10 the counter, pharmacy only? How are they available?

11 DR. MARSH: They're over the counter.

12 DR. LEONARD-SEGAL: Over the counter. So
13 you can just go in and pick them right up off the
14 shelf and buy them?

15 DR. MARSH: Yes.

16 DR. LEONARD-SEGAL: Okay. Thanks.

17 MS. SIPES: Thank you very much.

18 DR. MARSH: Thank you.

19 MS. SIPES: Appreciate it.

20 All right. I think we're going to move to
21 our next speaker, Mr. Anton. Are you here? Our
22 next speaker is Mark Anton. He is with What A

1 Smoke, LLC.

2 MR. ANTON: Good afternoon. I'm Mark
3 Anton, founder and president of What A Smoke, LLC, a
4 manufacturer and distributor of electronic
5 cigarettes. I'm here to urge the FDA to stop
6 protecting cigarettes from market competition by far
7 less hazardous nicotine and tobacco products, and
8 approve NRT products as temporary and long-term
9 tobacco harm-reduction alternatives to cigarettes.

10 More than 99 percent of all tobacco-
11 attributable mortality and more than 99 percent of
12 tobacco-attributable health care costs in the United
13 States are caused by repeated inhalation of tobacco
14 smoke, while less than 1 percent are caused by the
15 use of noncombustible tobacco and nicotine products.

16 Existing evidence also indicates that
17 cigarettes are considerably more hazardous than
18 nicotine in tobacco products marketed in the United
19 States, including smokeless tobacco products,
20 electronic cigarettes, and nicotine products.

21 While quitting all tobacco use may be the
22 best way for smokers to improve their health,

1 switching to nicotine products reduces smokers'
2 health risks nearly as much as quitting all tobacco
3 and nicotine use. Surveys indicate that more than a
4 million smokers have quit smoking by switching to
5 smokeless tobacco products, and sales reports
6 indicate that nearly half a million smokers have
7 switched to electronic cigarettes.

8 The FDA should encourage and approve the
9 marketing of nicotine products to smokers as long-
10 term cigarette alternatives, similar to the way
11 smokeless tobacco and electronic cigarettes are
12 marketed to smokers currently. This would allow
13 users to continue to get their nicotine without
14 going back to combustible tobacco products.

15 I urge the FDA to be aggressive in truthful
16 information to the consumer about alternatives to
17 tobacco cigarettes. Currently the FDA considers all
18 tobacco products to be equally harmful, regardless
19 of the science that has been conducted to prove
20 otherwise.

21 If the FDA were willing to modify the
22 requirements for MRTP and NRT products,

1 manufacturers might be willing to apply for
2 consideration. However, under the current
3 guidelines and onerous potential barriers, it would
4 cost tens of millions of dollars for an e-cigarette
5 manufacturer to even provide all the information
6 needed to be approved either by MRTP or for NRT
7 fast-track processes.

8 As it currently stands, it is very
9 difficult and confusing for an electronic cigarette
10 manufacturer to ascertain the most logical route to
11 take -- seek FDA approval as an MRTP under the
12 guidelines set forth in guidance for the industry on
13 applications for modified risk tobacco products?

14 As an example, Dr. Michael Siegel,
15 professor at the department of community health
16 sciences, Boston School of Public Health, states,
17 "The guidance makes it extremely difficult for
18 existing potential reduced-risk products to
19 successfully achieve modified risk status.

20 "Most notably, the company must
21 successfully address the two following points: the
22 effect the tobacco product and its marketing may

1 have on tobacco use initiation among non-users; and
2 second, the effect a tobacco product and its
3 marketing may have on tobacco use behavior among
4 current tobacco users."

5 He also points out, "To make such
6 demonstrations, a company would have to conduct a
7 clinical trial or a long-term observational quasi-
8 experiment in which the product was introduced into
9 the market as a reduced-risk product." Wouldn't
10 this be a federal crime?

11 In short, it is extremely onerous and
12 difficult to make an informed decision on spending
13 millions of dollars without true guidelines that set
14 benchmarks instead of conflicting testing
15 parameters, with no guarantee that the product would
16 be approved as an MRTP.

17 Also, would the e-cigarette manufacturer be
18 able to apply under the NRT fast-track program? In
19 light of the court ruling that e-cigarettes are a
20 tobacco product, the FDA also should stop trying to
21 ban electronic cigarettes by misclassifying them as
22 drug devices, which federal judge Richard Leon has

1 already struck down; and instead, the FDA should
2 look to work with the electronic cigarette industry
3 to come up with proper guidelines and opportunities
4 for the industry to work with the FDA.

5 The FDA could facilitate a potential market
6 segment that could help afford the smoker of tobacco
7 cigarettes far less hazardous alternatives,
8 significantly providing an alternative that in
9 testing has shown far less particulate matter and
10 carcinogens than a traditional tobacco cigarette. I
11 urge the FDA to consider working with the industry
12 to find solutions to this quandary of confusion.

13 A deeming regulation under Chapter 9 of the
14 Family Smoking Prevention and Tobacco Control Act
15 would effectively ban the electronic cigarette,
16 which is a breakthrough product coupling the tactile
17 feel of hand to mouth and addresses the nicotine
18 cravings associated with smoking tobacco cigarettes
19 that no other product has truly emulated.

20 Please don't put forth the deeming
21 regulations that would essentially ban the
22 electronic cigarette. Concurrently, the FDA should

1 eliminate the current warnings on nicotine
2 replacement products that urge consumers to
3 discontinue use if they also use a tobacco product,
4 and instead should encourage smokers to continue
5 substituting nicotine products for cigarettes as
6 often as possible.

7 The position that the FDA takes, that to
8 date no tobacco products have been scientifically
9 proven to reduce risk of tobacco-related disease,
10 improve safety, or cause less harm than other
11 tobacco products -- this statement should also then
12 be applied to NRT products such as lozenges, gums,
13 patches, as well as it is being applied to
14 dissolvable tobacco products and electronic
15 cigarettes, as they all use nicotine as the
16 substitute for cravings.

17 If the FDA doesn't take these long-overdue
18 actions by working in conjunction with the
19 manufacturers of all products, the agency will lose
20 out on significant opportunities to protect the
21 public health.

22 The FDA has an ethical duty to inform

1 smokers that nicotine is addictive, but that some
2 tobacco and nicotine products are far less hazardous
3 long-term and temporary alternatives to cigarettes;
4 and the NRT should be approved for short- and long-
5 term use. Smokers have a right to truthful health
6 information from the FDA.

7 I thank you for your time.

8 MS. SIPES: I have one question for you.
9 Thank you for your presentation. Can you comment a
10 little further on your statement that a deeming
11 regulation under Article 9 would effectively ban the
12 electronic cigarette?

13 MR. ANTON: Well, Mr. Godshall had dealt
14 with that in your questions earlier. But it goes
15 back to the timing of it, that all products would
16 have to be on the market by January 15th of 2007.
17 Most electronic cigarettes have entered the market
18 after that point in time. And if you were to go
19 back to probably the original version, that design
20 is long obsolete. It doesn't even exist any more.

21 MS. SIPES: All right. Thank you very
22 much.

1 MR. ANTON: Thank you.

2 MS. SIPES: All right. I think at this
3 point we'll take our afternoon break, and then we'll
4 come back and do our last two speakers and have the
5 public comment period.

6 Just a word before we go. Anyone who
7 speaks in the public comment period is welcome to
8 either come to the podium or speak there at the
9 microphone. You see the stand set up.

10 Let's come back at 3:00. We'll get started
11 again, and our next speaker will be Robert Jack.

12 Thank you.

13 (Whereupon, a brief recess was taken.)

14 MS. SIPES: We're going to get started.
15 Before our next speaker begins, I just wanted to
16 make a small request. There are two speakers who
17 have already gone that the panel has some very short
18 additional questions for.

19 Dr. Abrams and Mr. Anton, if you're still
20 here, would you be able to come up after the next
21 two speakers and briefly speak again? Is that okay?
22 Dr. Abrams, you're here? Mr. Anton, you still here?

1 Okay. Thank you very much.

2 All right. With that, our next speaker is
3 Mr. Robert Jack, who is with Blue Mist Vaping.

4 Thank you.

5 MR. JACK: Good afternoon. My name is
6 Robert Jack. I'm speaking on behalf of my business,
7 Blue Mist Vaping. We are a small company from York,
8 Pennsylvania, in business for just under three
9 years, and serving over 8,000 customers worldwide.

10 In October of 2009, I switched from smoking
11 to electronic cigarettes and felt for myself the
12 difference in my personal health. I believe in the
13 product and the principle of harm reduction, so much
14 so that just a few short months after making switch,
15 I decided to go into business in this fledgling
16 industry.

17 During the three years since I've launched
18 the business, I've spoken to our customers and
19 received many letters expressing gratitude for our
20 products and how e-cigarettes have made a positive
21 change in their lives and health. Many of them are
22 lifelong smokers who have tried a variety of

1 therapies and treatments to quit smoking.

2 Unfortunately, the common NRT treatment plans and
3 timetables often don't work, and they relapse.

4 These former smokers express gratitude for
5 the substantial harm reduction offered in electronic
6 cigarettes, ease of use, and the improvements they
7 are experiencing in their quality of life. I'd like
8 to read a few comments I've received back from them.

9 Jen in Pennsylvania told me, "You helped me
10 to quit."

11 Gregory from New York: "I'm a throat
12 cancer survivor, heavily addicted to nicotine. I
13 know if I run out, I'll be going to the store for a
14 pack of you know what."

15 Carrie of Missouri had this to say in her
16 letter to us: "I want you to learn how important
17 your products are to some people. I'm an Army
18 veteran, as you notice by my signature line. What
19 my signature line doesn't show is that I'm a
20 disabled veteran.

21 "One of my disabilities is multiple
22 sclerosis. This past Friday, I had an appointment

1 at my VA hospital, a four-hour drive round-trip. Of
2 course, I vaped the entire trip and while I was in
3 the hospital.

4 "MS has many ups and downs. My doctors
5 only see me for a short period of time after I've
6 been immobile from a two-hour drive. I've tried on
7 numerous occasions to tell them what has been
8 happening with my gait when I tire, get too warm,
9 walk too much, or stand too long.

10 "In June, during one of my bad walking
11 episodes, I yelled for my daughter to get my cell
12 phone and video what was happening. Friday I
13 learned, thanks to that video, that I'm also
14 suffering from something called paroxysmal
15 dyskinesia, secondary to the MS.

16 "I didn't fully understand what it meant,
17 so the discussion on the ride home was about how
18 they cast my leg for a brace. Once I got home, I
19 started researching, and what I learned was rather
20 frightening as I realized that apparently the first
21 actual indication was from the late '90s with my
22 vocal cords. Now my legs and even my left arm were

1 being affected.

2 "It's been one extremely difficult weekend,
3 with learning the implications of what is happening.
4 Had I not had your product, there is no doubt in my
5 mind that I would have used cigarettes. It kept me
6 from smoking, even under the extreme stress that
7 I've been feeling.

8 "I need to share with you, your product was
9 able to keep me from smoking. It helped calm my
10 nerves. I wanted you to know that behind the orders
11 are not only people but also lives that your product
12 affects. I now know I don't have to light up a
13 cigarette when major stress hits.

14 "I'm a stubborn old soldier. I know this
15 little incident was a mental setback. I am now
16 determined to fight the battle with this one also.
17 I've now had time to come to grips with it all, and
18 I'll find the humor in it because that's my way of
19 coping. I will do it all while vaping."

20 These comments illustrate the importance of
21 providing products that can make a positive impact
22 in their everyday lives. I recognize that quality

1 and safety are both major concerns. But I believe
2 that our industry is up to the challenge.

3 Several associations that include
4 scientists, researchers, and public health experts
5 have already been formed to meet these concerns.
6 They've set up the structures that can help to
7 define reasonable standards and policies by which
8 e-cigarette liquids are manufactured and sold.

9 The standard policy pushing for complete
10 abstinence from nicotine is limited. What the
11 consumers tell us is they want options for lower-
12 risk products and to be able to make those choices
13 for themselves. Reduced harm products allow the
14 consumer that greater flexibility of choice. Thank
15 you.

16 DR. HUSTEN: Thank you. So it seemed like
17 a lot of the comments are related to folks who had
18 essentially used the product to quit smoking.

19 So I guess I'll ask the same question I had
20 asked the gentleman this morning, about shouldn't
21 e-cigarettes have to do the same kind of studies
22 that NRT products have had to do in order to be able

1 to be marketed for cessation?

2 MR. JACK: I believe that we can actually
3 show that e-cigarettes are a safe product to use.
4 We know what is actually going into these products.
5 There are no unknown substances. We know what
6 nicotine is. We know what the carriers are. These
7 are very, very similar to the ones already used in
8 NRTs as they exist already. The only difference is
9 that ours work.

10 DR. HUSTEN: And do you have studies that
11 you could submit demonstrating the effectiveness?

12 MR. JACK: I've got over 7,000 repeat
13 customers. That's who tells me.

14 DR. HUSTEN: So I take it you're saying you
15 don't think you should have to do the same types of
16 studies that the NRT folks have done?

17 MR. JACK: I'm sure that as time goes on,
18 those studies are going to become very necessary.
19 But I think that banning the product outright simply
20 because the cigarette industry can't afford to pay for
21 those studies up front has got to be short-sighted.

22 DR. HUSTEN: Then related to that, what are

1 the types of data or studies that you think should
2 be required for these products to be on the market?

3 MR. JACK: Well, we can look at the long-
4 term after-use of people who have used these
5 products over a long period of time to see if they
6 are experiencing any side effects. But we can also
7 look at the product itself. Now, we know what's
8 going into it. We can track all that information.
9 I know there are others here who may be able to
10 better speak to that than I.

11 DR. HUSTEN: Then my last question was
12 related to getting a modified risk product
13 designation. What types of studies do you think the
14 industry should do in order to get that type of
15 designation?

16 MR. JACK: I'm not sure I'm qualified to
17 answer that.

18 MS. SIPES: All right. Thank you very
19 much.

20 MR. JACK: Thank you.

21 MS. SIPES: Our next speaker is Mr. Lou
22 Ritter with the American E-liquid Manufacturing

1 Standards Association.

2 MR. RITTER: Good afternoon. It's been a
3 long day. My name is Lou Ritter, and I'm here to
4 speak on behalf of the American E-liquid
5 Manufacturing Standards Association, or AEMSA.

6 I hold the office of president in this
7 recently incorporated association. My involvement
8 is as a volunteer, and I am not a vendor, and I do
9 not have any financial interest in this industry.
10 Our members are all listed on our website and a
11 matter of public record.

12 AEMSA is a newly-formed trade association
13 for e-liquid manufacturers. E-liquids as a
14 component of e-cigarette use, vaporized and inhaled
15 are an issue of relevance. AEMSA was initiated and
16 formation facilitated by consumers. Our association
17 has articles of incorporation as a nonprofit, filed
18 in the state of Ohio. An exemption application has
19 been submitted to the IRS.

20 AEMSA's self-regulated standards, posted on
21 our website, focus on accuracy of content, quality
22 of ingredients, professional and appropriate

1 manufacturing environments, professional and
2 appropriate packaging, and transparency.

3 Electronic cigarettes are one category of
4 innovative product, as referenced by the FDA 2012
5 and 114 docket notice summary. Some estimates
6 indicate over five million people around the world
7 are already using e-cigarettes in these products as
8 a tobacco harm-reduction alternative to smoking.

9 Some estimates indicate a \$2 billion global
10 market, with the U.S. holding the largest share.
11 Hundreds of thousands supportively participate in a
12 global community; multiple Internet industry forums
13 and online programming; three professional trade
14 associations here in the U.S., more in other
15 countries; CASAA; over 250 vendors here in the U.S.,
16 books getting published, and more, are all prime
17 examples. All focus on disseminating educational
18 information, supportiveness, encouragement to this
19 profound tobacco harm-reduction alternative.

20 On the AEMSA website, we have posted some
21 links to some profound current research performed by
22 one leading cardiologist, Dr. Konstantinos

1 Farsalinos, Clearstream project, and more. EC vapor
2 is proving to be exponentially less harmful than
3 tobacco smoke. Please see the links on our website
4 for the details of these studies and other relevant
5 information.

6 Research studies are showing exponential
7 reduction in the consumed harmful chemicals; for
8 example, almost undetectable nitrosamine levels.
9 Since the introduction of electronic cigarettes, we
10 are unaware of any deaths or even any illnesses
11 resulting from the use of these products, from
12 direct or secondhand exposures. There are
13 uncountable numbers of stories expressing how
14 profoundly these products are positively impacting
15 lives.

16 To my understanding, nicotine is an
17 alkaloid found in the nightshade family of plants,
18 Solanaceae, that acts as a nicotinic acetylcholine
19 agonist, that by a synthesis that takes place in the
20 roots, an accumulation occurs in the leaves of the
21 Solanaceae. It constitutes approximately only 0.6
22 to 3 percent of the dry weight of tobacco, and is

1 present in the range of 2 to 7 micrograms per
2 kilogram of various edible plants.

3 Given this minimal constitution and the
4 existence in other nightshade plants, some commonly
5 consumed, it raises the question: Is nicotine equal
6 to tobacco?

7 Granted, in its concentrated form, nicotine
8 is toxic and certainly justifies controlled and
9 professional handling and environments. However, in
10 the diluted concentration consumed by e-cig users,
11 the risks are exponentially reduced and often
12 considered comparable to caffeine.

13 Referencing U.S. Code 2010, Title 21,
14 Subsection 387, delineates the definitions for
15 tobacco and its subcomponents. We wonder how
16 electronic cigarettes fit these definitions of
17 tobacco and/or tobacco products. We believe that if
18 the products and/or their components do not fit the
19 definitions of tobacco, perhaps e-liquids deserve a
20 new approach to regulation.

21 Let's address some of your real and
22 substantive questions.

1 4.4(a) asks, how should the harm be
2 identified and measured? Well, for THR purposes,
3 tobacco harm reduction purposes, in direct
4 comparison to combusting and smoking tobacco,
5 Dr. Farsalinos' study shows comparable plasma and
6 nicotine levels. The comparative absence of
7 nitrosamines, carbon monoxides, and thousands of
8 other harmful chemicals verify the reduced harm
9 factors.

10 4.5 asks, what barriers exist to the
11 development and marketing approval? My answer would
12 be the looming threat of unreasonable, unrealistic,
13 and unsustainable regulation is by far the most
14 significant barrier.

15 4.6 asks, how can the FDA and other HHS
16 agencies act to protect and promote public health?
17 The FDA can work with industry-related associations
18 like AEMSA, CASAA, and others, as well as other
19 industry-knowledgeable and confident activists to
20 formulate and establish reasonable, realistic, and
21 sustainable regulations for the manufacture and sale
22 of refillable e-liquid products.

1 Different nicotine products carry
2 substantially different risks. The FDA can educate
3 people about these significant differences.

4 4.7 asks, how can these broader outcomes be
5 taken into account? Competent professional research
6 has been conducted and continues. These
7 professionals are willing to share their information
8 and results. Dr. Farsalinos and the Clearstream
9 project would be two likely sources. There are many
10 others who have substantive libraries of accumulated
11 research: CASAA, Dr. Michael Siegel, Bill Godshall
12 all come to mind. AEMSA is more than willing to
13 participate.

14 The harm smoking tobacco causes, both
15 first- and secondhand, is obviously unquestionable.
16 We already have substantive implications for
17 electronic cigarettes to scientifically prove
18 themselves a profound harm-reduction alternative, as
19 most e-cig users are already learning for
20 themselves. We implore this committee to advocate
21 for reasonable, realistic, and sustainable
22 regulations for the manufacturer and sale of these

1 refillable e-liquid products.

2 We are now presented with a rare
3 opportunity. We have the technology, means,
4 education, and the wisdom to offer this substantial
5 tobacco harm-reduction alternative. Yes, more
6 research is clearly warranted and justified.
7 However, to risk even diminution of this profound
8 harm-reduction alternative with over-regulation
9 would be a true injustice.

10 While abstinence is clearly the preferred
11 and healthiest alternative, the addictive realities
12 proven by relapse statistics, and continued harm
13 experienced by smokers and all of us touched in one
14 way or another by those harms, are absolutely
15 undeniable.

16 The axiom, "Quit or die," spoken or
17 implied, has proven unviable and inhumane. We as a
18 society have not only created the harms of tobacco,
19 we have permitted them to endure for decades or
20 longer, and we've done so through governmental
21 regulations.

22 Now, through this very same regulatory

1 process, we have a very real opportunity to mitigate
2 some of that harm. Don't we owe it to our society
3 and all of humanity to lead the way and facilitate
4 this tobacco harm-reduction alternative? AEMSA
5 offers to assist with, contribute to, and facilitate
6 the development of reasonable, realistic, and
7 sustainable regulations for the manufacture and sale
8 of e-liquid products.

9 Thank you all for your time and attention,
10 and I appreciate this opportunity to present this
11 information. If you have any questions?

12 DR. LEONARD-SEGAL: Thank you. You made
13 a statement, I think, that said that you're not
14 aware of any illnesses or deaths. By what mechanism
15 would you become aware of this information? How do
16 you garner this kind of information about these
17 products?

18 MR. RITTER: Well, that was a very honest
19 statement. I said, we are not aware. We're active
20 in the industry. We're very actively involved in
21 following the forums and following the news. We
22 have consumer advocate associations.

1 We have people that are putting together
2 documentary films that are traveling the world doing
3 interviews. We have direct access to some of the
4 people doing some of the most leading medical
5 research in this field. And so far, we have not
6 seen a single report.

7 That doesn't mean it doesn't exist. But to
8 our awareness, being pretty well dug into this
9 industry, we have yet to hear of any. So I think my
10 statement was true and honest.

11 DR. LEONARD-SEGAL: And can I have a better
12 understanding, I guess, of the time span over which
13 these products have been actively used in the United
14 States?

15 MR. RITTER: To the best of my knowledge,
16 they made their preliminary introduction in the
17 United States about six years ago, and they have
18 just absolutely exploded exponentially since then.
19 As I said, to our count, we've got over 250 vendors
20 of various natures here in the United States.

21 DR. LEONARD-SEGAL: And can you give me
22 some kind of an understanding of the -- when

1 somebody picks up a cigarette for the first time and
2 starts to smoke, or you have a population that does
3 that, over that period of time, say three years,
4 four years, five years, whatever it is, how much
5 illness and death does one see during that period of
6 time of smoking cigarettes? Would you have any way
7 of comparing that to what you might expect to see
8 with your e-cigarettes?

9 MR. RITTER: I can't speak to what the
10 population experience is. I'm not the population.
11 I can tell you my personal experience.

12 As my personal experience, I did smoke
13 cigarettes for 33 years. I have not touched a
14 cigarette in over two and a half years. Yes, I have
15 held someone in my arms as they took their last
16 breath from lung cancer. And I can tell you now
17 that since I no longer smoke after 33 years of
18 smoking, I don't get sick very often. I used to
19 gets colds three, four times a year. I don't get
20 any now; maybe one a year, if that.

21 I can tell you that I used to wake up with
22 hacking coughs. I couldn't run. I couldn't jog. I

1 would lose my wind easily. I now work out regularly
2 in a fitness center, and I get on an elliptical and
3 I run endurance seven-minute miles in succession. I
4 now run interval training at over 18 miles an hour
5 for a minute straight.

6 So, yes, I have held people in my arms.
7 Yes, I have seen people get sick and die. Yes,
8 I have seen people develop emphysema; a recent
9 friend of mine just died, who was a lifelong smoker.
10 She tried to quit many, many times. I tried to
11 introduce her to electronic cigarettes. She wasn't
12 ready. And she just passed of emphysema at the age
13 of 67 not two months ago.

14 DR. LEONARD-SEGAL: Yes. I'm just trying
15 to get a sense, over this brief period of time that
16 we've had information or some kind of experience
17 with these products, how they would compare if
18 cigarettes had only been available for three years
19 or four years as well. I'm trying to get a sense of
20 that relative difference.

21 MR. RITTER: With all due respect, ma'am, I
22 don't see that as a relevant question. The fact is,

1 tobacco has been around for decades. And we
2 promoted it. And we either regulated it or we
3 didn't. And we allowed it to be advertised.

4 It has gone on, and it has permeated our
5 society to the point of not only being socially
6 acceptable, but being socially attractive. And now,
7 today, it's become unattractive. But the damage is
8 done. The chemicals are in the tobacco. And those
9 chemicals are accelerated exponentially by the
10 combustion process.

11 So we have a combination of habit patterns
12 and addictions. And we have something that has
13 permeated our society to the point where you've sat
14 here all day long looking at statistics that show
15 43 million, 44 million people in this country
16 smoking.

17 With all of the increases in prices, with
18 all of the increases of taxes, with all the medical
19 knowledge that we have and information that we have,
20 this says that this is deadly. This is destroying
21 your life. And we do it again and again and again.
22 And children still continue to do it because for

1 some reason, they get it in their heads that this is
2 cool.

3 But that's not what I'm here to talk about.
4 I'm not a tobacco specialist. I'm not a scientist.
5 I'm not a doctor. But I am involved in this
6 industry, and I see what's going on. And I see the
7 hundreds of thousands of people that are actively
8 participating every single day; in the forums.
9 There are right now 30 pages of forum posts that
10 have been posted today, during this hearing alone,
11 by people following what's going on in this room,
12 live on the Internet.

13 People care. People need this. They want
14 this. This is something -- we don't have enough
15 proof, but we have enough proof to know that this,
16 by comparison to tobacco, compared to continue
17 smoking, that NRTs as -- yes, promote the NRTs. I'm
18 not saying stop them. But they're not working
19 enough.

20 In six years, we've got 5 million people
21 worldwide already using these products in one
22 variation or another. We've got social environments

1 and communities, support structures, that are
2 evolving at a rate that I have never seen happen in
3 any other facet of society. We have events that
4 take place, four or five of them a year here in this
5 country, where 6-, 7-, 8-, 900 people show up from
6 around the world. People fly in from England.
7 We've got doctors in Greece.

8 Dr. Farsalinos was chosen, he was honored
9 to be chosen, for the European Society of
10 Cardiology. I think there were thousands and
11 thousands of different studies that were submitted
12 to be presented at that cardiology event in August
13 of 2012. And here was Dr. Farsalinos holding up a
14 comparison on the cardiological impacts of tobacco
15 versus vapor. And the study is posted on our
16 website. The links are there.

17 I encourage you, I beg you, go to our
18 website. Look at this information. Is it enough?
19 No. It's not. You have a responsibility. We have
20 a responsibility. But the information's there.

21 Yes, sir?

22 MR. LINDBLOM: I apologize for my

1 ignorance. I don't know a lot about your
2 organization. And I'm just curious as to if you
3 could maybe speak a little bit more about what
4 you do.

5 I was interested in the core beliefs, and
6 it talks about, for example, verifying the accuracy
7 of the nicotine content, the quality and safety of
8 the ingredients, which is terrific stuff.

9 Do you actually do any laboratory tests
10 to check those kinds of things? Or are there
11 site inspections about the clean, sanitary
12 manufacturing facilities? I'm just curious as to
13 how those --

14 MR. RITTER: Yes. Yes. Yes.

15 MR. LINDBLOM: Great. How do you -- could
16 you just --

17 MR. RITTER: All of that is posted on our
18 website. We believe in 100 percent transparency.

19 MR. LINDBLOM: And you speak --

20 MR. RITTER: Now, while I am not a
21 scientist, I have been very active in leading and
22 facilitating the formation of this process because I

1 believe in it. And, as I said, I'm a volunteer. I
2 have no financial interest in this industry. But I
3 do it because I care. And I see the need for
4 regulation -- self-regulation, AEMSA -- it could be
5 a model. It could be an example.

6 But we brought in a professional chemist, a
7 professor with over 30 years' experience in
8 biochemistry, and we brought in leading -- we even
9 have nicotine suppliers that are very well-educated.
10 And so we sat down and we tried to study it and say,
11 how do we isolate the top quality of the nicotine?
12 We know that there's this variation, this range,
13 this scale of quality of nicotine. We have
14 pesticide grade. Do we want anybody using that?
15 No. How do we get to the top?

16 So we pulled a quantitative GCMS test. And
17 I had to go study what is a quantitative GCMS test
18 versus a qualitative GCMS test? And I had to learn
19 that in order to have an effective quantitative GCMS
20 test, you have to build a library of all the
21 potential contaminants. And then you have to create
22 a baseline.

1 Now, we realized that this was cost-
2 prohibitive to do on an item-by-item -- on a supply
3 level-by-supply level basis for per-order for the
4 manufacturers that are operating at our levels.
5 They're small, small business.

6 So what we realized was that there are
7 certain nicotine suppliers that are doing this as a
8 matter of course. They're already doing it on a
9 batch level. So we started comparing the
10 quantitative GCMS tests, and we said, okay, well, we
11 went and looked at the FDA requirements and we said,
12 if it was going to be USP -- if it was going to be
13 certified, it would probably have to be -- what did
14 we come up with -- 99.5 percent pure, I think.

15 Then we looked at the other guy and said,
16 well, wait a second. There's nobody selling USP
17 certified in the United States. There's nobody
18 going to certify it here in the United States. We
19 don't that kind of money. But there are people that
20 are doing USP grade.

21 So then we started looking at USP grade,
22 and we said, okay, 99 percent. And then we started

1 looking at some very, very specific contaminant
2 ratios within that 1 percent.

3 We talked to our nicotine suppliers. We
4 talked to our professional chemist, subject matter
5 expert. And we started isolating out very specific
6 levels of contaminants. And you can see this on our
7 website. It's all listed. All of our definitions
8 are listed.

9 So then, from there, we went and we said,
10 okay, well, we've gotta go even further. We gotta
11 verify not only the quality, but we got to follow
12 the accuracy. So in that quantitative GCMS test,
13 every single vendor, when they take in a batch, they
14 have to titrate their incoming level.

15 Now, none of them are bringing in pure, so
16 they're bringing it in at some working level or
17 something reduced closer to a working level. So
18 they have to titrate in. They may even be bringing
19 in their working level.

20 So if it is coming from the supplier at,
21 say, 100 milligrams, then the manufacturer, the
22 vendor, our member, has to have that titrated to

1 verify the accuracy before he begins to sub-dilute
2 it further. All diluents have to be USP-certified
3 through the chain of custody. They have to use
4 NIST-certified, calibrated equipment to measure the
5 nicotine.

6 So there are steps. I mean, I can't rattle
7 off our entire set of standards off my head, but
8 they're there on our website. And they were based
9 in a large extent off FDA commercial food
10 regulations, commercial food manufacturing.

11 Personally, I believe that some reasonable
12 set of standards can be developed, maybe straddling
13 U.S. liquor distillation and commercial food
14 handling. I mean, there's no doubt. Nicotine is an
15 ingredient of concern. And for me to stand here and
16 pretend that it isn't would not make much sense. It
17 is. In its concentrated form, it requires
18 professional handling and professional environments.
19 There is no doubt about it. But in the level that
20 it's diluted down, if you're using high-quality
21 ingredients -- we have a whole list of ingredients
22 we prohibit from being included in our members'

1 liquids.

2 We've evaluated the FDA standards for the
3 environment, the dedicated environment -- nonporous
4 surfaces, how we store chemicals and levels, how
5 often hands have to be washed, hair standards,
6 clothing standards, standards for abrasions.

7 If somebody's sick, they have to report it
8 to a person in charge, and they're not allowed in
9 the mixing room for three asymptomatic days or until
10 they're cleared by a medical professional; similar
11 to that of commercial food handling.

12 We've taken on the packaging issues, and
13 we've gone into childproof caps, tamper-resistant,
14 tamper-evident packaging. Smear-proof labels.
15 Batch ID numbers that are traceable on each bottle
16 back to the incoming batch of nicotine.

17 Yes, ma'am?

18 MS. SIPES: Eric, I don't want to cut you
19 off. Did you want to ask anything further?

20 MR. LINDBLOM: My only other
21 question -- that's all extremely interesting. So to
22 be a member of the organization, they have to meet

1 the minimum standards you set? Is that -- I'm just
2 trying to figure out what --

3 MR. RITTER: They agree to the -- the
4 standards are published. They agree to the
5 standards. They sign a membership agreement. We're
6 a very new organization. We have a set of charter
7 members; we've had some recent additions. Nobody is
8 actually required to be in compliance until January
9 15th, and the inspections will begin then. Every
10 single member agrees to scheduled and unscheduled
11 inspections.

12 MS. SIPES: And how many members do you
13 currently have, roughly?

14 MR. RITTER: I think the number is 13.
15 But, as I said, we only launched October 8th, I
16 believe.

17 DR. RAPPAPORT: On item 4.6, in your
18 comments you went pretty quickly over what you think
19 FDA and HHS agencies could do. I don't want you to
20 go through all of what we could do, and maybe not
21 focus on correcting what you see as we've been doing
22 wrong, but perhaps, say, focus on what regulatory

1 role you think the federal government should have,
2 if any, for these types of products.

3 MR. RITTER: Well, are you asking what role
4 I think the government should have, or are you
5 asking me how I think that these reasonable,
6 realistic and sustainable regulations can be
7 formulated?

8 DR. RAPPAPORT: Would you repeat the last
9 part more slowly?

10 (Laughter.)

11 MR. RITTER: I'm asking you the nature of
12 your question. Is your question to me, what do I
13 think the government's role should be in the
14 regulation, or are you asking me how I think these
15 regulations should be formulated?

16 DR. RAPPAPORT: I think it's what's the
17 government's role in regulating this group of
18 products.

19 MR. RITTER: I think that the government is
20 best served to work with those who are already
21 extremely knowledgeable. You've got wonderful
22 resources at your disposal: CASAA. AEMSA has

1 wonderful, knowledgeable experts. There are other
2 people in this room here today.

3 We've got Bill Godshall. We've got
4 Dr. Farsalinos in Greece, who's willing to
5 communicate and participate. We've got the
6 Clearstream project. Dr. Michael Siegel. There's a
7 long list of people who have been actively involved
8 and very knowledgeable, and we would be happy to
9 facilitate and participate.

10 I think that the regulations could very
11 well be developed, as I said, to perhaps maybe
12 straddle -- and this is my opinion; I can't speak
13 for the industry, I can only speak for our own
14 manufacturers, for our members for our association.
15 But we believe, as an association, that reasonable,
16 realistic, and sustainable standards might somehow
17 cross the borderline between liquor distillation and
18 commercial food manufacturing.

19 DR. RAPPAPORT: Okay. That's what I was
20 trying to get at. Thank you.

21 MS. SIPES: Thank you very much. I
22 appreciate it.

1 MR. RITTER: Thank you. Thank you for the
2 time.

3 MS. SIPES: All right. At this time,
4 Mr. Anton, are you there?

5 (No response.)

6 MS. SIPES: Perhaps not.

7 Dr. Abrams, would you have a moment to come
8 up and respond to an additional question? Are you
9 there? There he is. Take your time.

10 (Pause.)

11 DR. WINCHELL: Thank you, Dr. Abrams, for
12 coming back to speak with us.

13 There was something that you said during
14 your remarks that I wanted to return to and ask you
15 if you could expand on that a little bit.

16 You talked about individuals with 15 to
17 20 pack-years of exposure to cigarettes having
18 a risk curve that is so steep that any combustible
19 use would be a risk for those people.

20 So could you expand on that a little bit?
21 Is there a population of people for whom smoking
22 reduction would not be an appropriate treatment

1 approach, or wouldn't be expected to lead to
2 benefit? If you could just say a bit more about
3 that finding.

4 DR. ABRAMS: Sure. Well, first I'd say no.
5 Obviously, any reduction is still beneficial because
6 this is a risk curve and we're talking about
7 probabilities. But the reality is, from my
8 understanding of the epidemiologic literature, is
9 that in particular for lung cancer risk, the curve
10 of risk does exponentially take off a kind of
11 J curve around 20 pack-years of exposure.

12 So for older smokers with at least a
13 history of 20 pack-years of exposure, the dangers
14 and the risks of getting lung cancer become very
15 high even if they substantially reduce their
16 combustible cigarette use but continue to smoke
17 combustibles. Obviously, there's still some
18 reduction in risk. But the benefit is not for those
19 with 20 pack-years of exposure as opposed to those
20 with less.

21 I believe those data are available from
22 CDC. They've been presented at other conferences,

1 like the IOM report on cancer reductions and tobacco
2 that was held about six or eight months ago. And
3 I'm happy to share the actual epi data with you.

4 That's it?

5 MS. SIPES: I believe that's it. Thank you
6 so much.

7 All right. Mr. Anton has left? Okay. He
8 was the one person of whom we had additional
9 questions. All right. At this time we had asked if
10 anyone wanted to -- if anyone who hadn't already
11 spoken wanted to make any comments. We haven't
12 gotten any names so far.

13 If anybody else would like to come up and
14 say something, now is the time.

15 (No response.)

16 MS. SIPES: No? All right.

17 In that case, on behalf of the panel, I'd
18 like to thank all of the speakers for making their
19 presentations, which were very informative. I'd
20 like to thank the audience for your attention; this
21 has been a full day. We got a lot of very
22 interesting information, which we appreciate, and we

1 will take it all into consideration in our decision
2 making.

3 Today's meeting is concluded. Thank you
4 very much.

5 (Whereupon, at 3:43 p.m., the meeting was
6 concluded.)

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