

FOOD AND DRUG ADMINISTRATION

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CENTER FOR TOBACCO PRODUCTS

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TOBACCO PRODUCT APPLICATION REVIEW
PUBLIC MEETING

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MONDAY
OCTOBER 22, 2018

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The Public Meeting convened at the
Hilton Washington DC/Rockville Hotel and
Executive Meeting Center, 1750 Rockville Pike,
Rockville, Maryland, at 8:30 a.m.

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1 P-R-O-C-E-E-D-I-N-G-S

2 (8:33 a.m.)

3 MR. ZELLER: Good morning, and welcome
4 to FDA's Tobacco Product Application Review
5 public meeting.

6 I am Mitch Zeller, Director of FDA's
7 Center for Tobacco Products, and I want to thank
8 you all for attending this meeting, and, also,
9 for your understanding, as we changed the
10 location of the meeting from Silver Spring to
11 here in Rockville.

12 And for those of you who are familiar
13 with this hotel, and when we all used to work in
14 the Parklawn Building 800 years ago, this was the
15 only hotel that we could hold meetings. So, it's
16 sort of like for us old-timers old home day, even
17 though it's now a Hilton and it's undergone a
18 complete facelift.

19 In July of last year, as you all know,
20 FDA Commissioner Gottlieb unveiled the agency's
21 Comprehensive Plan for Tobacco and Nicotine
22 Regulation. Understandably then, much of the

1 discussion and the media coverage focused on
2 certain elements of the plan, such as the
3 potential for a nicotine products standard.

4 However, the announcement also had
5 several key efforts in the areas of tobacco
6 product application and review. For example, the
7 Commissioner promised that CTP would examine its
8 existing approach to what are called the
9 Provisional Substantial Equivalence Reports that
10 were still remaining in the review queue. And
11 less than 10 months later, we announced a new
12 approach to these products that allows for
13 increased efficiency, better use of resources,
14 and greater transparency, while still making sure
15 those products with the greatest potential to
16 raise different questions of public health will
17 still undergo the full multidisciplinary
18 scientific review.

19 This past summer, we implemented
20 additional efforts to improve transparency for
21 applicants. Previously, applicants needed to
22 file the Freedom of Information request to obtain

1 certain review documents. We heard feedback that
2 receiving this information more rapidly is
3 critical to the decision-making process on
4 whether to seek further supervisory review when a
5 company receives an adverse decision. And so, we
6 made a change. And as of August, copies of these
7 documents are now available to companies
8 following receipt of a final decision action.

9 We also continue to hear about the
10 importance of transparency from other
11 stakeholders, and we will continue to strive to
12 make our decisions and our processes as
13 transparent as possible.

14 These types of improvements and our
15 willingness to reassess existing policies remains
16 a key aspect of our plan. It's why we're having
17 this meeting, where we will have a two-way dialog
18 that can lead to a better understanding of the
19 tobacco product application process and
20 improvements that would benefit the public
21 health.

22 The Comprehensive Plan we announced

1 last year is based on the vision of a world where
2 cigarettes would no longer create or sustain
3 addiction, and where adults who still seek
4 nicotine can get it from alternative and less
5 harmful sources. But, to achieve that vision,
6 any potentially less harmful nicotine-delivering
7 products still need to be properly reviewed and
8 authorized through the premarket review process.

9 In order to best evaluate these
10 products, we're committed to continuing to
11 develop guidance and regulations that further
12 spell out the rules of the road, if you will, for
13 the companies who are submitting these
14 applications.

15 I'm sure that many of you have
16 questions about the current status of the
17 compliance policy for deemed products on the
18 market, as of August 8th, 2016, and the deadlines
19 for submission of those applications. I can't
20 say anything publicly beyond what the
21 Commissioner has already said, other than to say
22 that we are reexamining that policy and, as the

1 Commissioner has stated, all options are on the
2 table. I can assure you that we are working
3 expeditiously to make those decisions and to
4 announce them as quickly as possible.

5 Beyond that policy, we're already
6 working on additional improvements that we also
7 hope to announce soon, but we also want to hear
8 from all of you. The next days provide us with
9 an opportunity to engage in a dialog, and I'm
10 hopeful that the presentations from our staff
11 will answer some of your questions and clarify
12 some points of confusion.

13 All of us in CTP, from Matt Holman and
14 his team in the Office of Science, to me and my
15 colleagues in the Office of the Center Director,
16 look forward to hearing and learning about
17 practical feedback and suggestions that we can
18 use to make positive changes to our processes.

19 As we delve into the various review
20 processes over the next two days, I hope everyone
21 can keep this meeting's common goal in mind: to
22 leverage the collective knowledge in this room to

1 inform and improve the process for premarket
2 review of tobacco products.

3 Before closing, I do need to somewhat
4 abruptly shift gears and share some very sad news
5 that impacts part of CPT's participation in our
6 meeting today and tomorrow, and our apologies in
7 advance for having to make this announcement
8 publicly.

9 Over the weekend, a dear CPT
10 colleague, David Keith, passed away unexpectedly
11 following a very brief illness. David was the
12 Director of the Division of Enforcement and
13 Manufacturing in OCE, our Office of Compliance
14 and Enforcement, and was actually supposed to be
15 one of the speakers here tomorrow.

16 David was a wonderful leader in OCE.
17 His passing is a shock and a great loss for CPT
18 and to public health. As you can imagine, it's
19 taking a very hard toll personally and
20 professionally on his OCE colleagues, many of
21 whom will be joining me at his funeral tomorrow.
22 So, all of the OCE speakers on the agenda beyond

1 David will not be able to participate this
2 afternoon or tomorrow.

3 I'm very sorry to have to share this
4 tragic news in such a public way, especially for
5 many of you in the audience who knew David and
6 are learning of his passing for the first time.
7 My apologies.

8 So, to transition back to the purpose
9 of our gathering here today and tomorrow, FDA
10 remains committed to the principles of our
11 Comprehensive Plan, including efforts to improve
12 efficiency and transparency when it comes to the
13 review process.

14 And on behalf of the Commissioner and
15 everyone at CTP, I want to thank you all for
16 being here today and participating in this effort
17 with us.

18 With that, I will turn things over to
19 Jeff Walker for some of his opening remarks.

20 Thank you very much.

21 (Applause.)

22 MR. WALKER: Well, good morning to all

1 of you.

2 I didn't know David personally, but I
3 had spoken with him on the phone several times,
4 and I'm sorry for CTP's loss.

5 Well, it's my sincere pleasure to be
6 here with all of you today and with those
7 watching via the webcast. I want to thank FDA
8 for the invitation to speak and provide some
9 remarks on what I consider to be an unprecedented
10 two-day public meeting to discuss the
11 practicalities in the review of these new tobacco
12 product applications.

13 I'd like to start my comments by
14 mentioning that I've spent the last eight years
15 in tobacco regulatory science, five years at
16 Altria as their Chief Medical Officer, VP of
17 Regulatory Sciences, and the last two and a half
18 years as an independent consultant and the U.S.
19 agent for Philip Morris International for their
20 MRTTP and PMTA applications.

21 However, I want to make it clear that
22 my comments and perspectives during this meeting

1 do not represent the opinions or perspectives of
2 either company. Rather, my comments arise from
3 the totality of my two professional careers,
4 first, as a physician and, second, for over two
5 and a half decades working in FDA-regulated
6 companies.

7 I have a great interest and a great
8 enthusiasm for this meeting. I am happy to see
9 it happen. It's very timely. It's very
10 important. The fact that over 700 people share
11 this enthusiasm who have registered for this
12 meeting indicates how important it is and how
13 much we have to learn.

14 We can really focus over the next
15 couple of days on the practicalities and the
16 challenges of these applications, learning
17 directly from FDA staff, from industry, and
18 people who represent the perspectives of tobacco
19 control and public health.

20 Our collective interest is
21 understandable, because the regulation of tobacco
22 products continues to evolve, sometimes it seems

1 like on a weekly basis. But, in fact, it's very
2 dynamic. It's understandable. It's new. We're
3 just beginning to learn how FDA applies this
4 unique public health standard to the review of
5 tobacco products and other applications.

6 We've also seen that the science
7 behind these applications is highly complex. It
8 can be complex, really a nexus for different
9 disciplines, such as physical sciences,
10 biological sciences, behavioral science, law,
11 medicine, public policy, public health, just to
12 name a few of the disciplines that usually are
13 involved in these kinds of conversations.

14 And amidst of this, we find ourselves
15 in a world where, despite these uncertainties and
16 evolutions, the pace of submissions of new and
17 modified risk applications continues to
18 accelerate. And I think over the coming months
19 to years, you will see a continued acceleration
20 of these applications.

21 So, given this backdrop, what can we
22 expect from the next two days of conversation?

1 And I use that word because I think that's
2 exactly what FDA wants this to be, which is
3 really a dialog that's frank, it's honest, but at
4 the same time respectful, acknowledging that
5 there are different views, different opinions,
6 some of which are quite strongly held.

7 Now this conversation should allow
8 everyone in this room and everyone on the webcast
9 to feel that their issues and opinions are being
10 heard. So, I encourage each of you to become an
11 active participant in this meeting by submitting
12 your questions. They're anonymous, so you don't
13 have to worry about attribution. But please
14 submit them. Please participate in the dialog.
15 Because, in this way, the FDA will get a very
16 good sense of the broad range of opinions and
17 issues that confront the public about these
18 particular applications. I think this feedback
19 will be quite welcomed.

20 Let me offer just a couple of
21 expectations for the meeting, and these are my
22 expectations and may not be yours, but let me

1 tell you what I think we should get from the
2 meeting.

3 First of all, it's obvious we should
4 all walk away with a better understanding of
5 these application pathways, how they are used or
6 intended to be used, and, more importantly, to
7 hear the real-world experiences of FDA, industry,
8 and other people who've been participating in
9 these processes.

10 The second expectation I have is to
11 achieve some degree of what I'll refer to as
12 process transparency. The FDA process of review
13 can be quite active. Particularly when you first
14 submit applications, there's a lot of dialog and
15 engagement, but there are also times when the FDA
16 review process can be quite silent, sometimes for
17 weeks. And never quite sure whether that means
18 your application has been shelved or lower
19 priority, or what that actually means. So, I'm
20 hoping over the next couple of days we can have
21 the FDA roll back the curtain a little bit on the
22 scientific review process, so the public can

1 better understand the timing and the complexity
2 of review, as the FDA reviews these applications.

3 My final expectation for the meeting
4 is to listen carefully to the variety of
5 opinions. There are some very diverse opinions
6 you'll hear over the next two days. And I think
7 that allows us to engage in a better dialog and
8 have a better perspective on the issues that can
9 be or have been raised in the context of
10 applications.

11 Any company that wants to submit
12 applications can understand that these
13 perspectives can be very useful as they formulate
14 a new application, as they consider issues, they
15 design studies. I think it allows a more fulsome
16 dialog and a better process. Keep in mind that
17 it is likely FDA will receive these same comments
18 and perspectives about your tobacco product
19 application from the public, particularly in the
20 context of an MRTTP docket.

21 In conclusion, let me emphasize again
22 once more to you in the audience and you at home,

1 you on your computers, you have an important role
2 in broadening this conversation, enhancing the
3 learnings from the meeting. So, I urge you to
4 relax as much as that's possible in an FDA formal
5 meeting, contribute to the conversation, and
6 enjoy the dialog.

7 Thank you very much.

8 (Applause.)

9 MS. JOHNSON: Good morning, and thank
10 you.

11 My name is Eshael Johnson. I'm the
12 Director of Stakeholder Relations in the Office
13 of the Center Director, and I am one of your two
14 moderators for today and tomorrow. My colleague,
15 Karin Rudolph -- wave, Karin -- will be assisting
16 me with this.

17 And our job today is to help
18 facilitate this very important two-way dialog.
19 I'm going to give run of show for today and
20 tomorrow. I'll be your task mistress, along with
21 Karin.

22 First of all, for over the next two

1 days, we're going to have eight sessions. Within
2 these sessions, we will have our FDA experts come
3 up and present anywhere from two to three
4 presentations. Following the presentations, we
5 will have our panelists, and each panelist, in
6 alphabetical order, will introduce themselves and
7 have five minutes to make their comments or
8 statements on the topic at hand or on the
9 presentation that's being given.

10 So, we're going to have to stick to
11 that. So, don't be mad when I cut you off,
12 because I will. We will try very hard to follow
13 that agenda. We have a lot of information to
14 cover in a short period of time, but we will be
15 accepting questions, as Jeff encouraged all of us
16 to do.

17 There will be notecards being passed
18 around. We will not have microphones for
19 questions. You'll need to write your questions,
20 hand them back, and either Karin or I will ask
21 the questions, either of the panelists or the
22 presenters.

1 And really, that's all that I have to
2 do. I need to get back to my job. I want to
3 introduce Jennifer Schmitz.

4 Jennifer, are you ready?

5 MS. SCHMITZ: Good morning, and thank
6 you all for coming today.

7 My name is Jennifer Schmitz, and I am
8 a Regulatory Health Project Manager in CTP's
9 Office of Science.

10 I will be speaking today about the
11 request for exemption from substantial
12 equivalence pathway. Please note that you will
13 also hear the term "exemption request" and see
14 the abbreviation EX REQ throughout the
15 presentation and during today's panel discussion.
16 These terms are used interchangeably to identify
17 this pathway.

18 For this presentation, I will be
19 providing an introduction to the three pathways
20 available to market a new tobacco product,
21 information on FDA's statutory and regulatory
22 authority for the exemption request pathway, how

1 to determine if a tobacco product is eligible for
2 the exemption request pathway, an overview of the
3 processes and timelines, and finally, program
4 updates.

5 So, let us begin with an introduction
6 of the marketing pathways available to market a
7 new tobacco product. There are three pathways
8 available to bring a new tobacco product to
9 market in the United States: a premarket tobacco
10 product application, or a PMTA; a substantial
11 equivalence, or SE application, and a request for
12 exemption from substantial equivalence, or
13 exemption request. This presentation will focus
14 on exemption requests, while presentations later
15 today will discuss PMTAs and SE applications.

16 The exemption request process requires
17 the completion of two steps in order to market a
18 modified tobacco product. First, an exempt order
19 is issued by FDA and, second, the applicant
20 submits an abbreviated report. This process will
21 be discussed in more detail later in this
22 presentation.

1 Next, I will discuss FDA's statutory
2 and regulatory authority for the exemption
3 request pathway. FDA's statutory authority for
4 the review of exemption requests comes from
5 Section 905(j)(3)(A) of the FD&C Act. FDA's
6 regulatory authority for exemption requests comes
7 from, first, the exemption rule under
8 21 CFR 1107.1(b), which became effective on
9 August 4th, 2011. Currently, the exemption
10 pathway is the only program with specific
11 requirements. This rule established the
12 procedures required to request an exemption and
13 explains how FDA reviews requests for exemptions.

14 Second, the refuse to accept, or RTA
15 rule, under 21 CFR 1105.10, which became
16 effective on January 30th, 2017, applies to all
17 tobacco product application types. This rule
18 established when FDA would refuse to accept a
19 tobacco product submission or application because
20 the application has not met a minimum threshold
21 for acceptability.

22 So now that you have a basic

1 understanding of the types of marketing pathways
2 and the statutory and regulatory authorities for
3 exemption requests, how can a manufacturer
4 determine if their tobacco product is eligible
5 for an exemption request?

6 In order to obtain a finding that a
7 tobacco product is exempt from substantial
8 equivalence, FDA must determine the following:

9 One, the new tobacco product is
10 modified by adding or deleting a tobacco additive
11 or increasing or decreasing the quantity of an
12 existing tobacco additive.

13 Second, the proposed modification is
14 minor and is to a legally marketed tobacco
15 product.

16 Three, and SE report is not necessary.

17 And four, an exemption is otherwise
18 appropriate.

19 I would like to point out that, for a
20 tobacco product to be legally marketed, it should
21 meet one of the following criteria:

22 It is grandfathered.

1 It has received an SE order, exempt
2 order, or marketing order under PMTA.

3 Or it is a provisional SE tobacco
4 product which has not received a not-
5 substantially-equivalent, or NSE, determination.

6 To assist manufacturers on the CTP FDA
7 website, we have an interactive tool which will
8 aid in determining what premarket pathway may be
9 appropriate to submit for a new tobacco product.

10 So now that we have defined FDA
11 authority and pathway eligibility, I will provide
12 an overview of the exemption request and
13 abbreviated report processes and review
14 timelines.

15 The exemption request process requires
16 two review phases. First, the exemption request
17 is reviewed, and if an exempt order is issued,
18 the applicant submits an abbreviated report.
19 Both of these processes are divided into three
20 distinct phases: acceptance, notification, and
21 review. I will provide detailed information on
22 each of these steps and phases.

1 First, I will discuss the acceptance
2 criteria specific for an exemption request. FDA
3 may RTA an exemption request application if the
4 following criteria under the exemption rule are
5 not met:

6 So, in the first column of this table,
7 we discuss the format of the application, which
8 should include the following:

9 First, the application is legible. An
10 application may not be legible if, for example,
11 the application included scanned documents which
12 did not transfer completely or if they have low
13 resolution.

14 Second, the application is provided in
15 the English language. If any portion of the
16 application is submitted in a foreign language,
17 the application should also include an English
18 translation.

19 Third, the application is submitted in
20 an electronic format. What constitutes an
21 electronic format? Electronic formats include
22 submissions through the CTP portal; the

1 Electronic Submission Gateway, or ESG, and
2 physical media, such as CDs, DVDs, or hard
3 drives. You may refer to the FDA website for
4 additional information on electronic submission
5 file formats and specifications.

6 In a situation where a manufacturer is
7 unable to submit electronically, they may submit
8 a written request to CTP which should include the
9 following criteria:

10 Explain in detail why they cannot
11 submit in an electronic format.

12 Request an alternative format, and
13 include an explanation why an alternative format
14 is necessary.

15 This request should be granted by FDA
16 prior to submitting the exemption request
17 application.

18 In the second column of this table, we
19 will discuss what is needed regarding product
20 information.

21 First, the product identified in the
22 exemption request is a regulated product under

1 Chapter 9 of the FD&C Act, or simply, is this a
2 tobacco product?

3 Second, the tobacco product is legally
4 marketed.

5 Third, the proposed modifications are
6 to tobacco additives. Additional information on
7 this topic will be presented during tomorrow's
8 presentations.

9 Fourth, the applicant is also the
10 manufacturer of the original tobacco product.

11 And fifth, the full identification of
12 the product is included in this request. This
13 information includes the category and subcategory
14 of the product, the product name, package type,
15 and quantity.

16 In the third column of this table, we
17 discuss what content should be included within
18 the application.

19 First, the manufacturer's contact
20 information, which should include the name of the
21 manufacturer, the primary point of contact, and
22 the address and phone number to receive FDA

1 correspondence.

2 Second, rationale or an explanation is
3 beneficial for FDA to understand the purpose of
4 the modification to the tobacco product, why the
5 manufacturer considers the modification to be
6 minor, and why the manufacturer considers an SE
7 report is not necessary for this tobacco product.

8 Third, a certification statement is a
9 signed statement by a responsible official of the
10 manufacturer which provides the rationale for the
11 determination that the modification does not
12 increase the tobacco product's appeal or use by
13 minors, toxicity, addictiveness, or abuse
14 liability.

15 And finally, an environmental
16 assessment, or EA, is included in the exemption
17 request.

18 Now that we have discussed the
19 specific requirements under the exemption rule,
20 let's move on to the requirements of the RTA
21 rule.

22 Exemption requests will also be

1 reviewed for acceptance under the RTA rule. This
2 rule is applicable to all tobacco product
3 applications, PMTA, MRTPA, SE, and exemption
4 requests.

5 FDA may refuse to accept an
6 application of any of the criteria listed in this
7 table apply. I will note that Nos. 1 through 5
8 within this table were discussed in the previous
9 slide under the exemption rule. So, I will focus
10 this discussion on items 6 through 10 which are
11 specific to the RTA rule.

12 So, No. 6, if the submission is
13 received from a foreign application, an
14 authorized agent that resides within the U.S.
15 must be identified within the application along
16 with their contact information.

17 Seven, this regards a submission not
18 containing required FDA forms. Currently, there
19 are no required forms for exemption requests.

20 No. 8, the type of submission should
21 be provided by the applicant. Is the submission
22 requesting PMTA, SE, EX, or MRTPA? This should

1 be identified within the application.

2 No. 9, the submission must contain the
3 signature of a responsible official. A
4 responsible official is a person authorized to
5 make decisions and act on the application.

6 No. 10, for all submission types,
7 excluding abbreviated reports, the submission
8 does not include a valid claim of categorical
9 exclusion or an environmental assessment. At
10 this time, there are no categorical exclusions in
11 place for exemption requests. So, an EA must be
12 submitted as part of the application.

13 So now that we have a better
14 understanding of acceptance criteria, I would
15 like to introduce the exemption request review
16 process. The steps in the exemption request
17 review process are listed here.

18 First, an exemption request is
19 submitted by the manufacturer and received by
20 FDA.

21 Second, FDA makes a determination on
22 acceptance which includes either (a) accept the

1 application, issue an acknowledgment letter, and
2 continue the review, or (b) FDA will refuse to
3 accept the application for review and issue a
4 letter which will contain explanations for why
5 the application was not accepted.

6 Third, we have the notification phase.

7 And fourth, review and action phase.

8 The notification phase will not apply
9 to all exemption request submissions. This phase
10 is specific to exemption requests which reference
11 the original product as a provisional SE in which
12 FDA has not made a determination of NSE. The
13 purpose of this phase is to remove the specified
14 SE report from the queue for immediate FDA
15 review.

16 The notification phase will include
17 the following steps:

18 First, in requests where a
19 manufacturer proposes to modify an original
20 tobacco product legally marketed under a pending
21 provisional SE, they will receive a notification
22 letter from FDA. This letter notifies the

1 manufacturer that FDA will first review the
2 provisional SE report, and once a final
3 determination of the SE report is issued, FDA
4 will begin review of the exemption request. The
5 letter will also provide options for review of
6 the exemption request and a timeframe for
7 response. FDA intends to complete review of the
8 pending provisional SE report even if the
9 exemption request is withdrawn after the
10 notification period.

11 Next, I will discuss the review and
12 action phase of the exemption request process.
13 During review of the exemption request, FDA may
14 request additional information to inform their
15 decision on the application. If this occurs, FDA
16 will issue an advice information request, or AI
17 letter, to request the additional information to
18 complete scientific review of the application.

19 If the manufacturer provides a
20 response by the date requested in the AI letter,
21 FDA continues review of the exemption request,
22 and once review is complete, FDA will make a

1 determination on the application in the action
2 phase of the process. However, per the exemption
3 rule, FDA considers the exemption request
4 withdrawn if the information is not provided
5 within the requested timeframe.

6 Once FDA has completed substantive
7 scientific review of the exemption request, FDA
8 will provide the applicant with written notice of
9 the findings. FDA issues one of the following
10 letters during the action phase: an AI letter, a
11 cancellation or closure letter, an exempt letter,
12 or a not-exempt letter. The cancellation,
13 closure, exempt, and not-exempt letters are final
14 decisions and will end the exemption request
15 process.

16 It is important to note that FDA
17 intends to make exempt order letters, the
18 technical project lead, or TPL review, and the EA
19 publicly available on the FDA website, in
20 accordance with current FDA redaction procedures.

21 We will now move on to the second step
22 in the exemption request process, the abbreviated

1 report. There is an additional step for a
2 manufacturer to market the modified tobacco
3 product, the abbreviated report. If FDA issues a
4 found-exempt order letter for the new tobacco
5 product under Section 905(j)(1)(A)(ii) of the
6 FD&C Act, it requires that, 90 days prior to the
7 introduction or delivery for introduction of the
8 modified tobacco product, the manufacturer shall
9 submit a report which will demonstrate the
10 following:

11 The product is in compliance with the
12 Act.

13 All modifications are covered by
14 exemptions granted by FDA, or it has been issued
15 a found-exempt order letter.

16 The modifications are to a product
17 that is commercially marketed.

18 And actions have been taken by the
19 manufacturer to comply with the requirements
20 under Section 907, if applicable.

21 After FDA has received and reviewed
22 the abbreviated report, in general, FDA will

1 issue an acknowledgment letter to the
2 manufacturer. This letter acknowledges receipt,
3 so that manufacturers are aware of the 90-day
4 timeline that must elapse prior to marketing.

5 For the review phase of the
6 abbreviated report, FDA conducts a review to
7 ensure that all of the required information has
8 been provided. During this review, if FDA
9 requires additional information, they will issue
10 correspondence requesting the information from
11 the manufacturer.

12 The final phase for abbreviated
13 reports is when the 90 days have elapsed from FDA
14 receipt of the submission. If the manufacturer
15 has received no additional correspondence from
16 FDA within the 90 days, the manufacturer may
17 market the new tobacco product within the United
18 States.

19 FDA has seen an increase in
20 applications for this pathway and, in response,
21 has taken additional efforts to provide
22 manufacturers with an efficient and consistent

1 process. To ensure predictability, FDA has
2 established performance measures for the
3 exemption request pathway, and there are two
4 performance measures.

5 First, within 21 days of receipt of an
6 exemption request, FDA will complete its
7 acceptance determination and issue one of the
8 following letters: an acknowledgment letter, a
9 refuse-to-accept letter, or if the application is
10 withdrawn at any time during review, a withdrawal
11 acknowledgment letter.

12 Second, within 60 days of receipt of
13 an exemption request or start of a new review
14 cycle, FDA will review and act with the issuance
15 of one of the following letters: an AI letter, a
16 closure letter, an exempt order letter, or a not-
17 exempt order letter.

18 Performance measures regarding
19 exemption requests can be found on the FDA
20 website. FDA has exceeded the performance goal
21 to render an acceptance decision in 21 days for
22 this measure in the two years since its

1 implementation in 2017. Through fiscal year
2 2022, both performance measures will be at 80
3 percent.

4 For the same time period, the goal to
5 review and act on an exemption request within 60
6 days showed marked improvement between fiscal
7 year 2017 and fiscal year 2018. Please note that
8 FDA intends to revise the performance measures
9 website in early 2019 to reflect a correction to
10 reported 2017 values, along with inclusion data
11 for those exemption requests received within the
12 last fiscal quarter that are pending review.
13 Through fiscal year 2022, the performance measure
14 will also be at 80 percent.

15 FDA has gained additional experience
16 with the submission and review of abbreviated
17 reports. An appendix to the exempt order letter
18 is provided with FDA's suggested format for the
19 submission of the abbreviated report.

20 Manufacturers may use the suggested format to
21 certify that the tobacco product has met the
22 requirements in Sections 905(j)(1)(A)(ii) and

1 905(j)(1)(B) of the FD&C Act.

2 For exemption requests,
3 21 CFR 1107.1(b)(9) states that an exemption
4 request must contain an environmental assessment
5 under Part 25 of this Chapter, prepared in
6 accordance with the requirements of 25.40 of this
7 Chapter.

8 FDA previously refused to accept
9 exemption requests that did not include the basic
10 elements required for a complete EA. FDA
11 currently accepts exemption requests that include
12 an EA. However, an AI letter may be issued to
13 request additional information needed for the EA.
14 Additional information on preparing an EA will be
15 provided in tomorrow's FDA presentation.

16 So, this concludes the presentation on
17 the exemption requests and abbreviated report
18 processes. I would like to thank you for your
19 attention during this presentation, and I
20 recognize a lot of information was discussed.
21 So, I encourage you to ask questions during the
22 panel discussion later on today.

1 Thank you.

2 (Applause.)

3 MS. STARK: Good morning.

4 My name is Cristi Stark, and I'm the
5 Director for the Division of Regulatory Project
6 Management within the Office of Science.

7 Today my presentation is going to
8 focus on the Substantial Equivalence Program.
9 Within this presentation, I plan to discuss a
10 high-level overview for the SE program and share
11 some more recent program updates in response to
12 experience gained.

13 So, let's start with an overview of
14 the SE program. Manufacturers must submit new
15 tobacco products for FDA review. Generally, the
16 premarket provisions provide FDA with the
17 authority over a tobacco product before it enters
18 the market. A new product that does not meet the
19 statutory premarket requirements cannot be
20 legally marketed. If the new tobacco product
21 does not meet the statutory premarket
22 requirements and a manufacturer markets

1 themselves their tobacco product in the United
2 States, they will be in violation of the Act.

3 As you heard in the last presentation,
4 there are three pathways to market a new tobacco
5 product. Here, we're focused on substantial
6 equivalence, an alternative to a premarket
7 application.

8 Specifically, 905(j)(1) of the Federal
9 Food, Drug, and Cosmetic Act provides that, in
10 general, at least 90 days prior to the
11 introduction of your new tobacco product into
12 U.S. interstate commerce, an applicant should
13 submit an SE report.

14 So, for determination of substantial
15 equivalence, the manufacturer must demonstrate
16 that the new product has the same characteristics
17 as the predicate tobacco product or it may have
18 different characteristics than the predicate
19 tobacco product, but the information submitted
20 must demonstrate that that new product does not
21 raise different questions of public health.

22 As this pathway is based on a

1 comparison between a new and predicate tobacco
2 product, this generally means that products
3 brought to market will not present more harm to
4 the public health than the predicate tobacco
5 product it is found substantially equivalent to.

6 So, an eligible tobacco product is
7 either a grandfathered tobacco product, meaning
8 it was commercially marketed in the United States
9 as of February 15th, 2007, or a product FDA has
10 previously found substantially equivalent. It is
11 not a tobacco product authorized under a PMTA,
12 exemption request, MRTPA, or a pending
13 provisional product.

14 Of note, there are two types of SE
15 reports. They're known as regular and
16 provisional SE reports. The scientific standard
17 and review for both types of these reports are
18 the same. The main difference is when the
19 product subject of the SE report may be legally
20 marketed within the United States.

21 So, basically, regular SE reports are
22 applications for new tobacco products that

1 require marketing authorization prior to being
2 introduced into the U.S. market. This is the
3 majority of SE reports in-house.

4 In contrast, a new tobacco product
5 under a provisional SE report may be legally
6 marketed unless an order issues finding that new
7 tobacco product not substantially equivalent to
8 its corresponding predicate. In order to be
9 noted as a provisional product, the following two
10 criteria must be met:

11 First, the SE report must have been
12 submitted by March 22nd, 2011.

13 And second, the product, that new
14 product that the subject of that provisional SE
15 report, must have been delivered for introduction
16 into interstate commerce for commercial
17 distribution in the U.S. after February 15th,
18 2007 and prior to March 22nd, 2011.

19 So, in simple terms, for the SE
20 reports FDA is currently receiving, they're coded
21 as regular SE reports. And the new product
22 requires marketing authorization prior to an

1 order finding the new product -- I'm sorry. They
2 require an order prior to legal marketing.

3 So now, let's walk through a high-
4 level stepwise approach to the SE process. And
5 I'm going to note this is a snapshot in time, and
6 we expect to continue to improve our review
7 process through feedback and in meetings such as
8 this.

9 So, the SE process is broken into
10 three phases. Phase 1 is acceptance. Phase 2 is
11 notification. And Phase 3 encompasses the
12 substantive scientific review.

13 So, first, let's focus on the
14 acceptance phase. This phase includes three
15 steps, based on the type of substantial
16 equivalence report under review.

17 For all SE reports, the application is
18 received and sent to the assigned Regulatory
19 Health Project Manager. During this time, the
20 RHPM will actually perform an acceptance review
21 and determine if the product is under CTP
22 jurisdiction and if it contains additional

1 mandated items either from the statute or from
2 regulation. The findings in these reviews will
3 determine if the application should either be
4 acknowledged or receive a refuse-to-accept
5 decision.

6 So, step 3, the public health impact
7 review, occurred for provisional SE reports. For
8 regular SE reports, products are reviewed using a
9 first-in, first-reviewed approach. However,
10 because a large number of provisional reports
11 were received on the same date, and because these
12 products are currently on the market, FDA
13 determined that it was not practical nor
14 appropriate to use a first-in, first-reviewed
15 approach for these provisionals.

16 Therefore, a public health impact
17 review categorized each provisional SE report and
18 placed them into a tier meant to capture the
19 relative potential of raising a different
20 question of public health. Classification of a
21 report into one of these tiers does not mean that
22 the new product described therein does or does

1 not raise different questions of public health.
2 That determination can only be made after full
3 scientific evaluation of the provisional SE
4 report.

5 So, once an SE report is accepted, it
6 moves into the notification phase. During this
7 phase, CTP will conduct a review to ensure the
8 predicate tobacco product is eligible. Again,
9 that predicate tobacco product may either be a
10 grandfathered tobacco product or a product
11 previously found SE.

12 If the applicant stated that the
13 predicate tobacco product was marketed in the
14 U.S. as of February 15th, 2007, a grandfathered
15 claim, the Office of Science has sent a request
16 to the Office of Compliance and Enforcement for a
17 grandfather determination.

18 So, in addition, if you look at
19 provisional SE reports, CTP will also send a
20 notification letter to those applicants to inform
21 them that their SE report has entered this phase
22 of review. The purpose of this letter is

1 threefold:

2 First, it updates the applicant of
3 that SE report as to the projected start date of
4 the scientific review.

5 Second, it allows the applicant to
6 amend their SE report with any additional
7 information to support an SE determination prior
8 to the start of scientific review. This is
9 important because FDA is not obligated to review
10 amendments received after the start of scientific
11 review.

12 And third, it informs the applicant
13 that GF review is starting and they may be
14 contacted by a representative of the Office of
15 Compliance and Enforcement with respect to
16 grandfather determination if applicable.

17 So, Phase 3 is where the majority of
18 the scientific review occurs. Generally, SE
19 reports are assigned a chemist, toxicologist,
20 engineer, and environmental reviewer. Depending
21 on the contents of the report and the data
22 submitted, we may add other disciplines as

1 necessary. If necessary, a deficiency letter
2 such as an advice information request or
3 preliminary finding letter is also issued.

4 Now, once the reviewers have completed
5 their reviews, CTP will, then, determine if the
6 new tobacco product is scientifically
7 substantially equivalent or not substantially
8 equivalent to its corresponding predicate tobacco
9 product. When that final SE determination is
10 made, we move into the action portion of this
11 phase.

12 If the determination is a scientific
13 finding of SE, CTP will, then, review to see if
14 any additional information is needed to comply
15 with the National Environmental Policy Act. If
16 additional information is needed, in general, a
17 letter issues to the applicant. In addition, for
18 regular SE reports, FDA must determine that the
19 new tobacco product is in compliance with the
20 requirements of the Federal Food, Drug, and
21 Cosmetic Act.

22 Now, once these steps have been

1 completed, an appropriate order letter issues,
2 and the assigned RHPM will contact the applicant
3 and offer a courtesy copy of that order letter.
4 Additionally, for provisional NSE decisions, the
5 RHPM will also offer a courtesy copy of an
6 appropriately redacted Technical Project Lead
7 review -- this is the summary basis for that
8 decision -- and the last cycle primary discipline
9 review that serves as the basis for that NSE
10 decision. If those documents are not ready at
11 the time of the courtesy call, the Project
12 Manager will provide a general timeframe for when
13 they will be ready and submit at that time.

14 And finally, CTP will post the TPL
15 review and order letter with appropriate
16 redactions. In general, these documents are
17 posted for all SE decisions and for provisional
18 NSE decisions.

19 So now that we've seen a high-level
20 program overview, let's transition to some of the
21 updates. For this part of the presentation, I
22 would like to focus on what's been occurring with

1 both industry and FDA in the following areas:
2 unique identification, letter language updates,
3 focusing scientific resources, the response time
4 to our deficiency letters, common issues in SE
5 reports, and performance goals. These six items
6 are examples of program improvements over time
7 based on dialog between CPT and industry. Each
8 of these elements have enhanced the consistency,
9 transparency, and predictability of the SE
10 program, and they are a nice example of growth
11 over time.

12 So, let's move to unique
13 identification. One of the challenges we've seen
14 with the SE program was the lack of uniquely
15 identifying both new and predicate tobacco
16 products. It's been an issue, as CTP has been
17 unable to determine what specific products were
18 being requested for review and what predicate
19 tobacco products were being used for comparison.

20 For example, past applications for a
21 cigarette may only contain identification of the
22 brand name. It would lack identification of

1 properties such as the package type, the package
2 quantity, the length, the diameter, and the
3 ventilation. This could mean there could be
4 multiple products under review or being compared
5 to, and, as such, it wasn't clear what the
6 applicant was requesting FDA to do.

7 More recently, though, we've seen an
8 improvement in applications, as applicants have
9 been able to better understand what properties
10 FDA needs for identification of these tobacco
11 products. We've found success through an open
12 dialog with industry.

13 So, through this process, we provided
14 applicants with an opportunity to amend their SE
15 reports to provide unique identification for
16 their new and predicate products. We posted TPL
17 reviews on our website which provides examples of
18 unique identification categories, subcategories,
19 and properties. And RHPMs have been available to
20 assist applicants with questions around unique
21 identification. Additionally, as discussed in
22 Ms. Schmitz's presentation, the RTA rule

1 published, which provided further help regarding
2 product identification. Collectively, these
3 efforts resulted in improved identification of
4 tobacco products under review.

5 So, in addition to improving the
6 identification for tobacco products, we also
7 received feedback regarding our communications
8 with applicants. So, over the last seven years,
9 the correspondence for the SE program has
10 evolved. More recently, based on stakeholder
11 feedback, we've opted the language within our
12 letters to improve communication and expectations
13 between the applicant and FDA.

14 For example, we've stated the purpose
15 of our correspondence in the first paragraph,
16 used plain language where possible, clarified how
17 to submit an amendments, removed duplicative
18 language, clearly identified response due dates,
19 where applicable, such as in a deficiency letter,
20 included the RHPM email address for ease of
21 communications, and within the deficiency
22 letters, those AINP find letters for the SE

1 program, we have visibly identified the
2 difference between a deficiency, which is
3 something that must be responded to for that
4 scientific finding of SE, versus a request, which
5 is a nice-to-have.

6 So, let's quickly walk through one of
7 our updated notification letters, so you can see
8 what this looks like. I note this is not a
9 complete sample of our notification letter.
10 Instead, it's a snapshot of our template, and the
11 image on the screen includes excerpts to
12 illustrate some of the changes that I'll go
13 through.

14 So, as you can see, the purpose is
15 illustrated at the top of the letter within this
16 paragraph stating, "We expect to being our
17 scientific review of all information contained in
18 your SE reports, including amendments received
19 within 180 days from the date of the letter."

20 Other examples you'll see include
21 clear language for when the response is due here
22 on the screen. And you see it stated as, "If a

1 review cycle ends with us issuing a deficiency
2 letter, we expect to provide you with 180 days to
3 respond to the letter."

4 We've also updated the language
5 regarding amendments. You can see the paragraph
6 here. For clarity, we're now asking for
7 amendments in a single submission and providing
8 recommendations for how to organize the response.

9 And last is one of the most important
10 features of the letter. This is your assigned
11 Regulatory Health Project Manager. Their
12 information is listed at the bottom of all of
13 your letters. This is your liaison. They can
14 assist with any application-related questions,
15 and we have now updated to include their email
16 address for ease of communication.

17 So, as you can see improvement with
18 communication, we also looked for areas where we
19 could focus our scientific resources towards a
20 greater public health impact. One of the areas
21 we examined was our review of provisional SE
22 reports.

1 Unlike tobacco products subject to
2 regular SE reports, the tobacco products subject
3 of the provisional SE reports are legally sold
4 under the Act. CTP is not required by statute to
5 review or act on these reports. Although there
6 was no requirement for that, the agency initially
7 intended to review and act on all of them.

8 In July 2017, FDA's Commissioner noted
9 CTP would examine its existing approach to the
10 review of the approximate 2500 remaining
11 provisional SE reports in an effort to focus on
12 reviews with the greatest public health impact.
13 With the years of experience conducting thousands
14 of SE reviews, and with greater understanding of
15 tobacco products, FDA announced a change in its
16 approach. The agency would continue to review
17 the approximate 1,000 pending provisional SE
18 reports that were determined to have the greatest
19 potential to raise a different question of public
20 health and would remove from review approximately
21 1500 provisional SE reports that were determined
22 less likely to do so.

1 So, the purpose of this was twofold.
2 First, to maximize CTP's application review
3 capacity and, second, to focus on public health
4 goals by investing more review capacity to those
5 tobacco products which are more likely to raise
6 different questions of public health.

7 To date, through the remove-from-
8 review process, FDA has removed an estimated 1200
9 provisional SE reports. For those interested,
10 the complete list is available on our website,
11 and we'll continue to update the list as
12 additional applicants respond with the requested
13 information to have their product removed from
14 review.

15 So, I note this change in review
16 perspective is unique to provisional SE reports
17 and does not translate to regular SE reports.
18 Through this process, CTP is focusing its
19 scientific review resources and is prepared to
20 receive and review the upcoming applications for
21 deemed tobacco products.

22 So, under the remove-from-review

1 process, eligible applicants have received
2 correspondence from CTP. This means, if your
3 product met the criteria for RFR, you would have
4 received a letter from FDA noting if your product
5 was removed from review or if additional
6 information was requested in order to remove the
7 product from review.

8 For example, if you were missing the
9 date your new tobacco product was first
10 introduced or delivered for introduction into
11 interstate commerce for commercial distribution
12 in the U.S., that would be requested prior to any
13 decision to remove from review. If you've not
14 received a letter regarding information around
15 removing a provisional product from review, this
16 means that FDA intends to review your provisional
17 SE report in the order as determined by the PHI
18 tier. As such, you would receive a notification
19 letter consistent with the SE process.

20 Now, even if a provisional product was
21 removed from review, it can be brought back into
22 the review queue if any of the following occurs:

1 First, that product that was removed
2 from review could have another pending
3 application submitted by the same manufacturer,
4 such as an MRTPA.

5 Second, FDA could receive new
6 information, such as from its inspectional
7 findings, suggesting that that new tobacco
8 product is more likely to have the potential to
9 raise different questions of public health.

10 And third, FDA has reason to believe
11 that that new tobacco product was not introduced
12 or delivered for introduction into interstate
13 commerce for commercial distribution in the U.S.
14 after February 15th, 2007 and prior to March
15 22nd, 2011.

16 I do note, applicants that are placed
17 back into the review queue will receive a
18 notification letter consistent with our process.

19 So, as part of the RFR process, CTP
20 has focused its resources on certain SE reports.
21 To give you a sense of the criteria that was
22 considered for that product to remain in the

1 review queue, this slide lists some examples for
2 provisional products that continue to be
3 reviewed.

4 So, a non-conventional tobacco
5 product, an example could include a product that
6 had novel features, such as a crushable bead
7 within a cigarette.

8 With respect to inadequate
9 characterization between the new and predicate
10 tobacco products, it could be a product listed
11 that's not uniquely identified, such as only
12 identifying a brand and category, not listing
13 your subcategories or properties within the
14 product.

15 For differences in categories, it
16 could be something like a cigarette compared to a
17 smokeless tobacco product.

18 With respect to design changes that
19 may increase harmful and potentially harmful
20 constituents, this could be products compared
21 that have major changes in filter design or even
22 comparing a filtered cigarette to a cigarette

1 that does not contain a filter. Additionally,
2 we've seen some comparisons with large changes to
3 tobacco blends, which could increase nitrosamines
4 or PAHs, and those would also remain within the
5 review queue.

6 So, in addition to focusing our
7 scientific resources, CTP, then, started to begin
8 to examine if the response times within our
9 deficiency letters were appropriate. And as I
10 noted earlier, over the last seven years, the
11 correspondence for the SE program has evolved.
12 More recently, based on stakeholder feedback, we
13 understand that applicants have received advice
14 information request letters or preliminary
15 finding letters, what we term "deficiency
16 letters," with response times of 60 days or 30
17 days, respectively.

18 Many applicants have noted that, to
19 fully respond, additional time has been needed.
20 And to that point, FDA has received multiple
21 requests for extensions of time.

22 So, in examining the types of

1 information listed in these deficiency letters,
2 and the time needed to respond -- for example, to
3 perform necessary tests responsive to the
4 deficiency -- the timeframe within the deficiency
5 letters has been extended. All deficiency
6 letters issued post-October 1st, 2018 now provide
7 for 180 days for applicants to prepare
8 information and respond. We believe that by
9 extending the response time to 180 days
10 applicants now have sufficient time to respond to
11 all deficiencies within our letters. Therefore,
12 with the additional extension of time to 180
13 days, FDA does not intend to grant additional
14 extensions of time to respond to deficiency
15 letters.

16 And additionally, when examining the
17 amount of time to provide responsive information,
18 the notification letter, which issues to start --
19 it issues to signal the start of the scientific
20 review for provisionals -- has also been extended
21 to 180 days.

22 These changes in timelines were in

1 response to industry feedback. By extending this
2 timeframe and removing the extensions of times to
3 respond to letters, the SE process is more
4 predictable and allows for adequate time to
5 respond to deficiencies without significant delay
6 to the review process.

7 So now, let's look at how this
8 translates to the review process if the response
9 to a deficiency letter is submitted early or
10 late. So, if the applicant amends early, before
11 the 180 days has elapsed, the assigned RHPM will
12 process the amendment and verify if the applicant
13 has responded to all deficiencies. For example,
14 if there's 10 deficiencies listed within the
15 letter, and the applicant responds to all 10, the
16 scientific review will commence as of the receipt
17 date of that amendment.

18 However, if it's an incomplete
19 response -- so, for example, out of the 10
20 deficiencies, the applicant only responded to
21 five -- CTP will wait until either the applicant
22 respond to the remaining deficiencies or the 180

1 days elapses, whichever is sooner. That means,
2 if the applicant does not respond to those
3 remaining deficiencies, CTP will initiate
4 scientific review on day 181. This is the next
5 day after the response date.

6 In the event that amendments are
7 received after the 180-day response date, CTP
8 does not intend to review those amendments.
9 However, if there is another review cycle,
10 information may be incorporated into that cycle.

11 So now, we've touched on increased
12 communication to better identify products,
13 clarifying our letter language, focusing
14 scientific resources through the RFR process, and
15 increasing the amount of time to respond to
16 deficiency letters. One other area that we
17 identified for improvement with industry's help
18 was around communicating common issues seen
19 within SE reports.

20 So, many of these common issues have
21 previously been provided in webinars, posted TPL
22 reviews, and through meetings, but it may be

1 difficult for applicants to find one location
2 identifying all common issues. So, to ensure
3 applicants have the information in one location
4 for their products, starting October 1st, 2018,
5 FDA has revised both the acknowledgment and
6 notification letters to include appendices with
7 common issues identified in previous SE reports
8 for specific tobacco product category and
9 subcategories.

10 So, for example, if an applicant
11 submits a new SE report for a cigarette, they'll
12 receive an appendix with information to consider
13 for cigarettes. Some examples of information
14 included with appendix may have, but is not
15 limited to, evidence needed for an eligible
16 tobacco product predicate, addressing toxicity
17 caused by ingredient changes, use of a model, and
18 so on.

19 It's important to note that these
20 appendices reflect deficiencies frequently seen
21 in previous SE reports for that category. The
22 information may not be applicable to the current

1 products within the report. If a difference
2 exists between the new and predicate tobacco
3 products, it is the applicant's responsibility to
4 provide a rationale for each difference with
5 scientific evidence and a discussion for why that
6 difference does not cause the new product to
7 raise different questions of public health. To
8 the extent that it's applicable, the information
9 provided within the appendix can be used by
10 applicants to determine whether their SE report
11 should be amended or withdrawn prior to FDA's
12 review of the SE report.

13 So, here's a sample section of the
14 appendix for information to consider for
15 cigarettes. Here you'll see again the language
16 noted at the top, that it reflects deficiencies
17 frequently seen in previous SE reports for
18 cigarettes. Again, this is a sample that only
19 shows the top portion, and we begin with unique
20 identification. Here you're going to see
21 continued language around tobacco product
22 identification and the properties that should be

1 provided for the different subcategories.

2 And another section of the letter is
3 the start of information around the use of a
4 predicate tobacco product that you no longer
5 manufacture. You'll see the appendix lists out
6 potential options for providing data on that
7 predicate tobacco product.

8 Again, the addition of these
9 appendices were in response to industry feedback.
10 The goal was to collate information already
11 available from the TPLs posted on our website.
12 Tomorrow you'll hear from Drs. Rogers and Cecil
13 on the approach to CTP's scientific review for
14 the SE program, and they will discuss many of
15 these topics in more detail.

16 So, last, but not least, I'd like to
17 focus on the predictability of FDA review and
18 action. In April 2014, FDA announced the
19 development of a set of performance measures that
20 would help improve timeliness and predictability
21 for the review of certain applications, including
22 SE reports.

1 In April this past year, FDA extended
2 these performance measures for regular SE reports
3 to fiscal year 2022, and, as part of the
4 reexamination of the review queue for provisional
5 SE reports, FDA announced new performance
6 measures for them. The performance measures for
7 provisionals are similar to those for regulars,
8 but they're tailored for the unique
9 circumstances.

10 So, the goals are as follows: for
11 regular SE reports, within 21 days, FDA intends
12 to issue an acknowledgment, refuse to accept, or
13 withdraw acknowledgment letter. Within 90 days,
14 to issue a deficiency letter, a closure-type
15 letter, or an order letter.

16 For provisional SE report, within 21
17 days, FDA intends to issue withdraw
18 acknowledgment letters. There are no refuse-to-
19 accept or acknowledgment letters for these
20 because the reports were submitted in 2011, so
21 it's moot. And then, within 120 days, FDA
22 intends to issue a deficiency letter, a closure-

1 type letter, or an order, and it's 120 days of
2 commencing scientific review.

3 So, let's take a quick peek at the
4 performance goals for the 21 days for regular SE
5 reports. You're going to see that it was 70
6 percent for the goal to be met in FY17 and 80
7 percent in FY18 through FY22, and FDA has been
8 taking some great strides to meet them, and has
9 been successful. I will note that there is still
10 some open cohort data for FY18. It will close
11 shortly, and the data will be available in early
12 2019.

13 Looking at the 90-day goals for
14 regular SE reports, you'll see again in FY17 we
15 had a goal of 70 percent, and FY18 is 80 percent
16 through FY22. Again, you'll see, for both FY17
17 and FY18, FDA has met these goals. And again,
18 for FY18, we have an open cohort. That will
19 close by the end of the year, and data will be
20 available in early 2019 with the final numbers.
21 And looking at provisional SE reports, you'll see
22 that the goal is 50 percent, starting in this

1 fiscal year '19, and increases by 10 percent to
2 max out at 80 percent in FY22.

3 So, to close, I want to remind you of
4 the importance of your assigned Regulatory Health
5 Project Manager. They're your main point of
6 contact for your SE application and can assist
7 with general inquiries about your premarket
8 pathways, application submission and review
9 process, help with useful resources on the web,
10 clarify some of what's in our letters, provide
11 reference, and, also, aid you through the formal
12 meeting process, which you'll hear about later
13 today.

14 And just in case you've read all the
15 SE guidances, viewed the webinars, and wanted
16 additional information, this slide provides some
17 links to some of the resources that are out there
18 to give a little more information on what I spoke
19 about today, and a few other helpful things as
20 you're navigating through.

21 If you still have questions and you're
22 aren't sure where to go, please use our general

1 inquiries email at "Ask CTP".

2 So, this concludes my presentation.

3 Thank you.

4 (Applause.)

5 MS. JOHNSON: Thank you, Jennifer and
6 Cristi.

7 If I could have the panelists come
8 upfront here, we're going to hear from them.
9 Again, each speaker has five minutes to introduce
10 themselves and make comments or statements about
11 the presentations we just heard. Don't forget
12 alpha order.

13 Okay. So now that I know the
14 difference between No. 1 and No. 2 panel, but not
15 how to use the microphone (laughter), we will
16 start, as I said, in alpha order with Rosanna
17 Beltre, and with introductions.

18 And I just want to remind people, for
19 folks that are still filtering in, that we do
20 have some assigned seating for our panels.

21 And again, you will be using these
22 cards for you to put your questions on. Raise

1 your hand if you need a card, and someone will
2 walk by and hand you one, so that we can use them
3 for the question-and-answer session of the panel.

4 Rosanna?

5 MS. BELTRE: Good morning.

6 My name is Rosanna Beltre, and I am
7 the Deputy Director of the Division of Regulatory
8 Project Management.

9 MS. CUSHMAN: Hi. I'm Brittani
10 Cushman, Senior Vice President of External
11 Affairs for Turning Point Brands.

12 All right. Well, I will start then.

13 So, my name is Brittani Cushman, as I
14 said. I have had the experience of working on
15 the initial round of provisional applications
16 that were filed back in 2011, and I was certainly
17 one of those people who was working on them all
18 night long to get them out the door. Because one
19 of the issues that we've had in this process that
20 I think both the agency and companies have been
21 dealing with is kind of learning as we go and
22 working on these applications as we go. So, we

1 were getting new information right up until
2 pretty close to the filing deadlines and trying
3 to supplement as best we could.

4 And with the provisionals, the
5 experience was that it was a lot of silence for a
6 long time, which one of the speakers mentioned
7 earlier that there would be this event of
8 silence, and then, all of a sudden, in the mail
9 you would get this rubberbanded stack of letters.
10 And while 30 days might be okay to respond to one
11 or two of those letters, when you get the stack,
12 it's a little overwhelming, especially for some
13 of the small companies where one person might be
14 doing 20 different jobs, and then, all of a
15 sudden, have 60 letters to respond to.

16 So, I speak from that experience
17 firsthand, but also from the experience of
18 working with CITMO, which is the Council of
19 Independent Tobacco Manufacturers. And that's a
20 group of small tobacco product manufacturers
21 under the Act who have dealt with these issues.
22 So, we've gotten some feedback from all of their

1 experiences and kind of collectively put together
2 some thoughts.

3 And a lot of that has centered around
4 what I think the agency has rightfully recognized
5 is the issues of transparency and consistency.
6 And a lot of the comments today I think really
7 touched on that and were some really good
8 solutions.

9 One thing that stuck out to me was, in
10 talking about the response letters that have
11 these appendices, that have additional
12 information for various product categories, that,
13 to me, is a great idea. You know, it's been a
14 long time coming, but I'm really happy it's
15 coming into place. What I would recommend there
16 is that should be made public, not be something
17 that is received in a deficiency letter where the
18 company say, "Oh, well, now I have the map to
19 comply. So now, I can finally do these things,
20 but I only have 180 days."

21 Another comment I would make on what
22 Cristi had mentioned was this idea of getting rid

1 of extensions across all applications. And I
2 understand the thinking that went into that
3 decision. I appreciate that there is an
4 examination of deficiencies and why extensions
5 were needed, what timelines were needed, but I
6 think what that perhaps doesn't take into account
7 is we're about to move into a period of time
8 where a number of products -- and when I say "a
9 number," I mean thousands of products -- are
10 going to be going to labs and needing testing
11 done.

12 So, when you're talking about 180 days
13 in today's environment, I think that looks very
14 different when you're moving into a situation of
15 labs already being behind, and I'm sure many of
16 us on the panel have been in touch with labs on
17 HPHC testing and other PMTA-related testing
18 coming up. And they're already expressing major
19 concerns about capacity. So, that, I think,
20 needs to be taken into account in this idea of
21 getting rid of extensions.

22 With that, I'll pass along. I want to

1 make sure we leave a lot of time for Q&A because
2 I think that will be really useful to this
3 discussion.

4 MR. LINDEGAARD: Good morning.

5 My name is Thomas Lindegaard. I am
6 from Scandinavian Tobacco Group, a company
7 focused on cigars and traditional pipe tobacco.
8 I am the Senior Vice President responsible for
9 scientific and regulatory affairs.

10 First of all, thank you to FDA for
11 hosting this important event. I think it's
12 critical that we stay in close dialog in order to
13 get good and effective regulation in place.

14 I have a few comments as well about my
15 background here. I have 25 years of experience
16 within the industry working primarily in
17 scientific and regulatory affairs, as well as
18 product development. I have been deeply involved
19 in the SE applications that have been submitted
20 by our company as the sort of scientific
21 anchorman responding to many of the questions
22 from FDA.

1 While I know that the discussion here
2 today will be dictated by questions from the
3 audience, I would also like to raise a few points
4 to inspire the questions or the dialog.

5 The first point is really about I hope
6 we can move forward on making the SE process even
7 more efficient. One of the examples in this
8 context that we have experienced is that we have
9 been unable in most cases to transfer learnings
10 from one SE to a next SE. That means we have
11 produced data on a specific additive or product
12 feature, but when we get to the next SE, we have
13 to repeat it all over because there are possibly
14 minor changes to the blend or other things, which
15 produces an enormous amount of work for each SE
16 which probably is not needed.

17 The second point I have is, in my
18 view, some of the inconsistencies that are
19 created by the SE system in the sense that, an
20 example, we might want to increase as a part of
21 several modifications the level of an additive
22 from 1 percent to 1.1, and have to demonstrate

1 that there are no new questions of public health
2 associated with that, while in many other
3 products we have which are predicates or
4 grandfathered, this particular additive might be
5 used in 3 percent or 5 percent, perfectly okay
6 because we are not changing it. That doesn't
7 make much sense to me.

8 Also, I see that the way that the
9 reductions or increase of an additive is treated
10 in the exemption process seems to be quite
11 different from the way it is being assessed in
12 the SE process, which is also strange to me. So,
13 those are points I hope we can get questions on
14 and discuss.

15 I also had a point about the timelines
16 for deficiency letters, but that is somewhat
17 covered. But I do share some of the same
18 concerns, seeing that we have, just our company,
19 thousands of products coming into this process.
20 So, there are still some concerns there.

21 Thank you.

22 MR. MURPHY: Good morning, everyone.

1 My name is Patrick Murphy. I'm a
2 Senior Director within the Submissions and
3 Engagement Group, Scientific and Regulatory
4 Affairs of RAI Services company. RAI Services
5 company is a wholly-owned subsidiary of Reynolds
6 American, Inc., that bears primary responsibility
7 for regulatory compliance for RAI's operating
8 companies, including RJ Reynolds Tobacco Company,
9 American Snuff Company, Santa Fe Natural Tobacco
10 Company, and RJ Reynolds Vapor Company.

11 I thought I would begin by providing
12 just a brief description of my background at
13 Reynolds that informs my perspective. Since late
14 2009, I have been heavily involved in effectively
15 operationalizing and refining both the
16 substantial equivalence and exemption from SE
17 programs for Reynolds, Santa Fe, and American
18 Snuff Company.

19 Over that time, I've also involved in
20 or have led work streams with other submissions,
21 including PMTAs, regular and provisional SEs,
22 exemptions, the now-defunct same characteristic

1 SE submissions, and MRTPAs. I currently lead a
2 multidisciplinary team whose primary
3 responsibility is managing all provisional SE
4 reports on behalf of Reynolds and Santa Fe for
5 traditional combustible cigarettes, non-combusted
6 cigarettes, and roll-your-own tobacco.

7 So, to provide you a little bit of a
8 high-level overview of a Reynolds experience with
9 the SE and exemption request programs, I'll note
10 that we submitted our first SE report in June of
11 2010. That was nine months before the
12 provisional window closed, and that particular
13 application was assigned STN0000001.

14 (Laughter.)

15 Since that summer, we have experienced
16 the highs and the lows of the SE and exempt
17 request programs solely based on the information
18 that's publicly available. This includes
19 clearance orders for both provisional and
20 regulars, some level of success with our approach
21 to exemption requests, and, as most are aware,
22 for NSE orders.

1 Which leads me to make a couple of
2 observations, some general, some more specific
3 about areas where I think things are going well,
4 and, lastly, some things where I think there is
5 some room for improvement.

6 So, in general, as could be expected,
7 as both the agency and applicant stood up their
8 respective programs, things could be perceived as
9 fairly chaotic. I had the distinct impression
10 that in many instances we were talking past each
11 other through regulatory correspondence.

12 One of the things we learned fairly
13 quickly that is very critical in terms of
14 communicating with FDA, and CTP specifically, is
15 nomenclature and terminology. We at Reynolds
16 have a very specific way about how we describe
17 our products, our specifications, our
18 manufacturing processes. If terminology is
19 unaligned, we must, at a minimum, have a common
20 understanding of certain terms and their
21 respective use.

22 I recognize that in many ways both the

1 agency and applicants have significantly evolved
2 since 2009. Two good examples of this evolution
3 from a Reynolds perspective. One, our internal
4 vocabulary, at least in the submissions group, is
5 markedly different than it was pre-2009. Two, I
6 know that at Reynolds we consistently focus on
7 evolving the form, format, and content of our
8 applications in order to more clearly communicate
9 disparate types of product data and articulate
10 lines of argument, improve the quality of our
11 submissions, and facilitate FDA review.

12 So, I'll note three things that, from
13 our perspective, things are going well. I've
14 seen increased engagement through the use of,
15 quote/unquote, "informal" meetings. These are
16 usually brief teleconferences or email traffic.
17 We're pleased with the timeliness and the
18 responsiveness of our assigned Regulatory Health
19 Project Managers. And I'm not just saying that
20 because Jennifer is sitting here in the room.

21 (Laughter.)

22 Second, based on our experience and

1 CTP's stated priorities, review timeframes for
2 regular SEs and exemptions are accelerating and
3 demonstrate the viability of those particular
4 pathways.

5 Lastly, some exceptions
6 notwithstanding, consistency among various FDA
7 reviews and -- where was I? Consistency among
8 various FDA reviews and individual reviewers is
9 improving. This helps set expectations, which
10 ultimately is what a regulatory industry wants,
11 consistency and predictability.

12 So, lastly, I'll focus on a couple of
13 things that could be improved upon. Given the
14 D.C. District Court's ruling in Philip Morris
15 USA, et al., v. FDA, applicants have little
16 regulatory clarity on the same characteristics
17 prong of the SE pathway.

18 Second, to date, guidance documents
19 and webinars have lacked actionable information.

20 And lastly, in the majority of cases,
21 written regulatory correspondence is the only
22 form of substantive communication with the agency

1 in regards to provisional SE applications
2 currently under review.

3 Thank you.

4 MS. STARK: Short and sweet, I'm
5 Cristi Stark again, the Director for the Division
6 of Regulatory Project Management.

7 MS. JOHNSON: Just so we don't have
8 any more feedback issues, I'm just going to stand
9 up here.

10 So, we have a couple of questions.
11 Again, if anyone has any questions in the
12 audience, raise your hand, and you'll be given a
13 card and it will be brought up here to be
14 presented to the panel.

15 The first we got is, "In prioritizing
16 the review of provisional SE applications, what
17 are the classification criteria used?"

18 MS. STARK: I am assuming this to the
19 RFR classification that we placed out? Is that
20 in the question?

21 MS. JOHNSON: I read it as is.

22 MS. STARK: The PHI?

1 Okay. So, I'll start, and, Rosie, you
2 can jump in, if you would like.

3 So, for our tiers that are out there,
4 we actually in a past webinar have discussed what
5 the top tier was, PHI Tier 1, where they remain
6 in review. And the main ones that I actually had
7 bullets up on the slide were non-conventional
8 products. So, something that was novel that
9 wasn't out there more recently -- for a long
10 time. So, it was more recent.

11 We looked at products that weren't
12 fully identified. So, you may come in with a
13 tobacco product just with the brand name, and
14 it's two pages, rather than listing your full
15 ingredients and all of your design features,
16 other items, and then, comparing across
17 categories.

18 When we went into the next tier, some
19 of those elements were also listed on the slide,
20 where we talked about major blend changes. We
21 talked about large increases significant with
22 HPHCs. We had some changes with some of our

1 acids and bases.

2 When we get down to some of the lower-
3 level ones that we looked at for the remove-from-
4 review queue, we were looking at some smaller
5 things, such as we had some changes to papers
6 where there was no filler in there. They were
7 very small. We had a few others where we looked
8 at certain types of changes to packaging that
9 didn't necessarily translate into the product
10 itself.

11 Rosie, do you have anything to add?

12 MS. JOHNSON: Cristi, you have a
13 couple of questions directed to you. It asks,
14 "Can you speak to how deemed products will be
15 handled within the regular SE process?" It says,
16 "As SEs for deemed products are currently not due
17 until October 2020, will they be treated as
18 provisional SEs and be permitted to remain on the
19 market until SE or NSE final determination? What
20 will be the performance standards?"

21 MS. STARK: So, to hit the provisional
22 SE, to be a provisional product is a very

1 specific definition by statute. So, the report
2 had to be submitted by March 21st, 2011, and that
3 new product had to be introduced after February
4 15th, 2007, up to and through March 21st, 2011.
5 So, these will not be considered provisional
6 products.

7 With respect to the review process, we
8 are prepared to receive and review them. We're
9 prepared to look at them first-in, first-
10 reviewed. I cannot speak to any types of
11 potential compliance policies or anything else
12 that may arise or anything that the Commissioner
13 may state. As Director Zeller said this morning,
14 there's not much else we can give. However, we
15 will try to be proactive and engaged with
16 industry as we move through that.

17 MS. JOHNSON: The next question for
18 you -- did you have something else related to
19 say?

20 MS. BELTRE: I think that, as Cristi's
21 presentation alluded to, we are sort of going
22 through the program and evaluating our processes,

1 and making sure that we are ready. Unlike in
2 2011, where we were just sort of assembling the
3 Center, I think we're in a much better place now
4 in terms of the maturity of the programs and
5 finding ways for us to be more transparent and
6 expedient with our process, as best we can.

7 MS. JOHNSON: Thank you.

8 This question, also for you. It says,
9 "In an effort towards transparency, will CTP
10 provide details on the public health tiering,
11 like how this tiering was undertaken and what the
12 outcome is? And also, what is the basis for the
13 SE acceptance criteria? You mentioned that this
14 is being determined by CTP. Can it be shared
15 with industry?"

16 MS. STARK: Sure. So, for the tiering
17 itself, we had quite a bit for the Tier 1 in our
18 webinar that was out there, when we went through
19 all of those elements. My slide talked about a
20 few others.

21 I want to note that that PHI tiering
22 was based off of that report at that point in

1 time. We looked at that new product as compared
2 to the predicate, and we looked to see what the
3 differences were.

4 Applicants, in general, should have
5 received notification if they are in the tiers
6 where they are less likely to raise a different
7 question of public health. If they are
8 questions, they still can reach out to their
9 assigned RHPM.

10 With respect to the acceptance
11 criteria, for the SE program, there are two areas
12 that we look at for acceptance. We look at what
13 is needed from the statute. So, we're going to
14 look at the basis for SE. We're going to look at
15 is there a health information summary or
16 statement present, and we're going to be looking
17 at regulatory items, such as the RTA rule, as
18 well.

19 So, as you heard in Jennifer Schmitz's
20 presentation, we're looking at, is an EA present?
21 Are you going to be identifying your product? Do
22 we have a U.S. agent present, if this is a

1 foreign applicant? So, items such as that.

2 For any additional required items for
3 acceptance, that would have to be through
4 rulemaking. So, stay tuned.

5 MS. BELTRE: I think that industry has
6 matured, and so has the program. And we've seen
7 a marked increase in products that are accepted.
8 It's actually, I would say, almost relatively
9 rare to receive a refuse-to-accept through the SE
10 program. Through the webinars, and through
11 venues such as these, I think applicants have
12 definitely learned what are sort of the criteria,
13 the regulatory/statutory criteria necessary for
14 the program. So, there's definitely been an
15 increase in terms of industry and submitting
16 stronger applications that would make it through
17 that acceptance threshold.

18 MS. STARK: To give you a sense of the
19 most repeat offender for an RTA decision now,
20 it's really around environmental considerations.
21 And you're going to hear a presentation on that
22 later on in the program. I know people have had

1 experience. Please make sure, for any
2 application that comes in, you have that EA
3 submitted with your application.

4 MR. MURPHY: Can I ask a follow-up
5 question?

6 Is it a safe assumption that this was
7 a one-and-done process, meaning the tiering by
8 PHI for each particular application and how that
9 fit into the potential RFRs?

10 MS. BELTRE: It is a snapshot in time,
11 and it was done, it was conducted, it was a high-
12 level review conducted with the information that
13 we had at the time. I know that we've maybe
14 recently with the RFR efforts sort of talked
15 about it a little bit more, but that is not,
16 should not be interpreted as we are either re-
17 reviewing these applications or evaluating recent
18 information. It was conducted I think in the
19 spring of 2013 -- I'm looking for confirmation --
20 just about, with the information that we had at
21 that point in time.

22 MR. MURPHY: So, what I'm hearing is

1 that you are not reviewing that, but you're not
2 discounting the fact that that could happen at
3 some point in the future?

4 MS. BELTRE: PHI has been completed
5 with the information we had in 2013 at that time.

6 MS. JOHNSON: Okay. Was that it? All
7 right.

8 The next question, "Can you speak to
9 how to provide comments to the proposed SE rule,
10 which I understand is currently under OMB
11 review?"

12 MS. STARK: Sure. As soon as the
13 comment period opens up, we are soliciting all
14 comments. It would be helpful, when providing
15 them, that you provide rationale for your
16 position, so that we can take that under
17 advisement and respond appropriately.

18 There should be a Federal Register
19 notice out there. Dockets should be open when
20 it's available for comment.

21 MS. JOHNSON: All right. "For
22 provisional SE reports, can CTP confirm that,

1 going forward, the Office of Science's review
2 cycle is 120 days, as opposed to the previous 90-
3 day timeline for review? Also, can you please go
4 over the review timelines for regular SE
5 reports?"

6 MS. STARK: So, as you saw on today's
7 slide with the performance measures that we
8 placed out, the review timeframe for provisional
9 SE report cycles is 120 calendar days. I
10 contrast that with regular SE reports, which is
11 90 calendar days.

12 I think that gets to the whole
13 question?

14 MS. JOHNSON: Yes, yes.

15 MR. LINDEGAARD: This sounds
16 excellent. Our experience so far -- and we might
17 be in the percentages that have not hit the
18 target -- but, still, the SEs we have in place,
19 and partly on our own fault, I'm sure, have been
20 in process for more than six years and are still
21 not clarified.

22 So, I think, with the experience we

1 have, that it would be worthwhile discussing if
2 there are steps to take to really make the
3 assessment of these products dramatically more
4 efficient; for example, by doing like most other
5 countries around the world, saying, we look at
6 the additives, which additives are accepted to be
7 used in cigarettes, at what level, rather than
8 having to assess each additive for each cigarette
9 every time there is a new application. That
10 would really dramatically increase the
11 transparency for the industry and ease the work
12 for the agency.

13 Have you discussed such an approach?

14 MS. STARK: So, I heard two different
15 points. One is a fair point. With many
16 provisional applications that were received in
17 2010 and 2011, they've been sitting. I want to
18 note, for these performance goals for 120 days,
19 we were kicking them off starting this fiscal
20 year, October 1st, 2018. So, any applicant that
21 receives a notification letter, you're on the
22 120-day cycle. Any applicant that starts to

1 receive a deficiency letter, starting October
2 1st, 2018, or after, you're on the 120-day cycle.

3 For those such as some of the STNs
4 within your company that are beforehand, we are
5 actively trying to move through that queue and
6 get you an appropriate letter within a reasonable
7 amount of time, and we are trying to look at
8 those that have been languishing the longest to
9 get those out first, to be completely fair.

10 With respect to some of the standard
11 that you're looking at for the SE program, where
12 you contrasted it with the exemption request, SE
13 is a little bit different. You are taking a new
14 product, and you are comparing it to a predicate.
15 So, it really is that one-to-one comparison where
16 we're looking for differences between that
17 product that is already out there and the new
18 one.

19 I'm going to contrast that where you
20 look at an exemption request or you could look at
21 a premarket tobacco application where you don't
22 have that necessary comparator, and you are

1 starting to look at that appropriate for the
2 protection of public health standard. You're
3 also looking at are there certain additive
4 percentage changes or other items that may be
5 applicable. That may also get into some of the
6 categories that you're looking at for potential
7 areas for exemption, which would require some
8 thought and rulemaking to go into it.

9 We're open to feedback that you may
10 have with that. If you guys have ideas, this is
11 part of the meeting today. And I know that
12 there's going to be quite a bit more discussion
13 on that scientific standard in tomorrow's
14 presentation by Drs. Walters, Rogers, and Cecil.

15 Did that get to some of your
16 questions?

17 MR. LINDEGAARD: Yes and no.

18 (Laughter.)

19 But we will, obviously, pick up on
20 some of these points on tomorrow's Panel No. 6,
21 where they might fit more appropriately.

22 But it would just be sort of a type of

1 step that would really speed up the process, I'm
2 sure.

3 MS. BELTRE: All right. I guess I
4 would add, you know, I think that we throw our
5 own words, like there are a couple of tiers.
6 But, just to clarify, within each tier there are
7 hundreds of reports, hundreds. So, you know,
8 when we receive these reports, we receive over
9 3,000 of them, just so that everyone is here on
10 the same page. And even though we say two or
11 three tiers, we're talking about a substantive
12 amount of applications.

13 And within sort of those applications,
14 there is randomization, computer-based
15 randomization, to sort of put them in order, so
16 that we can organize the application in a way
17 that they can enter scientific review. So,
18 that's one clarifying point.

19 And two, in terms of Cristi alluded to
20 making sure that you do a side-by-side
21 comparison. So, I think organization of the
22 report, and tomorrow you'll hear a little bit

1 more about that, and explanation on why you
2 provided that information that you provided, and
3 in the form that you provided it, will go a long
4 way, instead of the agency trying to guess why
5 the information was provided.

6 MS. CUSHMAN: And I just had a follow-
7 up on some of the stats in the program updates.
8 Of those that have closed out in the projected
9 period of time, how many of those were
10 withdrawals, or do you have that figure, versus
11 those that actually went to either completion or
12 NSE?

13 MS. STARK: So, I don't have the
14 numbers on me right now. I didn't pull them in.
15 We can update our website with aggregate numbers.

16 I can tell you that there are a much
17 larger number of orders issuing now than in the
18 past. So, although our withdrawals have been
19 high, we are now starting to really increase the
20 number of SE/NSE determinations to hit those
21 stats. So, withdrawals have been decreasing, as
22 people understand what goes into what's needed

1 for an SE report.

2 MS. BELTRE: And when the cohort
3 closes online, it will be broken down by
4 withdrawals and actions and letter types. So,
5 you'll be able to have that information.

6 MS. CUSHMAN: And just as a clarifying
7 question on something in your presentation
8 earlier, you mentioned that, when someone doesn't
9 respond to a deficiency letter, it sounded as if,
10 from the presentation, that automatically is
11 deemed a withdrawal. Is that correct?

12 MS. STARK: No. So, there is a
13 difference between the exemption request program
14 and the SE application program. For an SE, what
15 we're looking at is, if they do not respond --
16 let's say they received a deficiency letter --
17 they may go into another cycle, and there may be
18 review, or it may potentially be enough for that
19 NSE decision.

20 With the exemption request program, by
21 regulation, we actually state, if you fail to
22 respond to that AI letter, the application is

1 considered withdrawn. So, that's in regulation.

2 MR. HOLMAN: I'm going to take
3 prerogative as the Office Director to ask a
4 question of the three industry panelists.

5 So, Cristi presented a number of
6 improvements. You guys all sort of touched on
7 them in your opening remarks. But I'm wondering
8 if you could just sort of elaborate on the change
9 in policy on the response times and what that
10 means, or doesn't mean.

11 She also highlighted some of the
12 changes that we're trying to make to the
13 communications. I heard that some of the
14 communication has not been all that helpful. If
15 you could respond to maybe some of the examples
16 she shared of how we're trying to clarify things
17 in the letters, and are there other specific
18 areas that you guys have in mind where maybe we
19 are communicating, but the communication isn't as
20 clear as it needs to be?

21 MS. CUSHMAN: So, as I mentioned in my
22 opening remarks -- and I appreciate the question,

1 and, Dr. Holman, you've been great about
2 soliciting feedback in this area -- the idea of
3 responding with this additional information in a
4 letter versus having it upfront, I guess, for me,
5 I'm not sure why there's a disconnect between not
6 having it at the front end, where companies can
7 submit a more fully defined SE application at the
8 outset.

9 I know in preparing the provisionals,
10 obviously, that wasn't available at the time,
11 which I completely understand, given the time in
12 which the agency had been in place. But, at this
13 point, I think that within the agency there is
14 enough information, whether it be through
15 reviewer guides, whether it be through these
16 appendices that were mentioned, that that should
17 just be made public.

18 There should be examples of
19 notification letters, even if they're redacted,
20 that outline some of the deficiencies you're
21 seeing in great detail; rather than just bullet
22 points, examples of each of these items. I think

1 as much information as possible makes the review
2 more efficient for you all, and certainly makes
3 it much easier for us to prepare the
4 applications.

5 MS. STARK: So, Brittani, one of your
6 opening statements was to make public some of
7 these appendices for information to consider. We
8 did not do that prior to the public meeting
9 today. That is on our list to do shortly
10 thereafter.

11 So, the appendices that individuals
12 will be receiving, you do not need to submit an
13 application to see what's in these appendices.
14 We will make them publicly available. And as
15 they're updated, we'll be updating what is on the
16 website at that point in time, so people do have
17 access to it.

18 The second item that I actually have
19 from your opening remarks was regarding
20 extensions, lab capacity, and everything else. I
21 know that we have now made recent changes to
22 extend the time for deficiency letters.

1 Can I hear a little bit more on your
2 perspective for what denial of an extension for
3 time to 180 days would do to you and what you
4 guys are concerned with?

5 MS. CUSHMAN: I think right now it's
6 probably a bit hypothetical. But I know many of
7 us in the room and industry have been, as I
8 mentioned, talking to labs, and labs just on the
9 newly deemed product site are already expressing
10 concern that there isn't -- and I will quote one
11 without attributing it -- but "There isn't enough
12 lab capacity in the world for what we're about to
13 see in the deemed product world."

14 So, if you have applications that are
15 still sitting there in the regular SE bin, and
16 you receive a deficiency letter that demonstrates
17 you need some additional testing, for example,
18 you may go to a lab and find that they're
19 backlogged two years. So, I think that's the
20 concern I have.

21 And a blanket, no-extension policy, I
22 just think the idea doesn't make sense

1 considering the amount of lab work that is going
2 to be needed upcoming. And often, deficiencies
3 do require some lab work to be done. So, I would
4 just say, revisit the policy of no-extensions
5 period and have it go back to a case-by-case
6 basis.

7 MS. STARK: So, let me throw something
8 out for discussion from the three of you to see
9 where we're at.

10 In general, in the past, many
11 applicants have received an advice information
12 request letter. They've gotten that. They've
13 responded. They received a preliminary finding
14 letter. Both of these are now going to have 180-
15 day timeframes.

16 If you guys are starting to see, in
17 the absence even of a pre-submission meeting
18 which is open to everyone, what is needed, and
19 you can plan for your testing -- so, before you
20 submit them, let's just state that you need to do
21 stability testing on something, and that may take
22 you a year before you get it in. How do you feel

1 about starting the testing when you first submit
2 the application, waiting for that first
3 deficiency letter potentially, if it's not there,
4 and then, responding to that when you have the
5 testing information? This way, you know upfront
6 and you can plan to test accordingly at the
7 start, rather than in response to that deficiency
8 letter.

9 MR. LINDEGAARD: Well, that would make
10 a lot of sense, seen from our perspective, if it
11 is clear to us what we would be expected to test.
12 That has not always been very clear to us. And I
13 also think it has been the result of a growing
14 skill set within FDA, in the Office of Science,
15 that we can see from the responses that we have
16 received that they have become a lot smarter.
17 They know a lot more detail about the products.
18 And by knowing a lot more details, they also know
19 a lot more questions to ask.

20 So, we got, in the year we, all of a
21 sudden, got very specific questions that we were
22 not prepared for and we could not have, I think,

1 anticipated earlier in the process, or we got
2 them at the preliminary finding.

3 So, yes, we try to look forward and do
4 the testing we think is needed, but we can't
5 always predict exactly what type of questions are
6 going to show up. That has been our experience,
7 anyway. So, we have been struggling with some of
8 the 30 and 60 days desperately. I mean, I've
9 lost sleep over some of these waiting for
10 extension, but the 180 days is going to resolve a
11 lot of things in the current situation. But I
12 also agree, with the potentially thousands of
13 products that need to be tested going forward,
14 just from our company, I don't know how the
15 timeline looks.

16 MR. MURPHY: Yes, so we're talking
17 specifically about applications within the
18 regular space, not these pre-submission meetings
19 and setting expectations. I think we've gathered
20 enough learning over the years that, you know,
21 when we start looking at potentially submitting
22 regular applications, that we pretty much, just

1 eyeballing the comparisons, know what types of
2 product data or test data may be required by the
3 agency. It doesn't necessarily mean that we would
4 submit that in our initial application, but at
5 least we would have some sense of what may be
6 needed and have that in our back pocket, if
7 needed.

8 But I want to go back to Dr. Holman's
9 question about this extension of time. Moving
10 from either a 30-day clock or a 60-day clock to a
11 180-day clock, it sounds great when you look at
12 it in isolation and kind of in the abstract.
13 It's kind of be careful what you ask for, because
14 a lot of these AINP finds, they're not on one
15 particular product. They're for 15 products at a
16 time.

17 And even though we within Reynolds
18 have grown over time as an organization, and we
19 have a lot of resources available to us, we've
20 broken it out where we've got groups focused on
21 provisionals; we've got groups focused on
22 regulars; we've got groups focused on smoke

1 lists. There are always a lot of balls in the
2 air. And all of these different submissions
3 groups are generally reaching out to the same
4 stakeholders across the enterprise.

5 So, it's a function of resource
6 constraints. Just because you give me more time
7 doesn't necessarily mean that I can still
8 generate what I need to generate in that
9 timeframe.

10 MR. LINDEGAARD: Can I add one point?

11 I think you should also be aware that,
12 when the deemed product comes in with pipe
13 tobacco, which is just an enormous amount of
14 different brands produced in very small volumes,
15 or cigars produced in a situation where it's a
16 very low-tech environment from those
17 manufacturers, they have no regulatory or
18 scientific department, most of these
19 manufacturers. It is going to be a different
20 scenario, even the most basic data on quality
21 control. I mean, the most advanced equipment
22 that is being used in this is a ruler and maybe a

1 scale. So, there is going to be sort of a gap of
2 knowledge which is going to be difficult to fill
3 up in 180 days, or 10 years, for that matter.

4 MS. BELTRE: So, I actually want to
5 piggyback on the point that you made in terms of
6 there be a learning curve. So, in Cristi's
7 presentation today, she went over these
8 appendices that we really hope are a great tool,
9 as applicants prepare new applications.

10 And I want to clarify a couple of
11 things. One, these are not a direct comparison
12 to your predicate tobacco product. And at the
13 end of the day, for the SE program, the predicate
14 that you select really is what's going to dictate
15 the kinds of deficiencies that you are going to
16 receive, right?

17 So, in thinking about sort of the
18 challenges that you're facing when you're
19 preparing these reports, I would encourage all of
20 you to think about your selected predicate. What
21 kind of comparisons are you making? What kind of
22 differences are between those two? Because that

1 would definitely dictate the kind of, the number
2 of deficiencies, or how extensive the
3 deficiencies are, or how far you may have to go
4 to justify those differences. That's one.

5 And two, the appendices that we have
6 sort of collated are years of work, of reviewing
7 an SE report, and sort of the program evolving.
8 And this is true for statutory products. And
9 it's going to take some time for us to get there
10 for newly deemed tobacco products. So, although
11 you're going to sort of start seeing these
12 deficiencies, and we'll post them, or these
13 common issues that we've seen in the past, I just
14 want to make sure that everyone is clear that,
15 for newly deemed tobacco products, that's going
16 to take some time. I mean, it took a long time
17 to get to these, and I think we've learned.

18 So, moving forward, it's something
19 that we would definitely keep in mind for newly
20 deemed tobacco products, that we have come to
21 consensus on common issues, that we would post
22 those more readily than we have in the past for

1 provisional. I mean, it took a long time.

2 But I just wanted to clarify that
3 point for you.

4 MR. LINDEGAARD: Thank you.

5 MS. BELTRE: You're welcome.

6 MS. JOHNSON: So, we've come to the
7 end of our time for the first panel,
8 unfortunately, just as soon as it was getting
9 going good. Thanks to Dr. Holman for lobbing
10 that grenade to the panel.

11 We're going to take a break.

12 We want to thank our panelists. Let's
13 give them a round of applause.

14 (Applause.)

15 Thank you so much.

16 And we're going to take a 15-minute
17 break. Let's all convene back here about 10:35.

18 Thank you.

19 (Whereupon, the above-entitled matter
20 went off the record at 10:24 a.m. and resumed at
21 10:39 a.m.)

22 MS. RUDOLPH: Folks, before we move

1 into our second panel, I'll introduce myself.
2 I'm Karen Rudolph, also with the Stakeholder
3 Relations Office in the Office of the Center
4 Director with the FDA CTP.

5 On the last page, for those who are in
6 person, you might note that there are some
7 helpful resources on your agenda. A couple of
8 folks have been asking about availability of
9 resources following this meeting, and just to
10 take note that the web cast will be available
11 probably first, and then we do anticipate that
12 the transcript and also the presentations will be
13 made available on our website. But there's a
14 helpful link that you can kind of take a look at
15 to be informed of what information is available
16 when.

17 Also it's been brought to our
18 attention that for those who are submitting
19 questions, it would be really helpful if you
20 could write really legibly because evidently some
21 folks who are trying to read that before they
22 come up to us are having a little bit of trouble.

1 Also be very, very clear in what you're
2 specifically asking so that we can ensure that
3 the questions that you all provide us can be
4 answered during this public session.

5 So it looks like everybody's settling
6 in. So as we get moving into our second panel,
7 why don't we go ahead and start with our FDA
8 colleagues and Nicholas.

9 MR. HASBROUCK: All righty. Good
10 morning and thank you all for coming today. My
11 name is Nicholas Hasbrouck, and I'm a regulatory
12 health project manager with CTP's Office of
13 Science. I'll be speaking today about pre-market
14 tobacco product applications, otherwise known as
15 PMTAs.

16 First, I will describe the statutory
17 requirements and explain the five review phases
18 for this program. Then I will go through the
19 program. Then I'll go through discussion of some
20 recent metrics and key features and wrap up with
21 the various resources CTP has made available to
22 applicants.

1 So now I will discuss the statutory
2 requirements for a PMTA as described in Section
3 910 of the Federal Food, Drug, and Cosmetic Act.
4 An order under Section 910(a)(2) is required to
5 legally introduce and market a new tobacco
6 product in the United States. You have
7 previously heard talks on the substantial
8 equivalence and exemption from substantial
9 equivalence pathways. This talk on PMTAs will be
10 the third talk on pathways to legally market a
11 tobacco product in the United States. The PMTA
12 pathway is the primary pathway for a new tobacco
13 product to come to market.

14 I keep looking up, but I have it right
15 here. Sorry.

16 For a PMTA, the CTP review is looking
17 at whether marketing of the tobacco product for
18 which an application has been submitted meets
19 four main criteria. First -- and the focus of my
20 presentation is if the product is appropriate for
21 the protection of public health.

22 Consideration for this is determined

1 with respect to the risks and benefits to the
2 population as a whole, including users and non-
3 users of the tobacco product. This consideration
4 also takes into account the increased or
5 decreased likelihood that existing users of
6 tobacco products will stop using tobacco products
7 and the increased or decreased likelihood that
8 those who do not use tobacco products will start
9 to use tobacco products.

10 Additionally, our review will look at
11 conformance to the requirements that apply under
12 Section 906(e), which deals with manufacturing
13 practices if they apply. The proposed labeling
14 should not be false or misleading, which may
15 render a product misbranded under Section 903.
16 And the product must conform to any product
17 standards under Section 907 which apply, or it
18 must contain an adequate justification for why
19 there are such deviations.

20 Now that we've discussed some of the
21 regulatory requirements of the PMTA pathway, I
22 will go through the five review phases of a PMTA.

1 The PMTA review process is divided into five
2 distinct phases. Just to note, the flags here
3 represent the phases. However, they are not
4 necessarily to scale and do not indicate the
5 portion of time required for review.

6 Phase zero, which is not required but
7 is strongly recommended, is the pre-PMTA
8 submission meeting. Phase one is the acceptance
9 review. Phase two is the filing review. Phase
10 three is substantive review and the action phase.
11 And phase four is the post-market reporting
12 phase. As described in Section 910(c)(1)(a), the
13 PMTA pathway has a 180-day review period. And
14 now I will go more in depth on the review
15 process.

16 Phase zero of the submission review
17 process is the pre-PMTA meeting between the
18 applicant and CTP. Again, this is considered
19 phase zero as it is not a required phase.
20 However, CTP encourages applicants to request
21 appropriate meetings as we find that after
22 meeting with FDA, an application may be more

1 complete at the time of submission and more
2 likely to be accepted and filed.

3 CTP notes that a meeting is best when
4 held well in advance of the planned pre-market
5 submission so that the applicant has an
6 opportunity to consider CTP discussion points and
7 feedback prior to preparing their full
8 application. This may include but is not limited
9 to discussions on appropriate samples,
10 inspections, study endpoints, and any clarifying
11 questions.

12 CTP issued a revised guidance in July
13 of 2016 on meeting with industry and
14 investigators on the research and development of
15 tobacco products, which may provide further
16 information on how to plan, request, and what to
17 expect from meeting with CTP. Additionally,
18 there will be a talk later today about meeting
19 with CTP.

20 Phase one of the review process is the
21 acceptance phase. During the acceptance phase,
22 CTP will review the application to ensure the

1 product falls under our jurisdiction. Then a
2 regulatory health project manager will complete a
3 high level preliminary review to determine if the
4 application on its face contains the statutory
5 and regulatory required information applicable to
6 PMTAs. This is per the refuse to accept
7 procedures for pre-market tobacco product
8 submissions, which were discussed earlier in the
9 exemptions from substantial equivalence talk.

10 At the end of this phase, CTP will
11 issue one of two types of correspondence. If the
12 application is missing a required element, the
13 applicant will receive a refuse to accept letter,
14 which will include a reason for the refusal. If
15 the application appears to contain all of the
16 required elements, CTP will issue an
17 acknowledgment letter, which will inform the
18 applicant of their submission tracking number and
19 the RHPM that is assigned to their application.

20 Just a note about the role of the
21 RHPM, we're your main point of contact for any
22 issues related to your applications, and we are

1 the ones that should be contacted if any
2 questions arise with your applications. The
3 acceptance letter will provide the RHPM's contact
4 information.

5 If refused, the applicant can submit
6 a new application once they're able to provide
7 all of the required elements. If the application
8 is accepted by CTP, it moves to the next phase,
9 which is the filing review. The purpose of the
10 filing review is to determine if the application
11 contains sufficient information to initiate
12 substantive review. FDA will conduct a more in-
13 depth, multidisciplinary review of the data as
14 submitted to determine if all statutory and
15 regulatory requirements have been provided as
16 outlined in Section 910(b).

17 Regulatory and scientific reviewers
18 will determine if the application includes, one,
19 full reports of all information published or
20 known, or what should reasonably be known to the
21 applicant, regarding health risks of the tobacco
22 product and whether the tobacco product presents

1 less risk than other tobacco products. For
2 instance, a social science reviewer may look at
3 use liability data to see if there's enough
4 information to review if the product is
5 appropriate for the protection of public health.

6 Two, the applicant should include a
7 statement of the components, ingredients,
8 additives, and properties and of the principle or
9 principles of operation of the tobacco product.

10 Three, a full description of the
11 methods used in and facilities used and controls
12 used for the manufacturing, processing, and, when
13 relevant, packaging and installation of the
14 tobacco product. This should include the address
15 of the applicant's manufacturing facilities.

16 Furthermore, we will determine if the
17 application includes an identifying reference to
18 any tobacco product standard under Section 907
19 that applies.

20 Five, samples of the tobacco product
21 and components thereof as may be reasonably
22 required. Suggested sample numbers may be

1 discussed at the pre-submission meeting if one is
2 held.

3 Six, specimens of the labeling
4 proposed to be used for the tobacco product and,
5 finally, any other information relevant to the
6 subject matter of the application. Again, other
7 information is a component that may be identified
8 during the pre-submission meeting that is held as
9 it may be unique to the tobacco product
10 submitted.

11 At the end of this phase, similar to
12 the acceptance phase, CTP will issue one of two
13 types of correspondence. If the submitted
14 information is inadequate to continue a
15 substantive review, the applicant will receive a
16 refuse to file letter, which will include the
17 reason for refusal.

18 If the application meets the filing
19 requirements for a PMTA seeking a marketing
20 order, CTP will issue a letter to notify the
21 applicant that the application has been filed.
22 If refused, the applicant has the option to

1 submit a new application once, again, they're
2 able to provide all the required statutory and
3 regulatory elements.

4 If the application is accepted by CTP,
5 it moves to Phase 3, which deals with substantive
6 review and an action by CTP. The substantive
7 review phase is a multidisciplinary approach to
8 review the data submitted by the applicant to
9 determine if such data is sufficient to
10 demonstrate -- sorry -- to demonstrate that
11 authorizing the marketing of the product would be
12 appropriate for the protection of public health
13 as previously described.

14 During this review phase, CTP may
15 conduct inspections such as of clinical or
16 manufacturing facilities in conjunction with
17 CTP's Office of Compliance and Enforcement. Also
18 of note, an application may be referred to the
19 Tobacco Product Scientific Advisory Committee,
20 otherwise known as TPSAC. If the applicant would
21 like TPSAC -- excuse me -- if the applicant would
22 like CTP to consider referral to TPSAC, they

1 should include the request in the cover letter of
2 the initial submission. It would also be helpful
3 to provide a reason as to why the referral is
4 warranted. CTP has the discretion to refer a
5 product under consideration to TPSAC and will
6 determine this during the substantive review
7 phase. And also testing of the new product may
8 be conducted by FDA.

9 After completion of the review, FDA
10 will determine if marketing of the product under
11 review is appropriate for the protection of
12 public health and if it may or may not be
13 introduced or delivered for introduction into
14 interstate commerce. In general, within 180
15 days, an applicant will receive either a
16 marketing authorization or no marketing
17 authorization.

18 If an application is denied, a
19 rationale for that decision will be provided.
20 The applicant will have an opportunity to
21 resubmit their application. If authorized, the
22 applicant will be provided a marketing order

1 notifying them that the product is appropriate
2 for the protection of public health and you have
3 met the requirements under Section 910(c) of the
4 FD&C Act. Under the provision of Section 910,
5 you may introduce or deliver your product for
6 introduction into interstate commerce. If there
7 are any restriction on sales and distribution,
8 these will be described in the marketing order.

9 If after review of the submission,
10 marketing orders are authorized, CTP will
11 generally request any post-market reporting in
12 the marketing order letter. These will vary
13 based on the product and the submitted data.
14 However, examples may include serious and
15 unexpected adverse event reporting, which we
16 typically request within 15 days after an adverse
17 event is received by the applicant, any
18 manufacturing deviations, and we also may request
19 any other reports such as annual or biannual
20 reporting or updates to ongoing studies. Again,
21 the marketing order will detail any specific
22 reports and timelines for these reports to be

1 submitted.

2 Now that we've had an opportunity to
3 discuss the statutory requirements and the review
4 process, I will discuss the metrics through the
5 last fiscal quarter, reiterate some key features
6 of the PMTA pathway, and wrap up with some
7 resources CTP has made available to applicants.

8 But first a note about withdrawals.
9 Applicants are allowed to withdraw their PMTA for
10 any reason at any time in the process prior to a
11 marketing decision by CTP. To withdraw an
12 application, a request must be submitted to CTP
13 in writing. Upon receipt, we will issue a letter
14 acknowledging the withdraw request, thus ending
15 review of the product.

16 Here I am showing some recent metrics
17 related to the PMTA Program. Just a note, there
18 are some applications at various stages in the
19 review process, as well as applications that have
20 been withdrawn. Therefore, these numbers may not
21 all add up.

22 As of September 30th, 2018, CTP has

1 received 396 PMTA applications and entered Phase
2 1 of the review process. Of the applications
3 received, 26 have been acknowledged and moved
4 into Phase 2, which, again, is filing, while CTP
5 has refused to accept 367 applications. Of those
6 acknowledged, 17 have been -- I'm sorry -- of
7 those acknowledged, 17 have been filed and moved
8 into Stage 3, which is substantive review, while
9 CTP has refused to file five applications. Eight
10 applications have received marketing
11 authorization, and thus far no applications that
12 have been filed have received no marketing
13 authorizations or a denial. Three PMTAs have
14 been withdrawn.

15 There are some features of a PMTA that
16 are important and/or unique compared with other
17 pathways that I wanted to reiterate and
18 highlight. Again, the PMTA pathway is a primary
19 pathway to legally market a new tobacco product
20 in the United States. This is because a PMTA
21 does not require a predicate tobacco product as
22 previously -- as is required in the SE pathway.

1 Rather, a PMTA is for a new product that is not
2 equivalent to something that is already on the
3 market. Also it is important to note that an
4 authorized PMTA cannot be used as a predicate
5 product for substantial equivalence submissions.

6 A PMTA may require post-market
7 reporting, which will be communicated in the
8 marketing authorization letter. Please be sure
9 to read this letter thoroughly as it will outline
10 any specific information. A PMTA may be referred
11 to TPSAC; however it is not required, such as is
12 required for an MRTP. Also samples may be
13 required. Again, CTP generally will act on a
14 PMTA within 180 days.

15 We also wanted to highlight an
16 opportunity for bundled submissions. This means
17 that if you plan to be prepare an application for
18 a number of products, you can submit one PMT
19 application. However to facilitate the review of
20 the bundled submission, please be sure your
21 submission identifies the unique characterization
22 for each product. CTP will make a determination

1 on the number of unique products and assign
2 submission tracking numbers as appropriate. And
3 for a bundled submission, an applicant can also
4 utilize the tobacco product master file if
5 appropriate, which you will hear more about later
6 today.

7 Here I have listed some helpful
8 resources CTP has provided for additional
9 information. I understand there was a lot of
10 information discussed, and I encourage you to ask
11 questions during the panel discussions later
12 today, in addition to listening to Dr. Murphy's
13 PMTA talk tomorrow, which will go deeper in depth
14 on the contents of a PMTA.

15 Thank you for your attention during my
16 presentation on pre-market tobacco product
17 applications.

18 MS. JACKSON: Good morning. All
19 right, so thank you all for coming today. My
20 name is Ebony Jackson, and I'm a regulatory
21 health project manager with CTP's Office of
22 Science. Today I have the great pleasure of

1 speaking with you about modified risk tobacco
2 product applications, otherwise known as MRTPAs.

3 So first I'm going to describe the
4 statutory requirements for the applications and
5 then explain the five review phases of the
6 program. I'll go through a discussion of some of
7 the key features, as well as highlight some
8 recent metrics, and then wrap up with various
9 resources FDA has made available to applicants.

10 So starting with the statutory
11 requirements for an MRTPA as described in Section
12 911 of the Federal Food, Drug, and Cosmetic Act.
13 Please note that unlike the other presentations
14 you have just heard, this is not a pathway to
15 market. This process is to obtain authorization
16 to utilize a claim for a modified risk.

17 Modified risk tobacco products or
18 MRTPs are defined as any tobacco product that is
19 sold or distributed for use to reduce harm or the
20 risk of tobacco-related disease associated with
21 commercially marketed tobacco products. This
22 includes products whose label, labeling, or

1 advertising represents explicitly or implicitly
2 that the product presents a lower risk of
3 tobacco-related disease or is less harmful than
4 other commercially marketed tobacco products, or
5 the product and its smoke contains a reduced
6 level of, or presents a reduced exposure to, a
7 substance or is not -- or does not contain --
8 excuse me -- or is free of a substance.

9 A tobacco product is also considered
10 an MRTP if light, mild, low or other similar
11 descriptors are used in its label, labeling, and
12 advertising or its manufacturer has taken any
13 action after June 22nd, 2009 directed to
14 consumers through the media or otherwise, other
15 than by means of label, labeling, or advertising
16 that will be reasonably expected to result in
17 consumers believing that the tobacco product may
18 present a reduced risk of harm, tobacco-related
19 disease, or exposure to a substance than other
20 commercially marketed tobacco products.

21 As previously mentioned, an MRTPA is
22 not a pathway to market. In order for an MRTP to

1 be legally introduced or delivered for
2 introduction into interstate commerce, that
3 product must have obtained authorization from FDA
4 through a marketing pathway such as SE, EX, or
5 PMTA which were all presented on previous to me,
6 or the product can be a grandfather product.
7 Additionally, in order to be legally introduced,
8 FDA must issue a modified risk order authorizing
9 the modified risk claim itself.

10 So now that we've discussed the
11 statutory requirements of the MRTPA, I will go
12 through the five review phases. The MRTPA review
13 process is divided into five distinct phases.
14 And just a note here, the flags represent the
15 phases; however they are not necessarily to scale
16 and do not reflect a period of time for review.

17 So phase zero which is not required is
18 the pre-MRTPA meeting. And while it's not
19 required, it is strongly recommended. Phase one
20 is the acceptance review. Phase two, filing.
21 Phase three is substantive review and action.
22 And phase four is the post-market surveillance

1 and studies review phase. Although not
2 considered a distinct phase, renewal and
3 resubmission is a unique feature to the MRTPA
4 process which I will cover as well.

5 So phase zero of the submissions
6 review process is the pre-MRTPA meeting between
7 the applicant and FDA. It is considered phase
8 zero as it is not required. But as stated, it is
9 strongly encouraged by FDA as it allows
10 applicants to ask specific questions and gain
11 feedback, and we find that after meeting with
12 FDA, an application may be more complete at the
13 time of submission, which in turn makes it more
14 likely that it will be accepted and filed.

15 A pre-submission meeting allows FDA
16 and the applicant to have a discussion about
17 samples. Applicants can learn how many samples
18 may be requested and the types of testing that
19 may be conducted. If you are seeking a certain
20 claim, applicants should ensure you have the
21 studies to back that claim. These endpoints can
22 be discussed during a pre-meeting. Although the

1 requirements for filing are outlined in the act,
2 the presubmission meeting allows applicants to
3 ask questions to gain a better understanding of
4 the expectations and requirements.

5 A presubmission meeting can also cover
6 the general process and expectations for the
7 inspections of clinical and manufacturing
8 facilities. FDA can outline what information is
9 useful to be included in the application such as
10 the name and address of each of the processing
11 facilities specific to that product.

12 A pre-meeting can also be useful to
13 the applicant to gain feedback on the format of
14 the application for FDA. During this discussion,
15 FDA can provide feedback on the technical
16 structuring of the application for ease of
17 submitting through Portal, as well as the
18 organizational structuring of the application for
19 ease of application review. And so these are
20 just some examples of how a presubmission meeting
21 can be useful to the applicants.

22 Similar to other applications, MRTPAs

1 have an acceptance phase. During the acceptance
2 phase, FDA will review the application to ensure
3 the product falls under the jurisdiction of the
4 Center for Tobacco Products. Then an RHPM
5 completes a high level preliminary review to
6 determine if the application on its face contains
7 the statutory and regulatory required information
8 applicable to MRTPAs.

9 At the end of this phase, FDA will
10 issue one of two types of correspondence. If the
11 application is missing a required element, the
12 applicant will receive a refuse to accept letter,
13 which includes the reason for refusal. The
14 refuse to accept or RTA procedures have already
15 been covered in previous presentations.

16 If the application appears to contain
17 all of the required elements, FDA will issue an
18 acknowledgment letter, which will inform the
19 applicant of their submission tracking number or
20 STN, as well as the regulatory health project
21 manager assigned to that application, along with
22 their contact information.

1 If refused, the applicant can submit
2 a new application once they are able to provide
3 all of the statutory and regulatory required
4 information required for that application.

5 If the application is accepted by FDA,
6 it moves into the next phase, which is phase two,
7 filing. The purpose of the filing review is to
8 determine if the application contains the
9 necessary information to initiate a full
10 substantive review. FDA will conduct a more in-
11 depth multidisciplinary approach to reviewing the
12 application as it's submitted to determine if all
13 the statutory and regulatory requirements have
14 been provided as outlined in Section 911(d).

15 Regulatory and scientific reviewers
16 will determine if the MRTPA includes the required
17 components as follows. Number one, a description
18 of the proposed product and any proposed
19 advertising and labeling. The product should be
20 uniquely identified, described the proposed
21 claim, and how the claim will be displayed or
22 marketed.

1 Number two, the conditions for using
2 the product. It's helpful to describe the
3 product's intended use, like heated and inhaled
4 or chewed, as well as the potential users.

5 Number three, the formulation of the
6 product. This could include manufacturing
7 process flows and ingredient information.

8 Number four, sample product labels and
9 labeling. An example of this would be actual
10 images and all views of the labels and labeling
11 with the proposed claim to be utilized for the
12 product.

13 Number five, all documents including
14 underlying scientific information relating to the
15 research findings conducted, supported, or
16 possessed by the tobacco product manufacturer
17 relating to the effect of the product on tobacco-
18 related diseases and health-related conditions
19 including information both favorable and
20 unfavorable to the ability of the product to
21 reduce risk or exposure in relating to human
22 health. For this, all other information is

1 something that could be identified in the
2 presubmissions meeting.

3 Number six, data and information on
4 how consumers actually use the tobacco product.
5 The data should be specific to the product type,
6 relevant to the claim, and take into account all
7 users and potential users.

8 And number 7, such other information
9 as the Secretary may require. Such other
10 information may include samples. This is another
11 item which would be great to discuss at the
12 presubmission meeting if held.

13 So filing ends in a decision, just as
14 the acceptance phase. At the end of this phase,
15 similar to the previous, FDA will issue one of
16 two types of correspondence. If any of the
17 aforementioned required components are omitted
18 from the application, the applicant will receive
19 a refuse to file letter, which will include the
20 reason for refusal. If refused, the application
21 is closed, and the applicant has the option to
22 submit a new application once they are able to

1 meet the filing requirements for an MRTPA.

2 Alternatively, if the application
3 meets the filing requirements for an MRTPA, FDA
4 will issue a letter to notify the applicant that
5 the application has been filed. Once filed, the
6 application moves into phase three, which
7 contains substantive review and action by FDA.

8 So once filed, the application will be
9 publically published on the FDA website redacting
10 any private or confidential or commercial
11 information. FDA's review utilizes a
12 multidisciplinary approach from disciplines such
13 as chemistry, toxicology, engineering, and
14 microbiology. And they'll review the data
15 submitted by the applicant and determine if the
16 modified risk claim presented by the applicant is
17 valid and can be substantiated. And Dr. Apelberg
18 will cover more on this in tomorrow's discussion.

19 So during this phase also testing of
20 the new product may be conducted by FDA. While
21 it is not required, FDA may conduct inspections
22 such as of clinical or manufacturing facilities

1 in conjunction with FDA's Office of Compliance
2 and Enforcement or OCE. As stated, this is also
3 a good thing to discuss during the presubmissions
4 meeting.

5 It is also during this phase that the
6 MRTPA will be referred to the Tobacco Products
7 Scientific Advisory Committee, also known as
8 TPSAC. In general, TPSAC is an open process.
9 However, there may be closed sessions for
10 discussion of certain items, which are trade
11 secret information such as ingredients of the
12 product.

13 Phase three is completed by FDA taking
14 an action towards the application. One of three
15 types of correspondence is issued at this time.
16 If after a substantive review, FDA determines
17 that the modified risk claim cannot be
18 substantiated, a denial letter is issued. The
19 applicant will not be able to utilize the
20 proposed modified risk claim. If FDA determines
21 that more information is needed from the
22 applicant, a response letter is issued. If a

1 denial or a response letter is issued, the
2 applicant has the option to resubmit when
3 sufficient information can be provided. And I
4 will talk a little bit more about resubmissions
5 in just a moment.

6 Upon completion of substantive review,
7 if FDA determines that the claim can be
8 substantiated, then a modified risk order is
9 issued. This authorizes the applicant to utilize
10 that proposed claim for that specific product.
11 The modified risk order is not permanent. It is
12 for a fixed period of time, which will be
13 specified in that order.

14 If a modified risk order is obtained,
15 the applicant must follow up with post-market
16 surveillance and study activities. Applicants
17 are required to conduct post-market surveillance
18 and study activities utilizing an approved
19 protocol and submit the results to FDA. FDA will
20 review these results and may collect further
21 information about the product's use and health
22 risk, as well as determine the impact of the

1 order on consumer perception, behavior, and
2 health.

3 If at any time FDA determines that it
4 can no longer make the determinations required
5 under Section 911(g) of the FD&C Act, FDA is
6 required to withdraw that order. Before FDA
7 withdraws a modified risk order, an opportunity
8 will be provided for an informal hearing as
9 required by the law.

10 As previously stated, modified risk
11 orders are not permanent. It is for a fixed
12 period of time, which will be specified in the
13 order. To continue to market a modified risk
14 tobacco product after that set term in the
15 modified risk order, the applicant would need to
16 seek renewal of the order. At that time, FDA
17 would need to determine that the findings
18 continue to be satisfied. No matter the action
19 letter received in Phase 3, be it the modified
20 risk order, a denial, or a response letter,
21 applicants also have the option to resubmit the
22 MRTPA. For ease of review, applicants can

1 reference the previous applications and indicate
2 any changes made for FDA to consider.

3 The withdrawal process of an MRTPA
4 mirrors that of the marketing pathways previously
5 discussed today. Applicants are allowed to
6 withdraw their MRTPA for any reason at any time
7 in the process prior to a marketing determination
8 by CTP. Once CTP receives a written request to
9 withdraw an application, we will issue a letter
10 acknowledging the withdraw request, thus ending
11 the review of that application.

12 So now that we've had an opportunity
13 to discuss some of the statutory requirements and
14 the review process, I'm going to reiterate some
15 of the key features of MRTPAs, provide some of
16 the metrics through the last fiscal quarter, and
17 wrap up with some resources that CTP has made
18 available to applicants.

19 So here are some of the key features
20 of the MRTPA process I would like to highlight
21 for you. FDA must make applications available
22 for public comment with the exception of personal

1 privacy, trade secret, or otherwise confidential,
2 commercial information. A redacted version of
3 the application is posted to the FDA website
4 shortly after filing. FDA must refer MRTPAs to
5 TPSAC for recommendations. As previously stated,
6 TPSAC is generally an open process, excluding any
7 trade secret or confidential, commercial
8 information. FDA intends to make a decision on
9 the MRTPA within 360 days. A decision is
10 indicated by the applicant receiving one of three
11 action letters as discussed in phase three.

12 Modified risk orders are issued for
13 individual products and not for a class of
14 tobacco products. The modified risk order will
15 authorize use of a claim for a specific product
16 for a specified period of time as outlined in
17 that order.

18 So here I am showing some recent
19 metrics related to the MRTPA program. Just a
20 note, there are applications at various stages
21 throughout the review process, as well as
22 applications that have been withdrawn and these

1 numbers are reflective of such.

2 As of September 30 of 2018, FDA has
3 received 37 MRTPAs and entered phase one of the
4 review process. Of that 37, 26 have been
5 acknowledge and moved to phase two, which again
6 is filing, while 10 were RTA'd. Twenty were
7 filed and moved to phase three, substantive
8 review, while four were RTF'd. Five applications
9 were withdrawn by the applicant somewhere in the
10 review process. Eight applications received an
11 action letter for response, and there are
12 currently applications in the review process with
13 FDA.

14 Here I've listed out some helpful
15 resources CTP has provided for additional
16 information. Later today, Ms. Sharyn Miller will
17 present on how to locate these and other
18 resources on the FDA website. Additionally, Dr.
19 Apelberg will be speaking tomorrow more in-depth
20 about the MRTPA process, as well as its contents.
21 I encourage you to listen to both and ask
22 questions during the panel discussions. Thank

1 you so much for your time today.

2 MS. RUDOLPH: So let's go ahead and
3 also give thanks to Nicholas. Great job. As the
4 panelists come on up and we'll get started into -
5 - we have about 30 minutes together. How's this
6 all sound? Sorry, guys, my ears are a little
7 clogged up with a little sinusitis.

8 Just as a reminder, we'll be going in
9 alphabetical order with our outside panelists
10 getting a chance to have five minutes to
11 introduce themselves and share their perspective.
12 And then our FDA colleagues will also introduce
13 themselves.

14 Could somebody change the panel slide
15 please to Session Two Panel Discussion?
16 Fantastic. Thank you. Thanks for noticing,
17 Cristi. Great, so let's go ahead, and, Patricia,
18 you're first.

19 MS. KOVACEVIC: Good morning and allow
20 me to thank the Center for Tobacco Products for
21 bringing together their expertise, as well as
22 industry's expertise to provide additional

1 transparency for the tobacco product application
2 process.

3 I'm Patricia Kovacevik. Historically
4 I've worked for Philip Morris International as
5 senior counsel, for Lorillard as head of
6 regulatory, and also for a domestic manufacturer
7 of newly deemed vaping products, Nicopure Labs,
8 as general counsel and chief compliance officer.
9 At present, I'm an independent consultant
10 continuing to consult for one of my former
11 employers and others in the industry.

12 My involvement with tobacco product
13 applications dates back to 2011 when the team I
14 had the privilege to lead applied for a regular
15 SE that received the very first pre-marketing --
16 or the very first marketing order since the
17 Tobacco Control Act. And I've also led legal and
18 regulatory teams that submitted comments to the
19 PMTA dockets. The various rules issued,
20 submitted successful product applications as
21 mentioned, and also scoped, prepared, recruited
22 consultants for PMT and MRTP applications.

1 I'll concentrate my brief remarks on
2 two areas of interest. First, a brief
3 perspective of the PMTA review process
4 opportunities to the applicant. And second, a
5 couple of suggestions regarding additional
6 guidance that would yield more robust actionable
7 product applications.

8 First, as an advisor to the industry
9 and in particular following today's workshop, I
10 can state unequivocally that the PMTA review
11 process steps are entirely clear to me. And I
12 hope they're clear to you as well. And from my
13 previous experience, at least as to the meetings,
14 the process does work as advertised. Our meeting
15 requests were addressed -- that were addressed to
16 FDA were extremely promptly answered, and the
17 meetings were extremely constructive and helpful
18 in connection with all kind of product
19 applications.

20 You've heard from the industry that it
21 would be very helpful -- I think on various
22 occasions, we've heard from the industry that it

1 would be very helpful to understand what are the
2 pass/fail criteria from a substantive review
3 point of view where the process is clear. But of
4 course, the details surrounding every product are
5 very important. We feel that at least the fail
6 criteria should be communicated clearly through
7 guidance documents.

8 Also if I might also add from previous
9 experience, one single presubmission meeting per
10 applicant is absolutely not enough given the
11 scope and number of studies that need to be
12 conducted in support of a presumably successful
13 PMT application.

14 Also last, but not least on the first
15 part of my comments, it would be extremely
16 helpful if FDA clarified that the 180 days
17 statutory deadline for issuing an action on a
18 PMTA is a deadline that works in favor of the
19 applicant, i.e. a deadline for the agency and not
20 the applicant. In other words, if an applicant
21 wishes to extend that deadline by, you know,
22 providing additional studies and so on, hopefully

1 the clock doesn't stop after 180 days and an
2 unfavorable finding is issued. Because I think
3 it's in anybody's interest to bring new products
4 to the market that may reduce harm.

5 The second area of my comments, the
6 PMTA guidance needs to be finalized. And also
7 for every single study mentioned in the guidance,
8 additional more detailed, more extensive guidance
9 must be provided as soon as practicable. To
10 elaborate for instance on study design, sample
11 size, demographics of the study that has to be
12 provided. That would really yield better
13 applications.

14 As an example, just this past month,
15 CDER published several guidance documents
16 detailing product specific or category specific
17 study designs such as -- just to quote --
18 assessing adhesion with transdermal and topical
19 delivery systems for ANDAs, contents of a
20 complete submission for threshold analysis and
21 human factor submissions to drug and biologic
22 applications, and master protocols, efficient

1 clinical trial design strategies to expedite
2 development of oncology drugs and biologics, and
3 so on.

4 So we would like those kind of
5 guidance documents for the PMTAs given that we
6 all acknowledge that a number of studies need to
7 be conducted. And of course given that the
8 Commissioner appears to contemplate perhaps
9 bringing forward the PMTA deadline for newly
10 deemed products from 2022 to perhaps earlier,
11 such guidance documents will be indispensable for
12 the industry. Honestly, no CEO wants to tell the
13 investors that it will have an answer from the
14 FDA within a certain period of time and then
15 realize the product application was so off the
16 mark as to require numerous revisions and
17 submissions. These are just a few suggestions.

18 If I may just add that harm reduction
19 is a desirable outcome for both industry and the
20 FDA. And the issuance of marketing orders for
21 products other than combustibles that may present
22 reduced harm, even if they don't advertise the

1 reduced harm, will send a clear message to
2 smokers who wish to switch and will help guide
3 consumers down the continuum of risk highlighted
4 by Director Zeller.

5 And of course additional further --
6 additional regulation that may further
7 differentiate more products would be helpful.
8 Thank you.

9 MS. RUDOLPH: Thank you. Jim?

10 MR. SOLYST: Started the time here so
11 I stay within five minutes. Jim Solyst. I was
12 new to tobacco in 2009. Really didn't know
13 anything about it. But what I did know was about
14 the -- it's not on? There we go. You didn't
15 miss anything.

16 I said I was new to tobacco until
17 2009. But I was not new to the regulatory
18 science process. I had worked for a bipartisan
19 organization and for industry in Washington since
20 the Reagan administration. And that was very
21 helpful because I knew how, for instance, EPA
22 worked, I knew how OMB worked, and I could apply

1 it to FDA.

2 I also had reasonable expectations in
3 interaction with FDA, and I also learned to put
4 yourself in their position. If you're going to
5 advise a client or your company, try to think
6 like CTP would think.

7 I was very much involved with the MRTP
8 and the PMTA process for our General Snus
9 product. It's eight different products within
10 the General Snus line. The PMTA process was
11 fairly straightforward. The MRTP process is
12 still ongoing. It was encumbered by a 1986
13 warning label law that required certain things
14 that we disagreed with, and that entered into the
15 MRTP process.

16 But let me give you sort of a
17 timeframe as to what has happened. We first
18 submitted our application for MRTP in June of
19 2014. A couple months later it was filed. It
20 was publicly available. In early 2015, we
21 submitted the same body of evidence, largely, for
22 our PMTA. And then in 2015, November, we

1 received the PMTA. With that was the technical
2 project lead report, which I cannot strongly
3 endorse enough that you should read that
4 document.

5 With the MRTP in December of 2016, we
6 received a partial decision, and we responded to
7 that partial decision with an amendment, which we
8 submitted in September of this year, and that is
9 pending right now. And we are now preparing a
10 PMTA for a different product. What we call ZYN,
11 Z-Y-N. It's a pouch product, very similar to
12 Snus, but nicotine only, no tobacco. So we are
13 once again going through the PMTA process.

14 Just some thoughts, some advice
15 perhaps. There's always going to be uncertainly.
16 We're the only company that received a PMTA.
17 We're doing a PMTA for ZYN and we still --
18 there's uncertainly. We don't know exactly how
19 many bridging studies we should be conducting.
20 We don't know how extensive our consumer
21 perception study should be. So you have to make
22 decisions. You have to use your best judgement.

1 You can listen to outside counsel and outside
2 advisers who will tell you they know what to do,
3 but they don't. This is a learning experience.
4 There's only been one decision -- There's only
5 been once decision document and that's what you
6 have to base it on.

7 Read the CTP documents. As I
8 referenced, the technical project lead report for
9 our PMTA was, I thought a masterful document.
10 They had a page and a half or page and a quarter
11 executive summary. And it said exactly why they
12 gave us a PMTA. When we're doing our ZYN PMT, we
13 go back -- I go back certainly to that TPL and
14 try to incorporate the main themes that were in
15 that document.

16 Other documents, the draft NNN rule in
17 smokeless -- if you're a smokeless product,
18 although that rule may or may not go anywhere,
19 it's still important. It gives you an indication
20 of the thinking of CTP. And the briefing
21 documents. For instance, most recently the Camel
22 Snus TPSAC briefing document I found very

1 interesting.

2 One thing reassuring and frustrating
3 is the AIRs, the advice information request. We
4 received eight of those for the -- probably both
5 PMTA and MRTP. The first one I received, I
6 thought oh my goodness. Do I have to do more
7 work for these people? And so it can be
8 frustrating. You get these things. You get a
9 deadline. You've got to scramble to address
10 them. But on the other hand, at least you know
11 that you're still in the game. You know that you
12 have the opportunity to provide additional
13 information. You know you can clarify things.
14 And so it's sort of a yin and yang on the AIRs.

15 As far as the meetings with CTP, yes
16 I agree with Patricia. More than one is
17 necessary. You have to -- but keep your
18 expectations in check. You go there and you
19 present information. You tell CTP this is what
20 we plan to do. And then you kind of look around
21 the room to see if you get any reaction. Usually
22 you don't. And then you focus on particularly on

1 matter, Ben Apfelberg and see what they're saying,
2 but they don't. But at least you have that
3 opportunity to present. And you hope that if you
4 were presenting something outrageous, they would
5 let you know.

6 But ultimately it is your own
7 decisions. You listen to people, read the CTP
8 documents and make a good judgement. Thank you.

9 MS. RUDOLPH: Thank you, Jim. Jeff?

10 MR. WALKER: Well thanks. Good
11 morning again. And let me just amplify my
12 introduction that might give a little more
13 perspective to my comments. So I was an ER
14 physician for many years. And then I
15 transitioned into industry and spent about 17
16 years developing combination drug device
17 products, which gave me some exposure to FDA, FDA
18 processes, particular in the medical device side.
19 Which I think has been useful as I have thought
20 about this tobacco regulation.

21 Then eight years ago, I transitioned
22 into really kind of two different phases of my

1 career in tobacco regulatory science. The first
2 was really thinking about this scientific
3 frameworks. How do you put together an
4 application? And I actually went back to my
5 training in medical devices and drugs, which
6 usually you start with a label. You start with a
7 claim. And you work your entire scientific
8 framework backwards to be able to support that
9 claim at the end of the day. So I think that was
10 very helpful to be able to spend a number of
11 years planning these applications, the scientific
12 frameworks, the clinical studies, non-clinical
13 studies.

14 And then fortunately for the last two
15 and a half years, I've really had much more
16 practical day to day experience with the
17 management of applications. So as a U.S. agent
18 for PMI, it's been my pleasure to be talking with
19 the project managers and managing the day to day
20 communications. The what happens? What do we do
21 now? I'll tell you it's a very interactive
22 process with FDA. At times, there's a lot of

1 activity. As Jim mentioned, advice information
2 letters. There's redactions to deal with.
3 Company inspections to deal with. It's a very
4 interactive process. So if you're a young
5 company, if you're thinking about filing these
6 applications, I encourage you to think carefully
7 about making sure you have enough resources to
8 manage all the various activities that go along
9 with submitting and managing an application.

10 I do want to touch real briefly on the
11 uncertainty issue since Jim had mentioned that.
12 And we are in kind of a study and contrast.
13 We're in a world where we only have eight PMT
14 applications that have actually been authorized
15 for really one basic product type. We have no
16 MRTPs to date. So we're just beginning to sort
17 of see how to do this and how FDA is thinking
18 about these kinds of applications. And I would
19 encourage you to try to minimize some of the
20 uncertainty by really going back and doing a lot
21 of reading. There's a lot of research. There's a
22 lot of stuff out there. It starts with the

1 preamble to the FSPTCA, draft guidance. It's not
2 only from CTP, but draft guidance is from drugs
3 and devices. Because they inform you of how FDA
4 might think about a process and how you can
5 interact with FDA at meetings.

6 I'd encourage you to read the FD
7 presentations. They've been very active over the
8 last number of years and going out to TMA and
9 other places. I know Matt was at TMA this year.
10 It gives you a lot of insight in how FDAs
11 thinking by just seeing what they present and how
12 they talk about these different topics. The
13 website is a lot of information, but you need to
14 read it. I think Jim alluded to TPSAC
15 transcripts. They're very useful to see how the
16 TPSAC members talk about issues, how FDA
17 responds, and how industry responds.

18 I would certainly encourage you to
19 read the FDA briefing materials, particularly the
20 briefing documents are very useful. Technical
21 project reports, these are -- You have lots of
22 nuggets in them to really point you to the

1 direction that I think you need to go in for
2 these applications.

3 And finally, I think certainly you
4 need to read the comments from Commissioner
5 Gottlieb and Director Zoeller. I mean they are
6 setting the north star for where FDA wants to go.
7 If you know that north star, if you can kind of
8 navigate towards it, I think you'll be in fairly
9 good shape.

10 So those are my opening comments. I
11 look forward to some of the questions, but I
12 encourage you to be active and engage with the
13 agency. And also seek out some of your industry
14 colleagues.

15 MS. RUDOLPH: Thank you. And now
16 colleagues from FDA. Would you like to re-
17 introduce yourselves?

18 MS. BELTRE: My name is Rosanna
19 Beltre. I'm deputy director of the Division of
20 Regulatory Project Management. I have no
21 additional opening comments, so I'll just hand it
22 over to Cristi.

1 MS. STARK: Again, Cristi Stark,
2 director for the Division of Regulatory Project
3 Management.

4 MS. RUDOLPH: That's great. Maybe
5 before we go to the questions that have been
6 turned in, in the room or provided online, I
7 would like to like to look to my FDA colleagues
8 and just say based on what you heard from our
9 panelists, do you have any additional comments or
10 things that came up for you as you were listening
11 to what they stated that you might want to
12 comment on at this time? Or would you rather go
13 to the questions?

14 MS. BELTRE: Yeah. Thank you for your
15 opening remarks. I think that particularly for
16 these two programs as they are relatively young,
17 I think that smaller companies can sometimes sort
18 of struggle reviewing the FDA information on the
19 website. Or sort of making the connection of how
20 something in drugs may potentially be -- give
21 them sort of something to know how the agency
22 thinks about things. And sort of taking a step

1 back and instead of thinking about well this is
2 how we've conducted our work, sort of thinking
3 more about how the agency and the role that the
4 agency plays and why things are sort of
5 structured the way that they are. Sort of the
6 boundaries of our regulatory authority -- the
7 regulations that we have out there and sort of
8 reading through all those documents.

9 I think that people definitely
10 struggle and I'm glad to hear that you guys are
11 doing that. I think it might potentially be a
12 little harder for other companies that are
13 relatively new to this -- to tobacco, but I'm
14 glad you guys are reading.

15 MR. SOLYST: One problem with
16 reviewing documents is there's a lot there and
17 you have to determine what's important and what
18 might be filler or cover yourself type of
19 language. I know that you can go through, for
20 instance, our partial decision for MRTTP, they
21 cited some deficiencies. That's what we had to
22 address. They cited some requests for additional

1 information, which is not as mandatory.

2 But also there's a lot of other
3 language in there. And how serious do you take
4 that? How do you narrow down what you should be
5 focusing on as you respond to CTP. And a lot of
6 that is just simply experience. But as you've
7 said, there's only one decision document right
8 now to base it on.

9 MS. STARK: So there's one other item
10 I'd like to touch upon. And this is in part to
11 Patricia's comments regarding timelines and
12 standard review pass/fail criteria and other
13 items. And also in response to Jim's comments
14 regarding the multiple advice information request
15 letters they received through their process.

16 Again, we do not have the robust
17 experience with these two programs as we have
18 similar to the SE programs. We're hoping to
19 learn from it. Our goal though is to take some
20 of the lessons learned from SE, apply them here.
21 So the goal would be to have more robust, clear
22 advice information request letters. So maybe you

1 don't see eight, you see far fewer. You see
2 things very clearly outlined to you.

3 Additionally, I'm looking at the time
4 for a presubmission meeting, what you use it for.
5 You don't necessarily have to look at it per
6 product. You may be looking at items across
7 multiple applications, especially looking at the
8 large number that may come in. Try to gather
9 those concepts together. Bring them in and ask
10 your specific questions to FDA. And note that
11 there are ways to get answers where you don't
12 formally have to meet face to face, but it may be
13 by a written response, which could be a little
14 bit faster than going the face to face method.

15 With respect to parsing through and
16 reading what's out there, one of the best places
17 to go first would be most recent TPL reviews. So
18 the one that we saw for the Snus products, it's
19 helpful to see how it was framed, looking at
20 recent meetings as well. That's really how you
21 want to start most current and then work
22 backwards. Also looking at recent items out from

1 some of other sister centers from FDA.

2 MS. BELTRE: Sorry.

3 MS. RUDOLPH: That's all right.

4 MS. BELTRE: The only thing that I
5 would add is that we've sort of shared a lot of
6 information here today. And talked a lot about
7 the SE program and sort of -- it's one of the
8 most utilized programs that we have. But when
9 applicants are looking to submit an application,
10 I highly encourage you to go to our website, look
11 at the bar for each one of these programs to
12 assess which one of these pathways is the best
13 for your product. It may be that, you know, PMTA
14 is not. And to think about the standard for each
15 particular program and what information you will
16 need to substantiate and to meet that bar because
17 they are different bars. So I encourage everyone
18 to sort of look at that. There are things that
19 you can sort of extrapolate and that you can
20 think across, but they are different bars for
21 each one of these particular programs.

22 MS. RUDOLPH: Thank you. So we've got

1 a couple of questions that are somewhat related.
2 And I'll put these out to the FDA colleagues.
3 Can you explain again the difference between
4 receiving an RTA and an RTF? And what are some
5 of the reasons for the RTA and RTF for PMTAs?

6 MS. STARK: So I'll take that. The
7 refuse to accept is really your first gate for
8 your pass fail criteria as you look at it. That
9 is a review that is in general done by your
10 regulatory health project manager. They are
11 going to be looking for basic items such as is
12 this under CTP jurisdiction, meaning is it a
13 tobacco product that we regulate? They're going
14 to be looking at items that are out in that
15 refuse to accept rule. So one of the reasons you
16 saw such a large number of RTAs for PMTAs, many
17 of them were missing their environmental
18 assessment. Not having that document present,
19 and you're going to hear about that in a later
20 presentation, would be a basis for RTA.

21 If you are passing phase one, you
22 received that acknowledgment letter, you then

1 move into that filing stage. So the end result
2 is the filing letter or the RTF letter. This is
3 a multidisciplinary approach, so you can have
4 anywhere up to 13 disciplines taking a look at
5 various parts of the application for what's
6 required for filing.

7 Looking through all your documents.
8 Are your studies there? Do you actually have
9 some of the source data? Is there anything
10 missing? So anything that's laid out in filing
11 criteria in 910(b) for your PMTAs and under 911
12 for your MRTPs is what they're looking at for
13 that RTF. If those items are missing, it would
14 be listed in that letter. If you passed that and
15 received filing, then you're in that substandard
16 review phase.

17 MS. BELTRE: Great. I would add to
18 that, clearly identify these sections in your
19 application. When we're talking about large
20 submissions such as the MRTPs and PMTAs that we
21 have received, it would help everyone involved in
22 this process if you can clearly identify what

1 this information is. The statutory requirements
2 are out there. The information is very clear on
3 what's necessary. The presentations here today
4 have clearly outlined that. So making sure that
5 you identify that up-front and that it's clear
6 would definitely help everyone involved in the
7 process.

8 MS. RUDOLPH: Okay, thank you. Jim?

9 MR. SOLYST: If I could comment on
10 Cristi's statement about conference calls versus
11 in-person meetings. When we were in the process
12 of doing our amendment to the MRTPs, it's now
13 publically available and I'm sure you've all read
14 it, we had a very effective meeting in March --
15 face to face meeting went very well. And then we
16 did consumer perception work to test various
17 marketing claims. And we requested another
18 meeting. And we got good feedback saying a
19 conference call will probably do. And a
20 conference call, I think worked well. I have my
21 colleagues here today who were part of that call.
22 And then more importantly, we got a letter of

1 course that addressed all of our concerns.

2 So sometimes a conference call
3 particularly given the response letter is just as
4 effective as a face to face meeting, depending on
5 the nature of the issue.

6 MS. RUDOLPH: And to that end then, a
7 question was raised is how does one request or
8 start a pre-PMTA meeting?

9 MS. STARK: So I don't want to answer
10 that. I believe we have a presentation coming up
11 from Ms. Banchemo regarding how you can go
12 through that formal process, in addition to the
13 guidance that's out there. So I'm going to let
14 her answer that question. And if it's not
15 addressed during that panel, we can hit it again.

16 MS. RUDOLPH: Okay. What about
17 marketing authorizations via PMTA, are these made
18 public?

19 MS. STARK: So for a PMTA, the
20 positive decision, meaning you're allowed to
21 introduce your product into interstate commerce
22 is made public, and you've seen that with the

1 past ones for the General Snus, in general will
2 post the copy of the order letter in that
3 technical project lead review, which is a summary
4 for the decision around that action.

5 With respect to a negative decision
6 where they may receive a denial, that is not
7 necessarily made public. That information,
8 similar to other FDA centers is held in and we
9 will be looking at has the applicant stated it's
10 been filed or not before giving any type of
11 inkling regarding what the decision is? I will
12 note though, we do release aggregate numbers with
13 respect to our decision. So if, let's say we
14 receive a large number and they receive denials,
15 that aggregate number would be posted out on the
16 web.

17 MS. RUDOLPH: Thank you. So here's a
18 good question that is listed here. When a
19 deficiency letter is issue for a PMTA, how does
20 that affect the 180 day clock for a PMTA? What
21 happens if we need more time than the 180 days?

22 MS. STARK: Okay, so I'm going to be

1 honest. I don't know if Dr. Holman's going to be
2 happy I'm up here or not. We haven't met some of
3 the 180 day goals that are out there. You can
4 see some of the numbers in there. We're doing
5 our best to get there.

6 In general when you're looking at a
7 clock, the clock is really with the applicant.
8 So if we're issuing a letter, the clock is not
9 with FDA, our timeframe has stopped. So
10 basically if that letter would come out and we
11 are 60 days into the cycle, when that amendment
12 is received back in, we would start at Day 61.
13 We're still working towards hitting the 180 days.
14 So I want to put that out there in case anyone
15 thinks we're trying to hide that. But that
16 should answer some of the clock questions. Go
17 for it.

18 MR. WALKER: So just a quick follow-up
19 on that. So if you had an advice information
20 letter you sent out, it effectively stops the
21 clock. You would give the applicant, let's say
22 30 days to respond. They send their information

1 back in. But now there's additional work for you
2 to review. You have additional information. So
3 does that add onto the clock, do you think, just
4 in a general sort of sense?

5 MS. STARK: So let me compare and
6 contrast some of the official clocks in other FDA
7 centers that you may be familiar with and what we
8 have in this center.

9 In this center, we don't have anything
10 official out. So if you were to go for a drug
11 application with an NDA and it was something
12 termed a major amendment, you would actually have
13 an extension depending if it is a Level 1 or
14 Level 2 amendment with time added. We don't have
15 that here. What we have been doing is trying to
16 make sure that we are finding efficient ways to
17 do our review and respond appropriately.

18 To one of the comments earlier though,
19 if it hits Day 179 and we realize we need to get
20 that order or decision out and there's more to
21 do, it's unlikely that we're just going to stop
22 everything and issue the order if there's more

1 work. We are looking at products that could have
2 the appropriate protection of public health. We
3 want to make sure we do our full review to get
4 out there with the understanding as well that we
5 are also trying to do this in a timely manner.

6 MR. SOLYST: If I could comment on two
7 issues that have come up. I believe for the
8 General Snus PMTA, FDA did meet the 180 day
9 deadline. On the question about is it public
10 knowledge if you get a PMTA, yes. My complaint,
11 my frustration is it's not public enough. I
12 would have liked to have seen a front page in the
13 Washington Post, FDA determines a product is
14 appropriate to the protection of public health.
15 But that just isn't the way it works. That is a
16 level of frustration. I assume hopefully that if
17 we got a MRTP, there would be more promotion of
18 that because I do think it meets Dr. Gottlieb's
19 initiative on discussion of nicotine and a better
20 educated consumer.

21 MS. RUDOLPH: Great, thank you. So
22 here is a question. If a product is on the

1 market -- Excuse me -- because it has a PMTA
2 order, if I change that product, how can I market
3 the modified product, even if it's a small
4 change? For example, SE type modification.

5 MS. STARK: Okay. So we're going to
6 talk about the three pathways to market briefly.
7 You have a PMTA. You have an SE report. And you
8 have an exemption request. The SE report, if
9 you've already been authorized under a PMTA is
10 off the table because it's not an eligible
11 predicate. You must either -- for the SE report,
12 be grandfathered or previously found SE.
13 However, there were two options.

14 You can look at a PMTA and there may
15 be ways where we could look at an abbreviated
16 process, depending on what that is, and FDA can
17 work with you. Or you can actually look an
18 exemption request if you have that minor additive
19 change. So remember when the Schmitz presented
20 earlier on exemptions, if you've modified --
21 you're allowed to modify a legally market
22 product. A PMTA would be one legally marketed

1 product that could come through that exemption
2 request pathway.

3 MS. RUDOLPH: Thank you. We have one
4 last question for our panel. Could you talk
5 about the communications with manufacturers
6 during the review process? Are there specific
7 communications and what are they?

8 MS. STARK: Okay. So I'm going to be
9 frank in the beginning as well. You were
10 assigned a regulatory health project manager, so
11 if you'd like to hear what's going on where
12 there's moments of silence -- because we've heard
13 sometimes there's frenzy and activity and other
14 times, you don't hear a lot, please reach out and
15 call them. I will tell you if you call them
16 every day, they will likely come back and state
17 check in with me once a week. This is similar to
18 what project managers will do for drugs,
19 biologics, and devices as well.

20 With respect to communication, you are
21 at least guaranteed to receive correspondence and
22 communication at each phase of review. So as you

1 go into Phase one, you should receive an
2 appropriate letter from a decision for
3 acknowledgment or refuse to accept. Phase two
4 for filing or refuse to file. And Phase three,
5 you're looking at potential advice information
6 request type letters, response letters, which we
7 had seen previously with one of the MRTPs. And
8 decision letters. There may be other
9 correspondence or items going on during that
10 time. Again, use your regulatory health project
11 manager to ask clarifying questions.

12 MS. BELTRE: I would clarify that once
13 an application has entered the scientific review,
14 if you are calling your regulatory health project
15 manager, they're going to tell you it's under
16 review. They're not going to discuss specifics
17 about what's happening in the scientific review
18 process, where they are in their review process.
19 That's all that they can say at that point in
20 time.

21 MS. RUDOLPH: Now Dr. Holman had
22 flagged me from the audience here, so let's give

1 him his moment here.

2 MR. HOLMAN: It's me again. A couple
3 questions I'd like to hear you guys discuss. One
4 is, you know, one of the points we've heard is
5 that it's very challenging. This is new.
6 There's not a lot of information. And Jim had
7 some good suggestions about looking at certain
8 documents carefully. I think Jeff also mentioned
9 looking at documents -- and even potentially what
10 other centers do and seeing how that might be
11 applicable to your tobacco product.

12 But I wonder, there was a lot of
13 discussion about our TPSAC meetings for the MRTPs
14 and how that has or hasn't been helpful as a
15 learning tool for industry. And so if you guys
16 could sort of comment on that, I guess both from
17 observing and maybe also participating to the
18 extent you'd like to share that.

19 And then I'd also like to jump in on
20 the last sort of meeting discussion point about
21 the clocks. You know, Patricia has basically
22 said hey, we don't want you to cut it off at 180

1 days, if you could go 200 and we'd get a
2 marketing order. Right? But we've also heard
3 that there are challenges with the clock. I mean
4 it stops. We need to get information. In some
5 cases, there's a number of deficiency letters
6 that get issued. So I just wondered if you guys
7 had thoughts about how we sort of balance that,
8 that these are very new.

9 As you've seen on the SE side, we
10 weren't as good about meeting our performance
11 measures in the early days. And we're much
12 better about it now. And I think we're kind of
13 going through a similar evolution for these two
14 programs. And so if you have thoughts more about
15 how to make it more predictable. How to improve
16 communication in light of all these challenges
17 that we're struggling on our end. And you guys
18 are quite frankly, I think struggling at your end
19 with. So if you had more thoughts on that, we'd
20 be happy to -- We'd like to hear them. Thank
21 you.

22 MR. WALKER: Sure. Let me just

1 address the communication piece. Everything you
2 said is correct. You will be told during the
3 scientific review phase, it's still under review.
4 But I think what I'd like to suggest would be
5 more useful, is could we just have at some point
6 in time, a little bit more detail on what is the
7 decision making process like within, you know,
8 the center? And also outside the center.

9 Because I'm guessing that when a CTP makes a
10 decision or has a scientific review completed,
11 there are other things that have to happen next
12 before a market order actually gets written.

13 So I would imagine there's other
14 government stakeholders. There may be other
15 processes that are navigated. And I think just
16 knowing that, that exists would be useful. So it
17 kind of helps you figure out where things are.

18 So number two communication, I agree
19 with you. Your project manager is your go-to
20 person. I have been guilty once or twice of
21 calling my project manager too often and I get
22 that same response. But I think what I've also

1 found is the CTP is highly interested in good
2 communications. And I've always felt comfortable
3 that they're to listen, answer questions, and
4 it's been a good process.

5 Regarding TPSAC, I'm candidly not sure
6 yet how that process works. And I think it
7 depends on the quality and the character of the
8 questions that are asked. I think it depends on
9 the background of some TPSAC members and whether
10 they are truly attuned to all the science or just
11 the particularly narrow focuses. And I guess I'm
12 still uncertain about the utility of that. I
13 think there is good conversation, I think that's
14 very useful to listen to the FDA briefing
15 documents. But in terms of how the TPSAC works,
16 I think it's clearly an FDA resources. But it
17 doesn't seem to always tie necessarily direct
18 back to the claims for me. So I'm sort on the
19 fence.

20 MR. SOLYST: I've attended each of the
21 TPSAC meetings for MRTPs. The latter two were
22 more interesting -- more enjoyable than the first

1 one. The first two days I went through, my
2 colleague, Lars-Erik Rutqvist is back there. I'm
3 sure he feels the same way. But most recently, I
4 went to the Camel Snus one and I wrote back to
5 Stockholm and Richmond as to what I thought.

6 And my lead was something that Mitch
7 Zeller said was that the discussion is just as
8 important as the votes. And I think that's a
9 very healthy way of looking at the TPSAC. The
10 votes in our case, they actually change the
11 nature of the questions that are voted on. But
12 you do get good discussion. You get a sense as
13 to what an educated group is thinking. Obviously
14 some have more expertise than others in certain
15 areas. But it's a good situation to sit through
16 and try to get a sense as to what is thought.

17 The other thing, the consultants I
18 find to be very useful. I mean I think that's a
19 good addition to the TPSAC that they have these
20 consultants who can advise the TPSAC members on
21 certain areas.

22 MS. KOVACEVIC: If I may, with respect

1 to the recent communication between applicants
2 and the center. You know, some types of
3 scientific review probably take longer than
4 others. So while there is benefit of having
5 fewer of AI requests, perhaps if some steps of
6 the scientific review such as for instance the
7 chemistry review is completed sooner, it would be
8 nice to get those questions immediately out to
9 the -- or those follow-up questions immediately
10 out to the applicants just because it will allow
11 them more time. And sort of reserve -- rather
12 than waiting for all of the various scientific
13 reviewers, you know, to bring their questions
14 back and issue one letter. Because again, that
15 may help applicants provide the answers in a
16 sequential matter, rather than struggle with 50
17 questions at once.

18 MS. STARK: So I want to clarify
19 because other centers have actually run pilot
20 programs where they will actually issue
21 discipline review letters, rather than a full
22 review letter.

1 MS. KOVACEVIC: Correct, correct,
2 correct.

3 MS. STARK: So are you proposing for
4 us to look at --

5 MS. KOVACEVIC: Yes, ma'am.

6 MS. STARK: -- a discipline review
7 letter, rather than the full --

8 MS. KOVACEVIC: Yes, ma'am. Exactly
9 right. Thank you.

10 MS. RUDOLPH: So we're coming to a
11 close here. Any last final thoughts from our
12 panel? Okay, thank you very much.

13 As our panelists transition back to
14 their seats, we will be having two more
15 presentations before we have lunch. So this is
16 Session three and we have got our colleague,
17 Barbara Banchemo, who will be talking about
18 presubmission meetings with the Office of
19 Science.

20 Somebody who's in charge of the
21 computer, can you find the presentation for
22 Barbara?

1 MS. BANCHERO: Bear with us. Okay,
2 good morning, almost afternoon. Thank you all
3 for coming today. My name is Barbara Banchero.
4 I am also a regulatory health project manager
5 within CTPs Office of Science. I will be
6 speaking today about the process for tobacco
7 product manufacturers, researchers, and
8 investigators to request meetings with the Office
9 of Science regarding their research and
10 development plans related to tobacco products.

11 Today I will orient you to currently
12 available resources and processes for CTP to meet
13 with industry. Then I will focus on the meeting
14 request itself. Specifically items applicants
15 may wish to consider when preparing their
16 request. This will be followed by a discussion
17 on how FDA intends to evaluate whether to grant
18 or deny a meeting request. Then we will continue
19 discussion of the meeting's process by reviewing
20 the types of communications applicants will
21 receive after submission of a meeting request.
22 And lastly, I will provide an update on the

1 performance goal for the meeting's program.

2 MS. BANCHERO: We need a little
3 technical support.

4 MS. RUDOLPH: Anybody who's presented
5 before, besides pressing the little arrows, any
6 other thoughts? Yes, and there's a -- there we
7 go.

8 MS. BANCHERO: Okay.

9 MS. RUDOLPH: Okay. And you may need
10 to click --

11 MS. BANCHERO: Okay, I'll just have to
12 click the button a lot. All right. Sorry about
13 that.

14 So in 2006, the FDA made two primary
15 resources regarding the meeting's process
16 publically available. First being the current
17 guidance dated July 2016. This guidance provided
18 editorial changes from the original May 2012
19 guidance and discusses among other things, what
20 information FDA recommends you include in your
21 meeting request. How and when to submit a
22 request. And what information FDA recommends you

1 submit prior to the meeting.

2 To accompany this document, FDA
3 maintains a dedicated landing page on the
4 guidance website for the meeting's program. Here
5 you will find hyperlinked questions and answers
6 that are frequently asked. And information on
7 how to access our electronic submission tools and
8 our contact information.

9 On CTPs tobacco compliance webinar, we
10 encourage you to review the 2006 webinar
11 entitled, "Meeting with the Office of Science"
12 which provides over 40 minutes of content
13 specifically for the meeting's program. It's
14 important to note that although the webinar
15 references the May 2012 addition of the guidance,
16 the content still aligns with our current
17 addition of the guidance. The guidance
18 frequently asks questions. Web site and webinar
19 were developed to provide consistent principles,
20 procedures for the meeting with the Office of
21 Science. We do encourage you to review them,
22 alongside today's presentation prior to

1 submitting your meeting request.

2 The meeting request process can be
3 viewed as occurring over three phases. First, a
4 decision is made to grant or deny the applicant's
5 request for the meeting. Second, if the meeting
6 is granted, the FDA performs a review of the data
7 and information submitted. And lastly, the
8 meeting is convened to provide feedback and
9 guidance on questions raised by the applicant in
10 their request.

11 So FDA recommends that meeting may be
12 held well in advance of a planned pre-market
13 submission so that the applicant has the
14 opportunity to consider FDA discussion points and
15 feedback prior to their full application.

16 Let's review some considerations to
17 aid you in preparing a complete meeting request
18 for submission and review through the Office of
19 Science. We suggest you clearly identify your
20 purpose for meeting with the FDA and include your
21 goals and objectives that you wish to achieve as
22 a result to the meeting. This information is

1 used for us to understand whether convening a
2 meeting will support the research and development
3 of tobacco products.

4 The Office of Science generally holds
5 meetings for two purposes. First, presubmission
6 meetings are beneficial to receive feedback on
7 your product development plan. In this example,
8 it would be appropriate for the FDA to meet for
9 pre-PMTA meeting to discuss questions regarding
10 the applicant's clinical study or sampling plans.

11 Second, the Office of Science holds
12 informational meetings, which are requested to
13 convene a listening session to gain scientific
14 knowledge on a topic of relevancy to FDA
15 programs. This may be initiated by industry or
16 FDA, but are not intended to discuss specific
17 tobacco applications or products. This
18 presentation will focus on presubmission
19 meetings.

20 Okay, when preparing your agenda, keep
21 in mind, the FDA intends to schedule meetings for
22 approximately one hour. Therefore we recommend

1 your proposed agenda provide adequate time for
2 discussion on these topics or you need specific
3 clarification from the FDA. In keeping with the
4 pre-PMTA meeting example shown earlier, here is
5 an agenda where the requestor plans to present
6 background information followed by a scientific
7 and regulatory discussion that aligns with the
8 objectives outlined in their meeting request.
9 Also note, additional time is allotted at the end
10 of the meeting for the applicant to summarize
11 their understanding of the meeting outcomes and
12 discussion.

13 It is also important for you to
14 include the professional background and
15 experience of your attendees. This information
16 helps us understand the scientific disciplines
17 necessary to review and evaluate your materials,
18 as well as additional CTP, FDA, or external
19 consultants that may be needed. Therefore for
20 each of your attendees, we recommend you include
21 their name, title, position, credentials, and
22 company that they're affiliated with. You are

1 welcome to request attendance of specific FDA
2 staff. However, if a meeting is granted, the FDA
3 will make the final determination of FDA
4 personnel assigned to the meeting request.

5 We recommend you propose a meeting
6 format for the meeting. However, based on the
7 amount of discussion needed, attendees, the FDA
8 will make the final decision on the format of the
9 meeting. And may change the format from what you
10 requested. Face to face meetings are held on
11 site at our FDA campus and our appropriate or
12 extensive discussion and clarification is
13 anticipated.

14 As an alternative perhaps due to
15 travel considerations, holding the meeting by
16 teleconference or phone is an option available to
17 you. You or the FDA may determine that based on
18 your questions or objectives, extensive
19 discussion is not anticipated. Therefore
20 feedback by letter or written response to your
21 question alone without further discussion is also
22 sufficient. You are welcome to include proposed

1 dates to hold the meeting based on your attendee
2 availability. However, the date of the meeting
3 will be scheduled to ensure that the FDA has
4 sufficient time to review meeting materials and
5 prepare responses to your questions.

6 Let's now look at what materials we
7 recommend you provide for the meeting. Your
8 meeting request should provide a preliminary list
9 of questions that are scientific or regulatory in
10 nature. And specific to your product development
11 plan and align with your objectives in your
12 request. Also consider how best to group your
13 questions, maybe by issue, study, or discipline.

14 FDA recommends final questions and
15 summary information and data relevant to your
16 products be submitted at least 45 days in advance
17 of the meeting. You also have the option to
18 submit your final questions and meeting package
19 within your meeting request. By doing so, if
20 granted, your meeting could be held within 45
21 days of the meeting request receipt.

22 Here are some recommended items to be

1 included in your meeting information package.
2 It's important to note that summarized material,
3 rather than full study reports and detailed data,
4 are appropriate for meeting packages. The FDA
5 understands the content of your meeting package
6 will vary based on the product application and
7 phase of tobacco product development. Therefore
8 we encourage you to review the previously
9 discussed resources, application specific
10 recommendations for the types of information that
11 could be included in your meeting information
12 package.

13 We recommend your meeting package be
14 current. Keep in mind, if you update your
15 meeting package and these changes are large or
16 complex, the FDA may choose to reevaluate whether
17 to postpone your meeting. For example, the FDA
18 might postpone the meeting to give staff
19 appropriate time to review the meeting materials.

20 Now that we've reviewed some
21 considerations of what to include in your meeting
22 request and meeting information package, I'd like

1 to take the opportunity to discuss how OS
2 considers whether to grant or deny a meeting
3 request. The evaluation factors were discussed
4 in detail within our 2016 meeting with the Office
5 of Science webinar. As an overview, when a
6 meeting request is received, the RHPM and the
7 technical project lead where appropriate, will
8 evaluate whether the meeting contains information
9 recommended in the guidance such as a list of
10 preliminary specific questions.

11 It is also useful for FDA to
12 understand whether the meeting is necessary or
13 appropriate. A meeting may not be necessary or
14 appropriate for example if the information
15 requested is already available to the requestor
16 such as guidance, regulation, or if a previous
17 meeting was held with the applicant for the same
18 purpose.

19 And lastly, it's recommended your
20 meeting be timely. A meeting may not be timely
21 for example, if the questions asked relate to
22 scientific disciplines and a pending application.

1 If the answer is yes to all these questions, the
2 meeting may be granted.

3 Meetings are beneficial to receive
4 feedback on your product development plan.
5 However the advice is not decisional. And
6 meetings are not intended to serve as a
7 substitute for an applicant's responsibility to
8 develop their own research plans or perform their
9 own data analysis. Therefore if the scope of the
10 meeting request or questions are intended for
11 these purposes, the meeting request may be
12 denied.

13 Similar to other programs, the FDA
14 intends to communicate its decisions for the
15 meetings program in writing. Therefore it would
16 be helpful to review the meeting process
17 alongside the types of communications that you
18 may receive following the submission. And
19 evaluation of your meeting request, as well as
20 leading up to following the meeting.

21 After evaluation of the meeting
22 request, the FDA will issue one of two types of

1 correspondence. If submitted information is
2 inadequate to continue scheduling a meeting with
3 the applicant, will receive a meeting denial
4 letter which will include the reasons for denial.
5 If denied, the applicant has the option to submit
6 a new meeting request once they have had the
7 opportunity to provide sufficient information.

8 If the meeting request is accepted by
9 the FDA, the applicant will receive a meeting
10 granted letter. Please refer to this letter for
11 logistical information such as the date and time
12 and location of the meeting. The date the
13 meeting package is to be received by the FDA. A
14 tentative list of FDA disciplines that will be
15 attending the meeting. And the name and
16 information of your RHPM who's assigned to your
17 meeting request.

18 FDA's review of the meeting
19 information package is multidisciplinary.
20 Individual disciplines will be assigned based on
21 the objectives and questions raised in the
22 request. In our pre-PMTA meeting scenario, the

1 meeting was to discuss biomarker endpoints and
2 inspections. And therefore include reviewers
3 such as a toxicologist, statistician, chemist,
4 and engineer. As well as members from our Office
5 of Compliance and Enforcement.

6 At the end of the review, FDA will
7 issue one of two types of correspondence. For a
8 final written response, the applicant will
9 receive a letter with feedback where appropriate
10 to each question raised in their meeting package.
11 This is a final correspondence and the meeting
12 request is closed. A face to face meeting is not
13 convened. If the requestor has new questions,
14 they may submit a new request.

15 A preliminary response letter is
16 issued prior to a face to face or teleconference
17 meeting. FDA provides its preliminary feedback
18 to the applicant where appropriate to each
19 question raised in their meeting request package.
20 Excuse me. The feedback is considered
21 preliminary because it is pending the applicant's
22 determination if additional clarification or

1 discussion is needed at the subsequent meeting.

2 If the applicant reviews the
3 preliminary response and determines no additional
4 discussion or clarification is needed from the
5 FDA, they may choose to cancel the meeting. In
6 this case, the response would be considered
7 final.

8 If following the preliminary response,
9 the applicant determines additional discussion is
10 needed, then the meeting will take place as
11 agreed upon. It is important to note that the
12 meeting is a forum to discuss questions raised in
13 the meeting request. If there are any major
14 changes to the product's development plan, the
15 purpose of the meeting or questions the FDA may
16 not be prepared to discussed or provide comments
17 on those changes to the meeting.

18 FDA intends to provide meeting minutes
19 within 45 days of the meeting. This document
20 will summarize discussion points, decisions,
21 recommendations, agreements, disagreements,
22 issues for further discussion, and action items.

1 Applicants can notify the FDA if their
2 understanding of discussion during the meeting,
3 differs from the meeting minutes. The FDA may
4 provide clarification of them in a letter. While
5 applicants may submit a copy of their own minutes
6 to the FDA, the FDA's minutes will serve as
7 official minutes of the meeting.

8 Oops. Yes, sorry. Prior to FDA
9 issuing a meeting granted letter or denied
10 letter, the applicant may decide to withdraw
11 their meeting request by sending a letter to CTP.
12 Once the meeting has been granted, the applicant
13 may decide a meeting is no longer needed and can
14 send a letter to CTP requesting the meeting be
15 cancelled. If the applicant submits subsequent
16 meeting requests, the FDA will consider this a
17 new meeting request.

18 The FDA intends to take reasonable
19 steps to avoid cancelling a scheduled meeting.
20 However, a meeting may be cancelled by the FDA
21 for reasons such as the meeting objectives within
22 the meeting request and meeting information

1 package are significantly different or meeting
2 information package is not received by the
3 requested due date.

4 In 2014, the FDA established
5 performance measures to improve the timeliness
6 and predictability for this program. For meeting
7 management, the current performance measure is to
8 respond to meeting requests within 21 days of
9 receipt. At fiscal year 2017 and through fiscal
10 year 2022, the performance measure is at 90
11 percent.

12 Responding means the FDA accepts or
13 denies a meeting request. It is important to
14 note that this performance goal refers only to
15 meeting requests from external entities of the
16 government such as regulated industry. Therefore
17 questions submitted through the CTP call center
18 are not subject to this measure.

19 And let's look at the requests we've
20 received for fiscal year 2018. Specifically for
21 the Office of Science. The Office of Science has
22 received 16 meeting requests. Nine meetings have

1 been granted. Two additional meetings were
2 granted, but cancelled by the applicant prior to
3 the meeting. And three meeting requests were
4 denied. Two meeting requests were withdrawn by
5 the requestor prior to FDA issuing a meeting
6 decision letter.

7 Thank you all for your time this
8 afternoon. I encourage you to ask questions
9 during the panel discussion, in addition to
10 listening to talks tomorrow on the content of
11 each application, which may inform your meeting
12 request. Again we encourage you to consider
13 meeting with the FDA well in advance of
14 submitting a pre-market application. Thank you.

15 MS. VICHENSONT: I think we're running
16 a little over. And everyone's probably really
17 hungry, so we'll take a lunch break now. And an
18 hour?

19 MS. RUDOLPH: We'll probably come back
20 -- let's see what time we are. Oh, look at that,
21 if we take that hour. Okay, so we'll all come
22 back at 1:15.

1 MS. VICHENSONT: 1:15.

2 (Whereupon, the above-entitled matter
3 went off the record at 12:16 p.m. and resumed at
4 1:18 p.m.)

5 MS. RUDOLPH: Welcome back from lunch
6 everyone. I hope everybody found something
7 enjoyable to nosh on.

8 As we head into the afternoon on our
9 first day of this public meeting we'll be
10 listening to an upcoming presentation on tobacco
11 product master files and then go on into the
12 panel discussion for Session 3.

13 Following that we have two more
14 sessions for the remainder of our day. So with
15 that note I am going to turn things over to
16 Sarah, although we do have some folks who are
17 filing in, just come on in.

18 MS. VICHENSONT: The slides, please.
19 The next set of slides. There we go. All right,
20 good afternoon, everyone. Hopefully everyone
21 enjoyed their lunch and ready to pay attention
22 about master files.

1 My name is Sarah Vichensont. I am
2 also a regulatory health project manager within
3 CTP's Office of Science and today my presentation
4 will focus on tobacco product master files, also
5 known as TPMFs.

6 This presentation will briefly cover
7 the following topics, an overview of the TPMF
8 program, some key terms, type of information to
9 include in a TPMF, the establishment process for
10 a TPMF, how and when a TPMF is scientifically
11 reviewed, the closure process, best practices for
12 TPMF owners, and some key take home points.

13 Let's start with an overview of the
14 TPMF program. CTP receives submissions required
15 by law, such as health documents, ingredient
16 listings, and applications.

17 To ensure compliance with the law some
18 of these documents include information that is
19 trade secret and/or confidential commercial
20 information for multiple sources.

21 For example, if a tobacco product
22 manufacturer was providing ingredient listing on

1 a tobacco product but purchased a component from
2 a component manufacturer ingredient information
3 on that component must still be provided.

4 So how could the component
5 manufacturer allow for use of this information
6 without the threat of substantial competitive
7 harm? The recommended approach from CTP is a
8 tobacco product master file.

9 A TPMF is a file that is voluntarily
10 submitted to CTP that contains trade secret
11 and/or CCI about a tobacco product or component
12 that the owner does not want to share with other
13 persons.

14 TPMFs are a beneficial tool for
15 manufacturers, component suppliers, ingredient
16 suppliers, and researchers and can assist in a
17 tobacco product's submission process.

18 So how does a TPMF -- No. A TPMF
19 owner call allow an authorized party the right to
20 reference a TPMF in support of a tobacco product
21 submission to CTP.

22 CTP can then access and review the

1 confidential information as part of their
2 submission but at no point in time does the
3 authorized party see or have access to that
4 confidential information.

5 Let's look at this through an example.
6 A cigarette manufacturer, Company A, intends to
7 submit a pre-market tobacco product application,
8 such as a PMTA, for a cigarette.

9 Company A utilizes rolling paper
10 purchased from Company B in their cigarette. For
11 the PMTA it is necessary to provide the full
12 listing of ingredients, materials, and
13 composition of the rolling paper.

14 However, Company B does not want to
15 provide that information to Company A. Instead,
16 Company B can establish a TPMF that includes all
17 of the rolling paper information.

18 Company B can provide Company A
19 authorization to reference its TPMF in a letter
20 of authorization, or LOA, and also provide a copy
21 of that LOA to CTP.

22 Now Company A can submit a PMTA and

1 CTP can look on behalf of Company A all of the
2 rolling paper ingredients, materials, and
3 manufacturing information located in Company B's
4 TPMF.

5 This benefits Company A to ensure a
6 complete application and benefits Company B by
7 allowing use of their rolling paper information
8 without disclosing it to Company A.

9 Additionally, the TPMF program
10 mutually benefits TPMF owners who can reference
11 their own master file rather than submitting
12 information separately for multiple submissions.

13 So by allowing FDA to keep certain
14 information on file within a TPMF it streamlines,
15 simplifies, and potentially reduces associated
16 costs and time related to administrative work
17 because a company would not need to resubmit data
18 for future applications, thus easing the
19 application burden.

20 For example, if a manufacturer,
21 Company C, utilizes the same tobacco blend in 50
22 products they can submit a TPMF that includes all

1 ingredients, composition, and manufacturing
2 information for that tobacco blend.

3 In lieu of recording this information
4 in 50 pre-market applications CTP could just
5 reference their own TPMF. This would save time,
6 reduce errors, as the manufacturer would only
7 have to provide this tobacco blend once rather
8 than copying it and pasting it 50 times in
9 multiple submissions.

10 In order to assist industry in TPMF
11 submissions the FDA has published a TPMF guidance
12 in May of 2016. This guidance document includes
13 information such as how to establish a master
14 file, considerations for TPMF owners and
15 maintaining TPMF submissions, how other persons
16 can use a TPMF, and FDA's role.

17 It is important to note that CTP is
18 encouraging regulatory correspondence
19 electronically via the CTP portal or electronic
20 submission gateway using eSubmitter, or,
21 alternatively, by mail through the Document
22 Control Center.

1 Electronic submission is generally
2 available 24 hours a day, seven days a week.
3 Therefore, it is encouraged to send TPFM
4 submissions electronically through the CTP
5 portal.

6 CTP also has a webinar on our website
7 titled "Using a TPFM for Ingredient Listing
8 Submissions" in September of 2018. This webinar
9 reviews examples of ingredient-listing scenarios
10 that a TPFM can address and how to cross
11 reference TPFMs for ingredient submissions.

12 There are three processes that can
13 occur over a life cycle of a TPFM, which I will
14 go into a little bit more detail a little later
15 in the presentation.

16 There is an establishment process, a
17 stage where a request to establish a TPFM is
18 received and submitted to CTP and CTP
19 acknowledges the receipt.

20 There is also a scientific review
21 process, the stage when a submission references
22 the TPFM. At this point a TPFM scientific review

1 occurs and ends with a determination of adequate
2 or inadequate.

3 Depending on the TPFM there may be
4 multiple scientific reviews occurring at the same
5 time if there are multiple submissions
6 referencing the master file.

7 And, lastly, there is a closure
8 process, the stage when a TPFM owner may choose
9 to close its master file or CTP initiates a TPFM
10 closure if it has not been active in three years.

11 Before I discuss the three processes
12 into a little more detail it is important to
13 describe and understand some key terms. CTP
14 considers a TPFM owner or owners as an entity.
15 For example, it could be a person, a company, or
16 a subdivision of a company that owns the
17 information contained within the master file.

18 Unless otherwise stated by the owner
19 an authorized representative is a person who is
20 authorized to reference and represent and
21 communicate to CTP on behalf of the owner and is
22 able to make decisions regarding the master file,

1 for example to grant or rescind a letter of
2 authorization.

3 CTP considers an authorized party a
4 person who has been granted authorization to
5 reference a TPMF, which is typically obtained in
6 writing within an LOA from the owner.

7 This LOA, which stands for letter of
8 authorization, is a document prepared by the
9 owner or authorized representative that grants a
10 person authorization to reference its master
11 file.

12 This LOA should also identify any type
13 of limitations to the authorization, for example
14 if the owner is only allowing the company
15 authorization to reference only certain sections
16 of the TPMF.

17 Now let me walk through some type of
18 information to be included in a TPMF. A TPMF can
19 be organized into two parts. There is an
20 administrative information section and a content
21 information section.

22 The admin information section contains

1 items recommended for the owner to establish a
2 master file, for example a cover letter, table of
3 contents, list of authorized representatives, a
4 list of authorized parties, and any limitations
5 to each of that authorization.

6 The second section, the content
7 information section, should contain information
8 that the owner wishes to be referenced.

9 Currently there are no requirements for structure
10 but CTP recommends the master file be organized
11 in a logical manner.

12 On the slide are some examples of
13 information you can include. For example, if the
14 master file contains specific tobacco products
15 this section may include information such as
16 tobacco blend information, HPHC methods, design
17 information, an ingredient listing, manufacturing
18 and process data, or research findings.

19 If a TPMF contains a clinical study
20 this section may also include information such as
21 the protocol, a statistical analysis plan,
22 subject information, data analyses, adverse event

1 reporting, and informed consent forms.

2 A TPMF can also contain information to
3 support grandfathered determination. I recommend
4 you refer to the other presentations that were
5 presented earlier this morning and tomorrow for
6 what to include in these types of submissions.

7 On the screen is an example of how to
8 present information within a cover letter. Note
9 that the subject line is clear, that it is a
10 request to establish a CTP tobacco product master
11 file.

12 The contact for the owner is present,
13 which includes a mailing address, phone number,
14 and email address. The submission lists
15 authorized parties and each company's
16 authorization for limitations and the submission
17 is signed by an authorized point of contact for
18 the company.

19 Using the same example here is how to
20 present information in an LOA. CTP recommends
21 that the applicant, Company A in this example,
22 include its LOA when submitting an application

1 that references a master file.

2 Note that the subject line is clear
3 that this is an attachment for an LOA from the
4 owner. The letter of authorization also includes
5 the TPMF submission tracking number, or STN, and
6 includes their limitations to the authorization,
7 for example only Section A for Rolling Paper X,
8 and the LOA is signed by the owner.

9 Now that we have an idea of what a
10 master file is let's move on to discuss the TPMF
11 establishment process. Upon receipt of a new
12 request to establish a TPMF CTP will review the
13 submission to ensure it contains enough
14 information to establish a master file.

15 As mentioned a few slides earlier CTP
16 looks for several items in the request cover
17 letter. For example, is the cover letter signed
18 by the owner and does the file support submission
19 to CTP, like PMTAs.

20 If information is present to establish
21 a master file CTP will issue an acknowledgment
22 letter in a timely manner to the owner confirming

1 receipt and establishment.

2 The letter identifies the owner, the
3 CTP assigned STN, and contact information for the
4 regulatory health project manager, or RHPM, and
5 information on how to update the TPMF.

6 Receiving an acknowledgment letter
7 means that the owner's file is established within
8 CTP and ready to be used as a reference by other
9 tobacco product submissions.

10 If additional information is needed
11 for establishment CTP will contact the owner. We
12 tend to work with the submitter to ensure all of
13 the requested information is present and
14 received.

15 So you may be wondering when does the
16 content within a TPMF undergo scientific review.
17 Consistent with other FDA centers CTP does not
18 intend to conduct a scientific review of the TPMF
19 at the time of its submission.

20 CTP intends to conduct a scientific
21 review of a TPMF only when the TPMF is being
22 referenced in an authorized party's submission to

1 CTP.

2 This is because different submissions
3 may have different information content needs.
4 For example, there are differences in review for
5 an ingredient listing versus a PMTA.

6 If the TPFM were referenced to support
7 ingredient listing CTP would focus on the review
8 of ingredient requirements such as product
9 identification, ingredient identification, part
10 to which the ingredient is added, and the
11 ingredient quantity.

12 Contrast that where the same TPFM are
13 referenced to support a PMTA. In this scenario
14 CTP would focus on the review of the components,
15 ingredients, additives, properties, principle of
16 operation, methods used in the manufacturing and
17 processing and testing data.

18 As you can see CTP takes a different
19 look at the same data based on the submission
20 that references it.

21 So how does the TPFM scientific review
22 process work? Upon receipt of a submission, such

1 as a PMTA that reference a master file CTP will
2 first verify that the applicant is an authorized
3 party and the extent of the applicant's
4 authorization, for example is the applicant only
5 authorized to reference a TPMF for a particular
6 PMTA or for all PMTAs.

7 If the applicant does not have
8 authorization from the owner CTP will inform the
9 applicant and CTP will not review the master
10 file.

11 To facilitate this process it is
12 recommended that the applicant include the
13 following within their application, a valid LOA
14 to reference the master file, a notation in the
15 cover letter of the TPMF STN being referenced,
16 and, if possible, where the information is being
17 referenced is located in the TPMF.

18 Once CTP determines that the applicant
19 is authorized to reference the master file CTP
20 will then begin scientific review of both the
21 application and the master file.

22 When reviewing the master file CTP

1 will review the extent of information authorized
2 in the letter of authorization and this review
3 based on the reference will result in CTP finding
4 the information adequate or inadequate.

5 So let's presume that in reviewing the
6 master file concurrent with the PMTA CTP
7 determines that the master file content is
8 adequate.

9 This means that the TPMF information
10 being referenced by the PMTA is sufficient and
11 CTP will continue scientific review of the PMTA.
12 Because there were no deficiencies in the master
13 file that was reference and reviewed CTP will not
14 send a letter to the TPMF owner.

15 So what happens if CTP determines that
16 the master file content is inadequate? If issues
17 are found within the master file during
18 scientific review CTP will send letters to both
19 the owner and the PMTA applicant.

20 However, information provided to the
21 PMTA applicant is limited. The owner will
22 receive a letter detailing each of the specific

1 deficiencies and a request to respond within a
2 requested timeframe to amend its master file.

3 In contrast, the PMTA applicant will
4 receive a letter that will simply cite that
5 deficiencies were found within the master file
6 which have been communicated to the owner already
7 and specific details about how the TPMF is
8 deficient is not relayed to the applicant.

9 Depending on the review stage this
10 letter to the PMTA applicant may request a
11 timeframe for a response. By following this
12 process CTP does not convey specific deficiencies
13 to the authorized party as to not disclose the
14 trade secret or CCI.

15 At this point two letters have issued,
16 one to the owner and one to the PMTA applicant.
17 The CTP review timeline is based on the PMTA.
18 Remember that this is the application with a
19 timeline in which CTP must make a final decision.

20 Therefore, once the date requested to
21 respond to the PMTA deficiency letter has passed
22 or CTP has received a complete response to the

1 PMTA letter, whichever is first, scientific
2 review of the PMTA and amended TPFM will
3 commence. CTP will then issue an appropriate
4 letter consistent with the PMTA process.

5 It is important to note that the
6 authorized party is solely responsible for
7 ensuring that their pre-market application and
8 supporting documents, which would be the master
9 file in this case, is adequate to support all
10 statutory requirements.

11 So in the example where we discussed
12 the PMTA applicant is referencing the master file
13 it is the PMTA applicant's responsibility to
14 ensure that the owner responds within the
15 requested timeframe and that all documents
16 support the statutory requirements for a pre-
17 market order.

18 If the TPFM owner does not respond or
19 fails to provide documents necessary to support a
20 pre-market order the order is likely to be
21 denied.

22 We encourage the authorized party and

1 the TPMF owner to communicate and coordinate
2 their responses to our letters so that CTP's
3 comments are adequately addressed in the
4 requested timeframe.

5 So far we have discussed the
6 establishment and scientific review of a TPMF.
7 Additionally, there is a closure process which
8 may be initiated by either the owner or CTP.

9 Being able to close a TPMF is
10 important and beneficial for owners because there
11 may be work associated with keeping the TPMF up
12 to date.

13 If an owner wishes to close its master
14 file the owner should notify CTP in writing and
15 include the reason for requesting closure of the
16 file and the date to which the TPMF should be
17 closed.

18 It is recommended that the owner also
19 notify all persons currently authorized to
20 reference the master file of the closure because
21 once closed the TPMF will no longer be available
22 for reference by an authorized party and CTP will

1 no longer review the content when referenced in a
2 submission.

3 CTP intends to begin a closure process
4 if the master file has not been referenced in a
5 three year period and the master file has not
6 been updated during this time.

7 This may occur, for example, if the
8 owner is not responsive to CTP's letters
9 requesting information for a reference
10 submission.

11 However, prior to CTP-initiated
12 closure of a master file CTP intends to issue a
13 notification letter to the owner of the intent to
14 close.

15 With this notification letter a
16 timeframe will be provided for the response. The
17 owner may choose to keep its master file open.
18 CTP encourages the owner to respond within the
19 requested timeframe with its intent.

20 If there is no response to the
21 notification letter CTP will move forward with
22 TPFM closure. Now that we have discussed the

1 closure process let's review some best practices
2 for TPMF owners.

3 In general owners are responsible for
4 three main items. One, serving as a point of
5 contact for the master file. This includes being
6 able to maintain a complete and current copy of
7 the master file.

8 Two, notifying CTP and authorized
9 parties of any changes in the master file. This
10 includes notifying CTP of any changes to the list
11 of authorized parties or changes to their
12 limitations or notifying CTP of a transfer of
13 ownership of the master file, and, three,
14 responding to deficiency letters within the
15 requested timeframe.

16 I would like to end with some key take
17 home points from this presentation. First,
18 master files are a beneficial tool for
19 manufacturers, component suppliers, ingredient
20 suppliers, and researchers and can assist in the
21 tobacco product submission process.

22 Secondly, the applicant or authorized

1 party at any point in time does not see or have
2 access to the TPMF content. Third, a TPMF is
3 reviewed when referenced by another submission.

4 Fourth, CTP reviews the master file in
5 the scope and context of the referenced
6 submission. And, lastly, timelines for a TPMF
7 review depend on the referencing submission.

8 This concludes my presentation. I
9 understand that was a lot of information to
10 consider. If you have any questions I recommend
11 you ask questions during the panel discussion.

12 You may also contact your assigned
13 RHPM. Their name and contact information is at
14 the bottom of the letters. If you do not know
15 who your assigned RHPM is or if you are new and
16 not have yet submitted a TPMF you may contact our
17 call center, Office of Small Business, Office of
18 the Ombudsman, or just email askctp@fda.hhs.gov.
19 Thank you for your time.

20 (Applause.)

21 MS. RUDOLPH: Okay, everybody. So as
22 we head into this afternoon we've got a nice

1 panel to get started with if the panelists will
2 come on up. Thank you.

3 As was stated previously in the
4 morning we are giving all of our outside guests
5 the opportunity to introduce themselves and use
6 five minutes of time to communicate their
7 thoughts on what we are talking about here today,
8 and we are doing this in alphabetical order, and
9 we get to start here with Bryan.

10 MR. HAYNES: Thank you and thanks for
11 having me here today and thanks for conducting
12 this meeting.

13 Sitting here and listening to the
14 remarks I keep thinking, boy, I wish I knew all
15 this stuff eight years ago when we started doing
16 all this stuff.

17 So my observations about meetings
18 first, pre-submission meetings. So first of all
19 we appreciate the opportunity to have these. We
20 think they are helpful, so it's good that we have
21 meetings.

22 I think that the process for

1 scheduling these meetings has improved. The time
2 from the request to the actual meeting my
3 observation, and I don't have any data to support
4 this, is that it is shortened, so that's good.

5 I think you do a very good job of
6 having the right personnel at these meetings to
7 answer the questions that are being put in front
8 of you and that probably influences the
9 scheduling, right, to make sure that all the
10 stakeholders are at the meeting, but you do a
11 very good job of that.

12 The written responses that we get in
13 advance of the meeting are helpful, including
14 whether we want to have a meeting at all, but
15 usually that helps at least narrow the issues
16 that you'll actually talk about, recognizing that
17 the time for these meetings is limited.

18 Coming from industry, we might like to
19 sit down with you for longer than an hour, maybe
20 two, maybe three. We are also mindful of the
21 constraints on your time.

22 And I think like Jim said earlier we

1 try to look at things from your perspective and
2 if you spend all your time in meetings you
3 probably wouldn't get anything else done, but
4 sometimes, you know, we would like to have more
5 time with you when warranted under the
6 circumstances.

7 Like any meeting, whether it's one
8 with the Office of Science or anybody else, these
9 meetings are more effective when you are better
10 prepared, and part of that is on us to be better
11 prepared, and as we have sort of gone through the
12 learning process with CTP over the last eight
13 years I feel like that's happened.

14 I think though about meetings and the
15 context of the deeming regulations and the newly
16 deemed products, obviously CTP will have some
17 outputs around that hopefully sooner rather than
18 later.

19 I think those outputs could inform
20 meetings and make applicants better prepared for
21 those meetings. So applicants might have a
22 chicken and egg issue, do you ask for a meeting

1 before you get more guidance from CTP, I think my
2 preference would be to get more guidance from CTP
3 before you conduct a meeting. So that would be a
4 preference.

5 Other areas of potential improvement,
6 maybe even shortening the time from the meeting
7 request to the meeting. In some circumstances
8 that would be very helpful.

9 More meetings. Somebody mentioned
10 earlier it could be good to have more than one
11 pre-submission meeting, particularly for a pre-
12 market review program that from start to finish
13 might be over the course of a few years.

14 You don't have all the answers in your
15 first meetings. Things come up. And so some
16 leeway in that regard would be good.

17 Meetings during the review process.
18 I have detected a strong bias against that. I
19 would like at times to have some relief from that
20 bias.

21 I have seen that the communication
22 process is less binary than it used to be. It

1 was kind of all or nothing either in writing or
2 nothing else that it's become less binary.

3 I would like it to become even less
4 binary. So in certain circumstances I think it
5 could be very helpful to have meetings during the
6 review process.

7 And then lastly I go back to my time
8 as a litigator, you know, you write a brief, you
9 can't put everything in a brief. Sometimes you'd
10 like to talk to the judge about what you did and
11 why you did it and I think you've spent three
12 years getting something together it would be nice
13 to sit in front of you guys and explain
14 everything we have done, why we did it, and
15 answer questions, and that might alleviate some
16 of the potential for miscommunication during the
17 review process.

18 I don't have much to say about master
19 files, which is good because I think my time is
20 short. We haven't spent much time submitting
21 master files mainly because of my concern about
22 submitting I guess what would be a partially

1 blindfolded submission that I can't see things
2 that we are submitting and it's always been my
3 concern that if something comes up in the review
4 process because it's proprietary or CCI that you
5 can't share it with me and then I don't know how
6 to respond to it.

7 Fortunately I haven't had to do that.
8 Maybe somebody could comment on how you deal with
9 that. Thank you.

10 MS. P. MILLER: So, first of all, I
11 want to thank CTP for having this workshop. I
12 think it's a great opportunity for two-way
13 communication and learning and I've already
14 learned a lot of things today, so thank you for
15 having it.

16 I'm Patricia Miller and I'm senior
17 director in law and regulatory affairs in Altria.
18 Altria, over the last several years, has had a
19 bit of experience with meetings as well as TPMS.

20 I'm going to limit my comments to
21 meetings, I'll let Russ deal with the TPMS. I
22 would guess that we've had, over the last five

1 years, a little bit more than half a dozen, what
2 I would consider, pre-submission meetings.

3 We think of pre-submission meetings as
4 a tool to encourage innovation in reduced harm
5 tobacco products, and that's a really important
6 goal for us as I know it is for CTP.

7 As FTA and applicants are preparing
8 their information to support authorization of
9 innovative tobacco products, two key things are
10 important. One is the need for clear
11 foundational rules. And preferably by notice in
12 comment rulemaking.

13 So to the extent that we have more
14 guidance on what we're supposed to be doing,
15 potentially there's less need to have meetings.
16 And when we do have meetings, they could be more
17 efficient and perhaps targeted. If we have those
18 clear foundation rules.

19 When it comes to meetings, what we see
20 is a need for meetings throughout the application
21 process that allow for two-way communication. So
22 when you talk about the opportunity for meetings,

1 if you look at a true pre-submission meeting.

2 So before you ever file anything you
3 may want to have an introductory meeting to talk
4 about a novel tobacco product and talk about the
5 general parameters of your application. You may
6 want to have meetings about particular studies
7 that you're conducting, you may want to have
8 meetings to conduct the, to discuss the structure
9 in content of your application.

10 Even while an application is pending,
11 and Bryan alluded to this, there may be
12 opportunities for communication, in person, with
13 FDA, that is more useful than responding to
14 written questions in an A/I letter. Sometimes
15 that two-way communication could be helpful.

16 And even post-authorization. I can
17 see opportunities, for example, for an applicant
18 to have a conversation with FDA about a
19 supplement for modifications to an authorized
20 tobacco product. So, we see the need for
21 communication throughout the application process.

22 What I'm having difficulty with is,

1 I've heard a bit of that today from CTP, which I
2 think is helpful, but when I look, for example,
3 at guidance documents that CTP has. The current
4 guidance document, which was the one that was
5 issued in 2012 and updated in 2016, really talks
6 about meetings to discuss scientific research.
7 And particularly meetings with Office of Science.

8 Now, it's encouraging to have heard
9 here, encouragement about having pre-PMTA
10 meetings and pre-MRTP meetings. But what appears
11 that we have is kind of a one size fits all type
12 of meeting in terms of asking for that meeting
13 and the construct of that meeting, that goes with
14 that 2016 guidance which is more about research.

15 Our experience has been, well, I'll
16 just say, what's worked for us in the meeting
17 process so far, when we have particular
18 scientific questions, and particularly research
19 studies that we want to discuss and we pose them
20 to CTP in the way that's requested in the 2016
21 guidance, we have gotten the meetings.

22 We've had really helpfully meetings.

1 We've had good suggestions from CTP. And we've
2 had documented results of those meetings through
3 the minutes process, which is great.

4 What we still see is the need to kind
5 of break out of that one size fits all meeting
6 structure. It can sometimes be a burdensome.

7 You know, from the time that an
8 applicant asks for a meeting to the time you
9 actually have the meeting, is at least two
10 months. And then the meeting process, at least
11 as outlined in the one guidance, is a bit stilted
12 or scripted.

13 In other words, you submit your
14 request, you get a response back from FDA in 21
15 days, you submit a meeting information package,
16 which can be pretty voluminous at times, and then
17 your meeting is limited to the topics that you've
18 raised there.

19 I will say too, part of that process
20 is you get responses back from FDA two days
21 before the meeting. And I don't know about
22 others but that can be quite a scramble. When

1 you get responses back two days before and your
2 digesting those responses, trying to understand
3 them, trying to know what you still have
4 clarifying questions on and being ready for a
5 meeting in just two days, it can be difficult.

6 So, we would like to see a process
7 that at times can adjust to the type of topic and
8 where you are in the application process. That
9 would be really helpful.

10 And I will note also, in CTP's PMTA
11 guidance, there is a limit stated of one to two
12 meetings per applicant that can really limit
13 communication, particularly with innovative
14 tobacco products.

15 So, I will summarize to say, it would
16 be helpful to have clear foundational rules that
17 may alleviate some meetings and we would love to
18 see an array of types of meetings.

19 MS. RUDOLPH: Thank you. Russell.

20 MR. WOLZ: Yes, hi, I'm Russ Wolz, I
21 am from Enthalpy Analytical in Richmond,
22 Virginia. I'm here just to share some of our

1 experiences with the TPMFs.

2 As the name implies, Enthalpy
3 Analytical, we do analytical work. All hundreds
4 of different types of chemical analyses as well
5 as toxicological analyses.

6 We do these as routine analyses and as
7 part of PMTA submissions. The benefits, Sarah
8 has described very well what the content of the
9 TPMF can be.

10 In our case, in our case our TPMF
11 includes our methods and the validations of those
12 methods and our accreditations. So many of our
13 methods are public but we include them in our
14 master file.

15 We have established a master file.
16 And we included our methods in the master file so
17 that people who use our analytical services can
18 reference those methods and validations of the
19 methods in their PMTAs.

20 So, as Sarah has also very well
21 stated, the master files are a benefit, both to
22 the manufacturers who are submitting the PMTAs as

1 well as to the support mechanisms. So, it saves
2 us time by not having to create multiple reports
3 and send the same set of SOPs and validations to
4 a lot of different clients, we can just send it
5 all to central, very secure repository.

6 (Laughter.)

7 MR. WOLZ: Then we assign the right of
8 reference to certain clients. And we're still
9 learning this process.

10 Our first submission was actually a
11 hard copy document. And we then later updated
12 that to do electronic submissions, primarily in
13 the form of PDF files.

14 So when we move to the electronic
15 submission, so now I'm going to move on to some
16 of the challenges we've encountered. Your first
17 electronic submission, after you've established
18 your, or been accepted to establish a master
19 file, is done through a test site.

20 So we created our master file and
21 submitted it through the test site. Then as it
22 turned out, we thought we had submitted it as a

1 formal submission but it turned out not to be the
2 case. And it wasn't for two or three months that
3 we found out that, oh, we need to submit it
4 through the real site.

5 So, again, that was just education for
6 us and that's why I'm sharing these challenges
7 we've experienced with you.

8 The other challenge is simply in
9 organizing these files. We have hundreds of
10 methods, like, 250 methods, to organize.

11 First of all, to create a document of
12 that size is very challenging and then to
13 organize it is the additional challenge. So
14 we've very recently updated our master file in a
15 new format, which is now a PDF format with
16 hyperlinks to the various sections.

17 And within each section we actually
18 have hyperlinks to the actual SOPs and
19 corresponding validations.

20 The only thing that we would
21 recommend, that might help, is instead of having
22 one giant master file, like I said, we've

1 submitted only 31 of our more than 200 methods,
2 we might recommend that there be separate files
3 corresponding, organized in different ways.

4 So, for example, we could have a
5 master file dedicated to e-liquid analysis,
6 another one for combustibles, another one for
7 smokeless tobacco. So we would have, rather than
8 one gigantic file, which is hard to wade through,
9 even with all the hyperlinks, we think it might
10 be better organized to use instead of having one
11 big file, to use the electronic depository as
12 more of a folder instead of just a file.

13 So, like I said, Sarah did such a good
14 job explaining all the other things, that's all I
15 have for you today.

16 MS. RUDOLPH: Great, thank you. And
17 colleagues from FDA, would you like to introduce
18 yourselves?

19 MS. RANDAZZO: Hi, I'm Joanna
20 Randazzo, I'm a lead science policy analyst in
21 OS.

22 MS. DOLLING: Good afternoon, I'm

1 Marcella Dolling, I am a branch chief within the
2 Office of Science, division for Regulatory
3 Project Management.

4 MS. RUDOLPH: Great, thank you. Well,
5 I guess before we get started with a few
6 questions that have been submitted, I guess I'm
7 going to look over to my FDA colleagues, and
8 based on what you heard from the panelist who are
9 sharing the table here with you, are there a few
10 things that come to mind that you think might be
11 of interest for you to address at this time?

12 MS. RANDAZZO: Yes, actually, I would
13 like to comment on a couple of the recurring
14 comments that we heard from both Bryan and
15 Patricia.

16 And part of it was about the time it
17 takes to get a meeting scheduled. And one way
18 that industry could actually help them reduce
19 some of their time to get a meeting on the books
20 with FDA is to submit their meeting information
21 package with the original meeting request.

22 Because we do prefer to have 45 days

1 minimum to prepare. We want to give you really
2 good responses.

3 And I think that I've heard through
4 several of the presenters, and Jim from Swedish
5 Match is one of them, thank you, that we do try
6 to give really good responses and we do try and
7 think about our responses and give you the best
8 feedback we can.

9 We do want a great submission from
10 you, it makes it easier to review, so we do want
11 to give you adequate and decent feedback on all
12 of your questions, as specific as we can get.
13 And so, so we don't want to short ourselves with
14 time either in order to give you a good work
15 product back.

16 And then one of the other items that
17 I was going to comment on was, regarding the
18 interest in possibly meeting with OS or CTP
19 during the review of a scientific application,
20 generally we try not to duplicate efforts that
21 are being undergone by the review team.

22 That is, working on preparing the

1 written questions and we're anticipating a
2 response back from the applicant. But there are
3 opportunities for clarifying questions during
4 this time and, I mean, you can work with your
5 regulatory health project manager to see if there
6 is anything specific that you are seeking
7 feedback on that we may be able to clarify that
8 wasn't as clear as we may have intended in that
9 letter.

10 And also, there are times when there
11 may be trends across where you're seeing that you
12 have certain questions that have come up in
13 multiple SE reports, for example, or across other
14 submissions that, if your questions are general
15 in nature and not related to a specific SE
16 report, for example, I mean, we would consider
17 granting a meeting for specific, or for general
18 questions as far as the research and development
19 plans for your tobacco product applications.

20 MS. DOLLING: Thank you, Joanna. I
21 would like to comment on your recommendation to
22 increase the time period from two business days

1 from receiving the preliminary response. Thank
2 you for that feedback.

3 We look at the preliminary response as
4 a way for applicants to understand our thinking
5 with the questions that were presented in the
6 meeting request. That's your time to review our
7 comments, and then we encourage you, and to
8 Bryan's comment regarding the one hour, to
9 utilize that document as a way to scope your
10 future meeting with us.

11 So for example, if you submitted ten
12 questions during your application and you only
13 need clarification of two items, we encourage you
14 to focus that meeting on those two specific
15 areas.

16 In addition to the meeting, that one
17 hour, we found that many companies spend a
18 majority of that time presenting their portfolio.
19 It will be helpful for you to possibly consider
20 cutting down the time that you plan to represent
21 information that's already given to us in that
22 meeting package and really utilize that

1 discussion time to focus on those areas in which
2 need clarification.

3 With respect to meeting logistics, I
4 do want to know, it probably wasn't mentioned
5 here, that Office of Science, in the next few
6 weeks, we will be relocating to Calverton,
7 Maryland. So currently all meetings that are
8 scheduled will take place at our White Oak
9 Campus, however, future meetings there may be
10 scheduled in that location.

11 It's about ten minutes from our White
12 Oak Campus. So we encourage you to pay attention
13 to that meeting grant it letter, which will
14 provide you with the address of any meeting that
15 may be held.

16 MS. RUDOLPH: Thank you. Based on
17 what you heard from FDA, Patricia or Bryan, did
18 you have anything else that you wanted to check
19 back in on? Okay. No? Yes?

20 MS. P. MILLER: I think we're fine.

21 MS. RUDOLPH: Okay, great. So we'll
22 take a question that got sent in to us. So, and

1 this, I think, may be for you, Marcella and
2 Joanna.

3 If there are multiple manufacturing
4 facilities or production sites under the same
5 company, how many TPMFs should we submit, one for
6 each site or a single TPMF that covers all sites?

7 MS. DOLLING: So, the decision to
8 establish a master file belongs to the owner. So
9 we encourage applicants, or TPMF owners, to look
10 at what's your best interest.

11 For example, we would be open to
12 establishing multiple master files. And that,
13 for example, you may consider, do I want to
14 establish one for one site, multiple sites, do I
15 want to establish one for cigarette products,
16 smokeless products for example.

17 However, we encourage you, when you do
18 submit a request for multiple master files, that
19 the information is presented in a logical manner.
20 And that applicant considers, and Russ is looking
21 at me --

22 (Laughter.)

1 MS. DOLLING: So, for example, Russ,
2 for your master file you may want to consider
3 would, for example, submitting my master files by
4 analyte or by flavor, for example, could that be
5 an alternative for me. So, it's something that's
6 manageable on your end but also something that
7 FDA could easily reference for future
8 submissions.

9 MR. WOLZ: Right. And so my question
10 to you then, I'm learning a lot today, would be,
11 so, in the example I gave we have maybe one
12 master file for e-liquids, combustibles,
13 smokeless, would those have to be separate master
14 files with separate applications or could they be
15 considered as, for example, appendices to the
16 main master file?

17 MS. DOLLING: So, you have a couple
18 options there, Russ. So, you can submit one
19 master file and you could have separate sections.
20 For example, you may want to have Section A be
21 for your flavors or you may have Section A be
22 specific for e-liquids.

1 MR. WOLZ: But that doesn't have to be
2 in the same document --

3 MS. DOLLING: That can be in either
4 the same document or we'd be open to establish
5 separate submission tracking numbers --

6 MR. WOLZ: Okay.

7 MS. DOLLING: -- for each one. For
8 your consideration, each master file, now, there
9 are different responsibilities for you as an
10 owner, to manage those multiple submissions.

11 MR. WOLZ: Thank you.

12 MS. RUDOLPH: Great. So the next two
13 questions are related and it deals with our
14 regulatory health, RHPMs.

15 So, the question really can be tied
16 together, these two. Before manufacturers
17 submits the first pre-submission meeting request,
18 is it possible to be assigned to an RHPM, and if
19 so, what is the process?

20 And subsequent to this, there was a
21 question related and it's, you know, when there
22 isn't already somebody who is assigned, is there

1 another way to communicate with CTP other than
2 the CTP mailbox, given the responsiveness
3 sometimes is not as timely as the applicant might
4 like it to be?

5 MS. DOLLING: Generally we assign
6 RHPMs upon receipt of the submission to CTP.
7 Currently that can be, for example, submitted
8 when an applicant requests an IM account.

9 So currently, if you do have an IM
10 account, you have already been assigned an RHPM.
11 If you need that information, you may contact the
12 Ask CTP and we'll be able to provide that to you.

13 When you receive an application
14 acknowledgment letter, in that letter, towards
15 the end, it will identify your project managers
16 name and their contact information.

17 MS. RUDOLPH: Great.

18 MS. RANDAZZO: I can answer the second
19 question --

20 MS. RUDOLPH: Sure.

21 MS. RANDAZZO: -- about additional
22 ways to contact CTP. Actually, one of the last

1 slides of Sarah's presentation did mention that
2 we have, yes, the Ask CTP email, but also the
3 ombudsman, Office of Small Business and our call
4 center. Those are all other ways to get in touch
5 and the correspondence will be routed
6 appropriately.

7 MS. RUDOLPH: Thank you.

8 MS. RANDAZZO: Yes.

9 MS. RUDOLPH: So we got just handed
10 two more questions here. So the first one, is it
11 possible to use a master file for product
12 registration, for example, if the same product is
13 used in 25 different brands?

14 MS. DOLLING: So currently we do not
15 intend to use TPMFs to reference registration
16 eliciting information.

17 MS. RUDOLPH: Thank you. Let's see
18 here. So what criteria does CTP use to determine
19 when a granted meeting is face-to-face versus
20 conference call or written response?

21 MS. RANDAZZO: So, when CTP receives
22 the meeting request we evaluate the scope of the

1 questions, and we take into consideration the
2 applicant or the requestor's preference for the
3 meeting, but we make the ultimate determination
4 of the format.

5 And written responses are generally
6 those where we do not anticipate extensive
7 discussion or clarifications and back and forth.

8 And as far as face-to-face and
9 telecom, I'm going to kind of lump those in
10 together because they really, neither one of them
11 are limiting as far as the amount of back and
12 forth discussion, it's just a matter of if you're
13 coming to FDA Campus or if we're on the phone.

14 And teleconferences can actually be a
15 really nice way to meet with CTP because it
16 alleviates the need for additional travel. And
17 on the company's end you can have additional
18 participants that you may not have been wanting
19 to all travel together or get airfare for the
20 meeting.

21 And also, it's kind of a nice
22 opportunity that if there is a need for internal

1 deliberation on a question that either party can
2 put each other on hold and make sure that you
3 give the proper vetted answer. And so, it kind
4 of has a couple of nice little features that
5 face-to-face doesn't provide because we're all
6 just sitting there looking at each other.

7 So, it really depends on the scope of
8 the questions. And generally, the written is
9 less back and forth, maybe anticipated.

10 MS. RUDOLPH: Thank you. So, I have
11 one last question. If I have other questions on
12 different topics that I can think of during the
13 meeting, can I ask them and get more information?

14 What if I provide more information in
15 my opening talk to FDA when we have the meeting,
16 can FDA provide me comment on the new
17 information?

18 MS. RANDAZZO: Generally FDA will
19 limit the discussion in a meeting to what we are
20 prepared to talk about, as outlined in the
21 applicant's meeting request and meeting
22 information package.

1 However, there may be some low hanging
2 fruit, I'll say, that if you're asking very
3 simple questions that we are able to answer
4 without further internal discussion or additional
5 scientific expertise that may not be in the room
6 with us that day. It really depends on the
7 nature of the question, but in general we tend to
8 stick to the scope of what the meeting topic was
9 as outlined in the request.

10 MS. DOLLING: And I will just
11 piggyback on that. And if there are comments
12 that we can vet after the meeting or there are
13 action items, we do intend to communicate those
14 in the meeting minutes.

15 MS. RUDOLPH: Thank you. And, Bryan,
16 did you have one other thing?

17 MR. HAYNES: Just one quick comment
18 because I'm aware of what's in the guidance
19 around supplemental information that you might
20 submit once the meeting has been granted and that
21 might cause the meeting to be rescheduled. Which
22 I'm always terrified about.

1 Inevitably you come up with things
2 when you're preparing for a meeting but then I
3 don't want the meeting to be rescheduled so I'm
4 hesitant to submit it.

5 My solution might be, well, we'll
6 submit it, please don't reschedule my meeting,
7 comment on it if you can but please don't
8 reschedule my meeting. Would that be a fair
9 middle ground?

10 MS. RANDAZZO: I mean, that sounds, I
11 mean, as long as the expectation is pretty clear
12 that you submitted this late --

13 MR. HAYNES: Yes.

14 MS. RANDAZZO: -- and you're not
15 expecting us to comment. But, I mean, it really
16 depends on what outcome you're seeking.

17 MR. HAYNES: Yes.

18 MS. RANDAZZO: If you feel the
19 information is really important for us to provide
20 an answer to, it may just have to be that we
21 reschedule or you can setup a separate meeting.
22 Yes, I --

1 MR. HAYNES: Fair enough.

2 MS. RANDAZZO: Depends on what you
3 want.

4 MR. HAYNES: Fair enough.

5 MS. RUDOLPH: Thank you. Any further
6 comments for the panel? Okay, thank you so much.

7 So, we'll be transitioning into our
8 Session 4. We'll have two presentations. The
9 first one is from Sharyn Miller, information
10 resources on application review programs.

11 And the second will be from Jeff Smith
12 on CTP electronic submission standards and
13 activities. And following that we'll have
14 another panel.

15 (Off the record comments.)

16 MS. S. MILLER: Welcome to the
17 presentation on information and resources across
18 application review programs. My name is Sharyn
19 Miller and I'm a regulatory health project
20 manager in the Office of Science.

21 In response to industry feedback, FDA
22 Center for Tobacco Products has provided

1 manufacturers with additional information and
2 helpful tools to assist in understanding tobacco
3 product regulatory requirements.

4 Navigating FDA's website, we will walk
5 through some of these resources and explain how
6 this information may benefit you. To accomplish
7 this, we will first walk through FDA's website to
8 see where guidance and regulation documents are
9 located. In addition to documents currently
10 available for public comment.

11 After that we will take a look at
12 marketing orders for pre-market programs. In
13 support of specific FDA actions, we will learn
14 how to access TPL reviews, order letters and
15 environmental assessments.

16 To further assist in addressing
17 regulatory and CTP specific questions, it may be
18 helpful to know that FDA offers webinars,
19 presentations and public workshops. We will
20 guide you through these online educational
21 materials and discuss ways to stay abreast of
22 ongoing CTP activities and initiatives.

1 Let's begin with locating regulatory
2 information using FDA's website. On CTP webpage
3 there is a gray box titled, navigate the tobacco
4 product section.

5 As shown here in the picture, there
6 are six options to choose from. Including
7 products, guidance and regulations, compliance,
8 enforcement and training, newsroom, public health
9 education, science and research, and about CTP.

10 Each option provides a brief
11 description on that topic. Selecting the first
12 option titled, products, guidance and
13 regulations, directs us to a web page that shows
14 information on marketing pathways, statutory
15 requirements and documents for public comment.

16 FDA offers direct access to all CTP
17 regulations and guidance documents. Selecting
18 rules and regulations from the navigation pane
19 displays all advanced notice of proposed
20 rulemakings, also referred to as ANPRMs, proposed
21 rules and final rules.

22 The Administrative Procedures Act

1 establishes the basic requirement for notice and
2 comment rulemaking. Notice of proposed
3 rulemaking, also referred to as NPRMs, make the
4 public aware of the agency's intentions for the
5 specific rule, while potential ANPRMs solicit
6 information to inform policy on future
7 rulemaking.

8 In summary, proposed rules explain the
9 agency's intent, provide CTP spaces for issuing
10 regulations and solicit public comments.

11 Selecting guidance allows anyone to
12 search for and download documents that represent
13 FDAs current thinking on a wide range of tobacco
14 related issues. These documents usually discuss
15 more specific products or issues that relate to
16 product design, production, labeling, promotion,
17 manufacturing and submission of regulated
18 products.

19 Guidance documents help industry
20 understand and comply with all laws and
21 applicable regulations. Unlike final rules,
22 guidance documents are not binding.

1 What this means is that you may use an
2 alternative approach if that approach satisfies
3 applicable statutes and regulations. Typically
4 for draft guidance documents, the agency
5 designates a comment period, generally 60 to 90
6 days so that comments can be considered as the
7 draft is finalized.

8 One important aspect in reviewing
9 guidance is to consider whether FDA has made any
10 revisions. Revised guidance demonstrates a
11 change in FDA's current thinking on that topic.

12 For example, effective April 13, 2018,
13 FDA issued a revised listing of ingredients in
14 tobacco products guidance. The purpose of this
15 revision was to assist manufacturers of deemed
16 tobacco products with the required ingredient
17 listings under Section 904(a)(1) of the Federal
18 Food Drug and Cosmetic Act.

19 In this revised guidance, FDA
20 announced the intent to enforce the ingredient
21 listing requirements, only with respect to those
22 components or parts, one, made or derived from

1 tobacco, or two, containing ingredients that are
2 burned, aerosolized or ingested during tobacco
3 product use.

4 When reviewing these regulatory
5 documents, note that the date listed reflects the
6 effective date. Regulatory documents may be
7 available for public viewing prior to the
8 effective date, to solicit public comments.

9 Your feedback plays a critical role in
10 helping shape tobacco policy and regulation.
11 Because FDA regulatory decisions are based on
12 science and law, agency reviewers look for logic,
13 good science and other evidence as they evaluate
14 comments.

15 To be sure comments have the greatest
16 possible impact, we suggest reviewing our tips
17 for submitting effective comments beforehand. A
18 few tips for submitting effective comments
19 include, adequately explain the reasoning behind
20 your position. This helps the agency formulate
21 the best policy.

22 Identifying credentials and experience

1 that may distinguish your comments from others.

2 If you are commenting in an area in which you
3 have relevant personal or professional
4 experience, say so.

5 When disagreeing with a proposed
6 action, suggest an alternative. Including not
7 regulating at all. And include an explanation
8 and/or analysis of how the alternative might meet
9 the same objective or be more effective.

10 On that same navigation pane, you will
11 see a section to submit comments on certain
12 tobacco related products. If a tobacco related
13 document is available for public comment, it is
14 shown here.

15 Currently, FDA is seeking public
16 comment on the public meeting, on tobacco product
17 application review and also requesting member
18 nominations to serve on the tobacco products
19 scientific advisory committee.

20 These links will direct you to the
21 federal registrar website where you can find
22 additional information on the submission process.

1 Also open for public comment are
2 several modified risk tobacco product
3 applications. Including Copenhagen snuff, fine
4 cut smokeless tobacco product, six Camel Snus
5 smokeless tobacco products and three iCO systems
6 with corresponding heat sticks.

7 Similar to public comments on guidance
8 and proposed regulations, application related
9 comments are submitted through regulations.gov.
10 Selecting any of the application links will
11 automatically direct you to a web page where
12 immediate feedback may be provided.

13 When considering resources that
14 improve public understanding of the scientific
15 principles involved in application review, it may
16 be helpful to know that FDA also posts relevant
17 documents to explain the basis for certain
18 actions.

19 Let's navigate CTP's website to
20 identify where these resources are located. On
21 the products, guidance and regulations navigation
22 pane, we can select review and evaluation

1 process.

2 When we select this item, several
3 additional options are displayed, including
4 questions and answers, misbranded and adulterated
5 NSE products, tobacco product marketing orders
6 and three CTP marketing pathways.

7 To view marketing order reporting
8 numbers across CTP programs, select tobacco
9 product marketing orders. This shows the number
10 of marketing orders, refused-to-accept and
11 withdrawals for pre-market product applications,
12 substantial equivalence and exemption from a
13 substantial equivalence programs to date.

14 In cases where CTP has issued an order
15 for any of the three marketing pathways, we can
16 access relevant documents to better understand
17 the application review process. To view this
18 information, select the specific CTP marketing
19 program, followed by marketing orders.

20 Let's take a look at marketing order
21 information for CTP's most active marketing
22 pathway, substantial equivalence. Shown here is

1 the general representative sample for the types
2 of SE marketing order information available.

3 More specifically, order letters,
4 decision summaries, environmental assessments,
5 also referred to as EA, and finding of no
6 significant impact, also referred to as FONSI,
7 are available for public viewing.

8 Clicking the product's name provides
9 the SE, or NSE order letter, for that tobacco
10 product. The order letter acknowledges
11 scientific review completion, explains marketing
12 order status and reminds applicants that the new
13 tobacco product specified are subject to the
14 requirements of Chapter 9 of the Federal Food,
15 Drug and Cosmetic Act.

16 The decision summary, also referred as
17 the TPL review, captures the regulatory
18 compliance and scientific review conclusions from
19 that tobacco product application. Reading TPL
20 reviews may be useful to understanding the scope
21 and depth of CTP's application review process.

22 In addition to the order letter in TPL

1 review, FDA provides the corresponding EA to
2 address environmental impacts that may be caused
3 from tobacco product manufacturing, use and
4 disposal.

5 In support of the EA, a FONSI may be
6 prepared. Which includes that the marketing
7 order for this new tobacco product will not have
8 a significant impact on the quality of the human
9 environment.

10 For more information on EA, please
11 refer to Dr. Chang's presentation this afternoon.

12 Prior to website posting, FDA redacts
13 information from these documents to protect
14 confidential and trade secret information. In
15 accordance with applicable statutes and
16 regulations.

17 Additionally, these documents are
18 reviewed to ensure compliance with Section 508.
19 Which requires that all website content be
20 accessible to people with disabilities.

21 For these reasons, the review time for
22 posting may vary, based on the content in each

1 document.

2 With a comprehensive approach, CTP
3 uses a variety of platforms for information
4 sharing and educational training. Let's explore
5 some of the information and training resources
6 available to you.

7 With the ingredient listing compliance
8 date of November 8th, 2018 looming for small-
9 scale manufacturers, CTP created a new ingredient
10 listing web page to provide additional
11 information and updated forms, to assist with
12 electronic submissions.

13 The creation of this webpage was a
14 result of a bolus in inquiries regarding the
15 ingredient listing submission process. To
16 address industry concerns, the webpage includes
17 the April 2018 revised guidance for industry,
18 criteria for submitting one listing that
19 corresponds with multiple tobacco products and
20 product specific ingredient listing spreadsheets.
21 Which are available for direct download here in
22 an eSubmitter.

1 More recently however, CTP developed
2 three webinars to account for the following.
3 Examples of ingredient listing spreadsheets by
4 product category, using a tobacco product master
5 file for ingredient listing submissions and using
6 FDA tools to submit ingredient listings
7 electronically.

8 As we continue to identify industry
9 knowledge gaps, CTP updates this webpage on a
10 regular basis to include general information on
11 topics received through public inquiries. For
12 additional CTP webinars, select compliance
13 enforcement and training on the left navigation
14 pane.

15 This webinar series provides
16 compliance, education and training on a variety
17 of topics so tobacco retailers, importers and
18 manufacturers learn all the steps necessary to
19 comply with the statutory requirements for the
20 marketing and sale of all tobacco products.

21 FDA considers new webinar topics based
22 on public inquiries and ideas. To share an idea

1 for a future webinar, please contact Ask CTP Help
2 Desk.

3 For a list of CTP press releases,
4 meetings and workshops, we encourage you to visit
5 the CTP newsroom. The top of the webpage
6 highlights featured stories on tobacco product
7 application review, steps taken to address youth
8 epidemic of e-cigarette use and a spotlight on
9 science.

10 Scrolling down the webpage shows
11 additional information sorted by date. Each item
12 will direct you to a page where you can find more
13 information on that topic.

14 For example, if we select the first
15 item, a public meeting tobacco product
16 application review, we see information on the
17 meeting location, objective, audience and
18 registration. Topics to be addressed in the
19 meeting are also noted here.

20 To ensure the most up to date
21 information, we recommend you monitor the CTP
22 newsroom periodically. To broaden our reach with

1 important updates, CTP is also active on a
2 variety of social media platforms, including
3 Twitter, Facebook and YouTube. In addition, we
4 offer the option to subscribe for email updates.

5 Whether you're a tobacco product
6 manufacturer retailer looking for compliance
7 information, a parent in need of resources to
8 educate your child about the dangers about
9 tobacco use, or a scientist interested in
10 learning more about the latest tobacco product
11 research, we have the information you're looking
12 for.

13 By subscribing to receive email
14 updates from us, you will stay informed about all
15 things tobacco products. The four unique email
16 lists include CTP News, CTP Connect, Spotlight on
17 Science and Modified Risk Tobacco Product
18 Application Updates.

19 Signing up for CTP News allows you to
20 be among the first to receive news from the
21 center, as it happens. Including information
22 about regulations, guidance, enforcement actions

1 and other compliance related announcements.

2 With CTP Connect, you can expect to
3 receive a regular newsletter that includes
4 messages from CTP leadership, a regulatory news
5 roundup, featured articles on current tobacco
6 issues and educational resources.

7 To stay current on CTP tobacco
8 regulatory science and research efforts, we
9 recommend the Spotlight on Science. This email
10 subscription provides tobacco science
11 publications, study findings and CTP grants.

12 If you want to know when materials
13 from any MRTP applications under review have been
14 posted, sign up for the MRTP application updates
15 email list. But, be sure to sign up for the
16 email list that best interests you.

17 To evaluate the usefulness of our
18 public facing materials and address issues
19 raised, we want to hear from you. There are
20 multiple ways to contact us.

21 For general questions, CTP encourages
22 you to reach out to the call center phone lines.

1 Staff are readily available to assist between the
2 hours of 9:00 a.m. and 4:00 p.m. Eastern Daylight
3 time.

4 Callers should select Option 1 for
5 general questions, such as questions related to
6 marketing application pathways and compliant
7 states or Option 2 for questions regarding
8 eSubmitter and CTP Portal.

9 General questions can also be sent by
10 emailing AskCTP. For specific inquiries, CTP has
11 several help desks available to ensure inquiries
12 are routed to the appropriate person who can get
13 you the response you need.

14 To prevent duplicative help desk
15 tickets, which may delay responses, we recommend
16 submitting individual inquiries through one
17 channel. For tobacco industry questions, such as
18 application submission process and timelines,
19 please contact Tobacco Industry Help Desk.

20 If you're considered a small-scale
21 tobacco product business and seeking more
22 information on the regulatory process, you may

1 send questions to Tobacco Industry Help Desk or
2 the small business office.

3 CTP stakeholder relations office helps
4 increase stakeholder awareness and understanding
5 of the Tobacco Control Act, including regulatory,
6 science, communication and enforcement
7 initiatives.

8 For questions on stakeholder
9 engagement and awareness, please contact CTP's
10 stakeholder relations. All regulatory
11 correspondence, including written and electronic
12 submissions, are processed through CTP's document
13 control center.

14 Note that delivery hours are from 8:00
15 a.m. to 4:00 p.m., and deliveries received after
16 4:00 p.m. will be date stamped the following
17 business day. Please refer to Mr. Smith's
18 presentation on electronic submissions and
19 associated forms for more information on
20 eSubmitter and CTP Portal.

21 This concludes the presentation
22 regarding information and resources on

1 application review programs. Clarifying
2 questions will be addressed during the panel
3 discussion for this meeting session. Thank you.

4 (Applause.)

5 MR. SMITH: Thanks, Sharyn, and thanks
6 for fixing this remote. Let me see if we can get
7 moving here. I'll probably refer to some things
8 that Sharyn mentioned, and as well, Barbara.

9 It's cozy in here and --- very cozy.
10 And your sugar is probably diving after lunch so
11 I'll try to amp it up a little bit.

12 My name is Jeff Smith, I'm with the
13 Office of Science Division of Regulatory Science
14 Informatics. I'll be presenting about some
15 electronic submissions, issues and
16 considerations.

17 And Deborah Sholtes, who's a branch
18 chief, will be sitting on the panel to entertain
19 questions. So, after I give my presentation I'll
20 duck for cover.

21 I want to mention a few things about
22 where we came from. Some of the challenges that

1 we had standing up a new center and dealing with
2 a newly regulated entity. To put it in context.

3 And then highlight one of our more
4 recent advances, which were really in response to
5 the feedback we've received from industry and
6 from you, to try to help in your submission
7 submittal part and communications.

8 Then some technical considerations,
9 lessons that we've learned, that we'd like to
10 share. Many of those lessons we've actually now
11 put out in documents.

12 You also get some of those lessons in
13 those pre-submission meetings that Barbara spoke
14 of as well. Then that's important for those
15 people who, the technical people who are actually
16 putting together these submissions to submit to
17 us.

18 Okay. Then, I want to talk about
19 where we're headed toward an existing electronic
20 submission standard. And that's very important
21 for, also those technical people as well, but
22 also important for the commercial marketplace of

1 solutions that we'll be building and providing
2 tools built around those standards.

3 So, the Tobacco Control Act was
4 enacted in June of 2009, and within six months we
5 had to be prepared to receive this. We were all
6 challenged on both sides. You in assembling and
7 submitting and us, we, on receiving.

8 And so we actually began receiving
9 other kinds of submissions within three months,
10 even before we were staffed very well. So we had
11 to track those and whose, what the status of
12 those. So we had to beg, borrow and steal pretty
13 much, from across centers.

14 Government contracting can be slow.
15 All contracting can be slow. And so that's why,
16 and then developing only begins to occur after
17 that.

18 So, eSubmitter was a good choice. I
19 think it's really helped. It's been well
20 received. eSubmitter is the TurboTax like tool
21 that you can fill out questions and answers, who
22 are you and what is this about. Then you can

1 begin to attach those files.

2 And it's been very well received and
3 it's served us well for the creation part of the
4 submission.

5 Next is the transmission part. The
6 agency already had an electronic submission
7 secured gateway. And we got a lot of feedback
8 about that.

9 And Russell alluded to that issue. It
10 requires a high technical capability and in a
11 newly regulated industry, especially with a lot
12 of small businesses that's not always available.
13 So we heard you and we responded.

14 Internal systems and building what we
15 could in-house so we could begin to track
16 everything we began to receive. And then of
17 course the FDA unified registration listing of
18 which, soon thereafter, the tobacco TRLM module
19 under that was established.

20 So, in response to concerns and
21 questions and frustrations, we rolled out, in
22 August of 2016, the CTP Portal. And it really

1 was a first for FDA.

2 It's more like your HMO where you go
3 in, it's an environment that your company and all
4 the users that your company assigns can share in
5 that environment, in their interaction with
6 Center for Tobacco.

7 And it allows you to easily click and
8 upload. So you don't have to negotiate the ESG
9 any longer, you simply click on a button and
10 upload it.

11 That was well received also, but more
12 than subjectively. When we rolled that out we
13 were majority paper. More than 70 percent paper.
14 After, just after a year, that had flipped. We
15 were 70 percent electronic.

16 Companies and people who had never
17 submitted electronically were submitting it. It
18 was easier than mailing. So that is a real
19 testament to that. And CTP loves data. So I had
20 to tell you that.

21 In order to make this fly, because we
22 appreciate the concerns about confidentiality of

1 company material, we did not want to put
2 ourselves in a position of assigning all of the
3 accounts within that company, knowing whose
4 coming and going. So we created the concept of
5 the industry account manager, and then put it in
6 the hands of the companies. Put it in your
7 hands, to manage who in your company can and
8 cannot get access.

9 A little screenshot there. So, when
10 you go into the home screen you'll see different
11 areas. Pretty self-explanatory here.

12 It lets you see the actions, the
13 letters that were issued. It doesn't let you see
14 the content of the letters yet, but it does give
15 you administrative information about the letters.

16 To the right you will see some
17 notifications and the bottom you'll see the most
18 recent files that your company has uploaded. So
19 anybody with that account that that company is
20 given will see these screens.

21 I've clicked on the submission screen,
22 so across the top actually. You can't really see

1 it, I feel sorry for you folks in the back, but
2 the submission screen across the top.

3 And what is good about this is not
4 only you can easily upload whatever you have
5 created with eSubmitter, but you can also see
6 when it was assigned in STN. You can see that
7 submission tracking number, STN.

8 If you click on that hyperlink, for
9 the STN, it will drill down and give you more
10 information about it. It won't tell you and show
11 you the content, but it will show you the
12 administrative information.

13 So you can say, yes, FDA received it,
14 they assigned this STN to it. And you can even
15 see what files you had uploaded, the files names
16 that are associated with that STN. So there's no
17 doubt.

18 When you're ready to upload, the
19 pointer is not going to do me any good here, so
20 to the upper right there's a little button,
21 orange button. And you'll get a screen showing
22 you the list of the files that your company has

1 so far uploaded. And if you're sharing this role
2 with another person in your company you can say,
3 oh, she hasn't uploaded it yet, so now I'm going
4 to upload that submission.

5 And you click. And then you browse to
6 your hard drive or your file share and you click
7 and you upload it.

8 What are you uploading? What are you
9 attaching within eSubmitter?

10 Now, I'm no fan of electronic.
11 Actually I, going from molecules to electrons, I
12 like my molecules, they serve me well. They're
13 allowing me to stand right here. I'm sure you
14 love your molecules too.

15 But it's really only when those data
16 can be provided in a form and format that can be
17 further utilized by computers. So we have to be
18 able to open, we have to be able process, read,
19 archive.

20 It's great if it provides more
21 capability than paper because then, now the
22 electrons have more capability than paper. So,

1 if they're searchable.

2 So, here are some of the most common
3 file types, the extensions for PDF is an
4 excellent, I think, standard everybody is aware
5 of. It's an open format.

6 Great for the narrative body, for
7 telling your story, for guiding a reviewer
8 through. And then of course you may refer them
9 to associated data which there are formats
10 appropriate for those SAS transport, unopened SAS
11 format. Excellent for data, comma separated
12 values.

13 Excel if you have to. But anything
14 but PDF because, believe it or not, we do get
15 some of those still with paginations and we're
16 taking our time pulling the data out rather than
17 reviewing, and that serves nobody any good.

18 So, also nonproprietary. When we get
19 submissions in SAS, that's proprietary format.
20 We prefer SAS transport. That's what the Center
21 for Drugs, Biologics and Devices have been
22 receiving for years. We're simply following

1 their lead.

2 Naming the files is important. You
3 wouldn't believe how difficult it can be just
4 knowing the entry point for the reviewer of where
5 to go and dive in and begin reviewing. And these
6 files number in the hundreds. It's just a
7 swimming pool of files.

8 And so, naming it explicitly, MainTOC
9 or MainBody, MainTOC would be good, has your
10 table of contents, your main body from there. It
11 can link to other pieces of your submission and
12 reference.

13 So, we've had much difficulty with
14 special characters and foreign characters. And
15 when we start to have to rename files, that can
16 break your links.

17 You may be referencing the files
18 somewhere deep in your submission, now we cannot
19 find the file because we renamed the file. We
20 don't want to be in the business of doing that so
21 that could slow things down and we'll have to get
22 back with you about possibly resubmitting a

1 portion or more of the submission.

2 We're a Windows shop right now, we're
3 hoping to change that, but there's a limit to the
4 kind of files we can read and the length of the
5 file names and the overall path. The overall
6 path is folder, folder, subfolder, subfolder,
7 subfolder/file name.

8 And when it goes too long we can see
9 it, you can try this at home if you have a Linux
10 machine and open it on Windows, you can see it
11 but you can't get a handle on that file, Windows
12 won't let you open it, it says, file cannot be
13 found, but I'm looking right at it.

14 So, that's been a problem for us and
15 we've had to work around those problems. So,
16 keep it down to 180 characters in total. It's
17 consistent with the other centers.

18 We're actually offering you more
19 characters than the other centers. We think we
20 can do that based on the way we're managing our
21 files.

22 I'll refer you to some documents in a

1 couple of slides that detail some of this much
2 better.

3 When you do create your submission
4 file, your main body, it's helpful to you, and it
5 saves time to generate it directly from the
6 source rather than print it out and scan it in.
7 It provides what's called a functional PDF.

8 It's searchable, but the great thing
9 about PDFs you generate from the source is, you
10 can zoom up, see letters and they don't pixelate,
11 it just, so they don't become fuzzy. Sometimes
12 things are scanned at low dots per inch and it's
13 unclear and then when you zoom in it's just
14 bigger but it's still unclear.

15 So, minimally, if you do scan it 300
16 dots per inch at least. And then OCR it because,
17 again, that makes use out of those electrons.

18 It gives an advantage over paper then,
19 and that's to all our benefit. And even in the
20 company, if they have to search for the
21 submission themselves and find information, which
22 they often have to do too.

1 Table of contents is very important in
2 that you reference every file throughout. We
3 cannot presume the intention of a particular data
4 set or file, we really need you to tell us why
5 it's there and how it supports your claim. We
6 cannot presume what you intended with the file.

7 So, everything has to be referenced in
8 some way. Hyperlinks and bookmarks, I've heard
9 mentioned here several times they're very
10 helpful.

11 Existing templates. A minute ago,
12 Sharyn talked about some resources available.
13 One of those is the ingredients template.

14 Ingredients template, use that when
15 you submit your ingredient submissions. But,
16 that template is available on the CTP
17 manufacturer website. You can find a lot of this
18 on the CTP manufacturer website so I don't need
19 to give you all these little links. You can find
20 it there.

21 And that spreadsheet could also be
22 used in support of your MRTP or your SE. It's an

1 ingredients template. Use it for your other
2 application pathways. It benefits everyone.

3 Please test also. Often, well, not
4 often, a few times we have had to open a
5 submission, we've had difficulty. And the
6 company discovered they could not open it either.
7 Because people have third parties create some of
8 these things and submit, so it's helpful if the
9 company knows it can be opened as well.

10 And virus scan also, as regulated.
11 We're also regulated. The federal government has
12 information security, regulations and laws. And
13 that's good for you because your data is secure.

14 And we do scan everything as it comes
15 in, but we also require that, and the agency has
16 made this a requirement, so CTP has to follow
17 suit, that you scan and indicate what you used to
18 scan it with if you're sending physical media in.
19 If we do receive something that is virus
20 contaminated, it is going to create a problem
21 receiving anything further from that company
22 until we can work this out.

1 And no need to encrypt or password
2 protect. The portal encrypts at the point of
3 origin. It goes over the wire encrypted, and
4 when it's received it's decrypted. It uses
5 secure socket layer.

6 Also, FDA has a long history of
7 maintaining confidentiality. Okay.

8 So, here is some references, I'm not
9 going to get into them, but they're references of
10 what I've been talking about. And also, the pre-
11 application meetings are important for that
12 purpose.

13 But when you're ready, you can
14 download eSubmitter, learn it. When you get
15 ready to submit you'll need a portal account. It
16 takes some lead time, ten to 14 days.

17 You'll need to submit a letter from
18 the company, on company letterhead, appointing an
19 industry account manager, and rules of behavior.
20 And then you're ready to go. Open up the portal,
21 browse to where your file is and upload it.

22 So now I'm going to try to speed this

1 up because now we're looking toward the future.
2 Toward a structured electronic submission that
3 can even stage us for more benefits.

4 And there's generally four areas of
5 standards. One is a laboratory standards test,
6 protocols and such, ISO and Caressa (phonetic)
7 and so forth.

8 There is a submission content, which
9 is how the data is arrayed and coded. You'll
10 hear acronyms like CDISC, STTM, HL7.

11 Analysis standards, statistical
12 standards, statistical assays. But what I want
13 to comment here on is the container. The actual
14 submission. The electronic submission itself
15 that breaks a part a submission, assembles it,
16 packages it and send it to us so everything
17 you've attached is sent to us.

18 FDA does try to make use of standards
19 whenever possible. 21 CFR 10.95 requires us to
20 participate, and utilize when possible and
21 appropriate, and we do. And the eCTD, the
22 electronic common technical document, is one such

1 standard that has been in use for almost 15
2 years.

3 The regulated product submission
4 builds upon that standard but it still uses eCTD
5 as the underlying code.

6 Now, we're going to have to modify
7 this slightly to avoid confusing and angering
8 people in eCTD. We're calling it the electronic
9 tobacco technical document.

10 The eCTD breaks a submission into
11 several discrete units. Not just theoretically,
12 several separate files by area, by discipline,
13 administrative area, clinical, quality, which
14 would be CMC manufacturing and so on.

15 Going into each of these modules, it
16 breaks it down even further. And for our
17 purpose, we may have to remove some. Pediatric
18 does apply here but we might need some behavioral
19 studies, population health studies and we'll have
20 to modify what we can without messing too much of
21 the standard up and getting people angry at us.

22 The RPS builds on this, so not just an

1 individual submission standard, but all the
2 submissions pertain to a product lifecycle. So
3 it has a file cabinet or a dossier, where all the
4 information pertaining to the life of that
5 product would be stored.

6 So you had drawers for different
7 application types. If SE applied you'd have SE
8 here. In this case it probably would be SE
9 exemption if there's a PMTA.

10 Then, a folder as a submission unit.
11 The first one to come in might create that PMTA.
12 An amendment would be another submission unit
13 folder. Documents within it are the content.
14 And so, it's fully metadata driven and so there's
15 no need for folders.

16 The good thing about this is, the
17 companies know where to put stuff, irregardless
18 of the application pathway, and we know where to
19 find stuff. And we can avail ourselves of more
20 automation and tools to do that.

21 We can actually reference one piece
22 within a submission to another piece within

1 another submission. And this is valuable instead
2 of just referencing one application to another.

3 The most important thing, take home
4 message is that, by subscribing to this type of
5 standard, we both avail ourselves of a whole
6 commercial marketplace of tools and solutions to
7 create, submit and review and analyze these data.
8 And it has served other parts of FDA well.

9 Just an example, how you have your
10 documents and then you have your metadata file.
11 So, a metadata file is simply saying, hey
12 document, here's stuff, here's how to use it,
13 this supersedes the previous one we sent and now
14 when you look at your application you'll see this
15 one and what it's to be used for.

16 A little bit of code here, and I'm
17 almost done, a little bit of code just to show
18 you some code. But actually, your email looks a
19 lot like this if you were to look under the hood.

20 Computer communication is like this
21 for financial data and medical data. And we're
22 currently working on several technical documents,

1 highly technical documents, for those software
2 firms and for the technical folks.

3 And I list them out here. And some
4 sample files. Which is what was done for eCTD.
5 And we're building in-house the databases and
6 architecture to receive it.

7 We've actually completed a successful
8 receipt of an eCTD from pilot participants in a
9 software industry that support the pharmaceutical
10 industry with these tools. They were able to
11 figure out, from our technical specification, how
12 to build an electronic eCTD and submit it to us.
13 And we were able to receive that.

14 And then of course, we will go to the
15 standard part of the good guidance process and
16 make these documents available for public
17 comment. But Dr. Holman wanted us to put our
18 ducks in a row and validate this before we did
19 that, and that's what we've done.

20 So, I think I'm two minutes over but
21 thank you very much for your time. And I think
22 this is going to benefit, as it has with CDER and

1 CBER, both sides and all parties, in the end. So
2 thank you very much.

3 (Applause.)

4 MS. RUDOLPH: Before we head into our
5 panel we're going to take a ten minute break. So
6 if everybody could come back at about 3:05 that
7 would be great.

8 (Whereupon, the above-entitled matter
9 went off the record at 2:53 p.m. and resumed at
10 3:07 p.m.)

11 MS. RUDOLPH: So welcome back
12 everyone. We're coming to the end of Session No.
13 4 with our distinguished panel and we will give
14 -- as we have previously -- each person who's an
15 outside representative five minutes to introduce
16 him or herself -- actually herself in this case
17 -- and to have an opportunity to kind of reflect
18 on the session. And then we will move into
19 questions from the audience, both in person and
20 on the Web.

21 Paisley?

22 MS. CAMERON: Thanks. Paisley

1 Cameron. I'm with JTI USA. I've been working
2 with this -- Matt and CTP for I guess since
3 inception in 2009 now. So I wanted to thank both
4 Matt and everyone here for having such a
5 workshop. I think it's absolutely a great
6 opportunity, and obviously we've come a long way
7 since -- over the last eight years that we're now
8 being able to collaborate on these items.

9 I'll just touch very briefly on both
10 topics. The first one with the eSubmitter, and
11 I'll qualify that by saying I don't really have
12 the direct experience myself. Fortunately we
13 have other people with better technical expertise
14 than I do within our organization who handle
15 these things. But my understanding is that we
16 have used them for certain -- in certain
17 instances. The ingredient submission for
18 example, which Jeff had talked about earlier.

19 And there is a template that's there
20 to be used, but in our case we found that the
21 information -- how we, let's say, keep it in our
22 systems, don't necessarily match with the way CTP

1 puts it in their template. So we then had to
2 build like an interface and a mapping tool so
3 that we could get it from our system into a
4 template or into an Excel format that could then
5 be easily uploaded in to the eSubmitter format.
6 So it takes a little bit of time to do that, but
7 in our case it made it easier for the long run.
8 And also even just setting up the eSubmitter
9 gateway in the first instance took a little bit
10 of time as well.

11 And I think I heard a number of times
12 sort of the technical expertise -- there is a
13 fairly high level of technical expertise that's
14 required for this. So I would encourage people
15 to have sort of dedicated people within their
16 organization who can do this, especially -- it
17 sounds like in the future it's going to be more
18 complex and although more beneficial I think
19 because that way you're not going to lose track
20 and you can more easily, let's say, track where
21 your submission is at and you can get your STN
22 numbers more quickly. And so -- and it will make

1 it easier for both CTP and for industry.

2 The one thing I would recommend is
3 that there is sort of this continued dialogue and
4 to understand -- or at least for CTP and industry
5 to make sure that the system allows for let's say
6 some flexibility for different product types of
7 categories and for different information that
8 needs to be loaded through the system for these
9 different products as they come up for either
10 substantial equivalent or PMTA or MRTP.

11 On the web site, look, there is a
12 significant amount of valuable information out on
13 the web site, clearly. There is everything from
14 submission data to webinars to product metrics.
15 I mean, you name it, it's there. It's just not
16 always easiest to find. I mean, if you looked at
17 the categories, they're not always let's say
18 intuitive of how you can find information, so it
19 does take a little bit of hunt and peck at times
20 to go through and find the right information that
21 you're looking for.

22 So one of the suggestions we might

1 have is maybe some quick links so that you can
2 find information much more easily, say for
3 example, the NSE determination summary, which I
4 think was addressed by Christi this morning, that
5 they're going to look at that as far as -- I
6 think they're now calling it Appendix of Common
7 Deficiencies that will be submitted or out there.

8 But one of the things that's let's say
9 maybe even lacking in the past is a versioning of
10 that. What's the actual date? What's the most
11 recent version of that information that's out
12 there. It was hard to know is there anything
13 new? Is there anything different? And then if
14 there was, sort of you had to look and see what
15 your old version said and compare it to your new
16 one. So if there was some way that CTP could
17 version those or give us dates so that we would
18 know when things were updated, even sometimes
19 when to go look for information.

20 We don't always -- like I said,
21 because there's so much information out on the
22 web site and a lot of it's, like I said, really

1 valuable information that can be used by the
2 industry. When those things are updated it would
3 be nice to get a flag or a notice somehow that,
4 okay, there's new information out there. Maybe
5 on the main page a list of what's been put up
6 recently, and then an actual link to that
7 information I think would be very helpful.

8 And just a note on those sort of
9 deficiency lists, I think if we could get a
10 little bit more substantive information on what
11 exactly it is that CTP is looking for in each of
12 those instances. A lot of times it would just
13 say the information is deficient. But if we
14 could get some insights onto exactly what was
15 missing, what would have been the solution, what
16 would maybe CTP be looking for in that particular
17 instance, it would provide some more transparency
18 and clarity to the industry so that they would
19 have let's say more complete applications in the
20 first instance, and it would be an easier,
21 quicker review time for CTP. And I guess that's
22 -- my time is up.

1 (Laughter.)

2 MS. CAMERON: My cue. Thank you.

3 MS. RUDOLPH: Leann?

4 MS. CAMPBELL: Good afternoon. My
5 name is Leann Campbell. I'm from RAI Services
6 Company. I'm a senior manager in the
7 eSubmissions Group and the Scientific and
8 Regulatory Affairs. I also want to thank CTP for
9 giving us this workshop and this opportunity to
10 talk to you.

11 So my comments are mostly confined to
12 the areas of MRTP and PMTA, of which I have
13 direct experience dating back to my time working
14 on clinical studies as a bio-statistician through
15 converting some old legacy data for use in one of
16 these type of applications, and then the actual
17 compilation of these applications.

18 And then as for what has been working
19 well with both of those application types, the
20 available tools that are from FDA we feel like
21 more or less we've been able to successfully use
22 them or adapt them. For example, the ECTD

1 structure. It wasn't put together necessarily
2 for us, but it does lend itself very well to
3 providing a structure for an application of this
4 type, particularly the scientific studies
5 sections.

6 Another area that I think we have been
7 able to have a successful adaptation is
8 translating the guidances into a submission
9 format absent a standalone guidance that's
10 specifically for the tobacco product applications
11 and absent a common table of contents. So it's
12 sort of left to us to -- or and to our own
13 devices to devise a submission structure for
14 these applications.

15 And then speaking to something that
16 came up in Jeff's talk, he didn't -- I don't
17 remember hearing him say the word "flat folder
18 structure," but that is the environment that we
19 are building our applications in now and I feel
20 like even though the eCTD structure utilizes
21 folders, you're able to take the logic from the
22 eCTD and translate into a flat folder environment

1 and then add metadata on top of that so you have
2 a nice -- he's giving me a thumbs up --

3 (Laughter.)

4 MS. CAMPBELL: -- so you have a nice
5 organized way to present hundreds and hundreds of
6 files that go into a product application of these
7 types.

8 And then one area that we've been
9 limited thus far is using eSubmitter for either
10 of these types of applications. I don't
11 personally have experience working with the HPHC
12 reporting and the ingredient listings, and I know
13 our company has been able to use eSubmitter for
14 those. We have not been successfully using them
15 for MRTPs or PMTAs.

16 MS. RUDOLPH: Anuschka?

17 MS. MERSON: Hi, I'm Anuschka Merson.
18 I work for ITG Brands. First I'll start with the
19 FDA website. I've set up a process where we
20 track the FDA website on a daily basis -- it's
21 the CTP to understand what has changed. And
22 there is a date at the bottom of each page, but

1 sometimes it's really hard to understand what has
2 changed. It's not always clear. So if we could
3 have something like that says new and the section
4 that's changed currently. We have a printout of
5 each page, and we compare that to determine if
6 like something small changed. And if it's no
7 worry, to let your stakeholders know.

8 Also I have experience in the
9 eSubmitter tool and the CTP Portal. We love the
10 CTP Portal. The ESG we never used because we
11 weren't confident in it. The eSubmitter, the
12 forms are very easy to use, and it tells you when
13 you've made a mistake and what you need to go
14 fix. I think the only thing where we would like
15 some more guidance on PDFs like the submission,
16 like a general format of how to submit an SE
17 submission, for instance. Do you want it in
18 smaller documents? Just a general format I think
19 would be very helpful. Thank you.

20 MS. RUDOLPH: Thank you very much.
21 And you heard from Sharyn, but would you like to
22 introduce yourself?

1 MS. MILLER: Hi, everyone. Sharyn
2 Miller, Regulatory Health Project Manager in the
3 Division of Regulatory Project Management within
4 the Office of Science.

5 MS. RUDOLPH: Thank you. Deborah?

6 MS. SHOLTES: I'm Deborah Sholtes.
7 I'm a Branch Chief with the Division of
8 Regulatory Science Informatics in the Office of
9 Science.

10 MS. RUDOLPH: Fantastic. So before we
11 get into -- and in case you all have not had a
12 chance to write down your question, write it down
13 now because we have got a little bit of room. We
14 have one question so far submitted. So if you
15 have anything, send it on over to your folks here
16 on the ends of the rows.

17 But before we get into this one
18 question that we do have, or others that may
19 come, Deborah, as you were listening to the
20 panelists talk, the other folks, do you have any
21 comments or thoughts about what you heard them
22 say?

1 MS. SHOLTES: I do. There are a
2 couple of things that people tend to get confused
3 because their names are so very similar. One is
4 the Electronic Submission Gateway -- it's also
5 called the ESG. And that's a very technical
6 piece of the infrastructure, and that is very
7 different from the eSubmitter tool. And the
8 reason it gets confused is not just because the
9 names are similar, but they're used in the same
10 process of submitting an electronic submission to
11 FDA.

12 So our portal actually is a simplified
13 way of accessing the ESG, the Electronic
14 Submission Gateway. It keeps you from having to
15 have that really high technical expertise in
16 house and makes it the simple point and click,
17 attach your files. The type of files to attach
18 are files you've created using the eSubmitter
19 tool. So the names are very similar; the tools
20 are quite different.

21 MS. RUDOLPH: Very helpful. Thank
22 you.

1 And Sharyn, do you have anything to
2 comment on from what you heard from the other
3 folks at this point?

4 MS. MILLER: Yes, I think I'll
5 piggyback on what Deborah was saying. And just
6 to clarify with the holidays quickly approaching
7 I think that it's easy for us to put into
8 perspective eSubmitter, ESG and CTP Portal in
9 terms of packaging gifts. So I'm going to do
10 that for you.

11 If you want to think about eSubmitter
12 as packaging that gift for the holiday season and
13 then ESG and the CTP Portal as a way to get that
14 gift to your designated recipient, I think that's
15 just an alternative way to consider and think
16 about those two different --

17 (Simultaneous speaking.)

18 MS. SHOLTES: So the portal is Santa's
19 sleigh. Is that what you're saying?

20 (Laughter.)

21 MS. SHOLTES: I'll take that.

22 MS. MILLER: And to Paisley's point

1 that she mentioned the website not always being
2 the easiest to find information, we certainly
3 acknowledge that and want to continue having
4 proactive discussions and collaborative efforts
5 to ensure that our website enables for and allows
6 intuitive navigation to find you the information
7 and resources you need to complete the submission
8 process and also to become more familiar with the
9 regulatory items we have available.

10 That being said, I'd just encourage
11 everyone to periodically check back with our web
12 sites as we are continuously looking for areas to
13 improve and continue quality enhancements to make
14 that more intuitive.

15 One item that we've recently done and
16 have in the past done -- Deborah can probably
17 speak to previously -- is usability testing of
18 some of our systems in place to see how
19 manufacturers and industry are able to navigate
20 through the information we have available and to
21 use that as a resource and way to identify areas
22 that further require improving. So continue to

1 check back.

2 I'll also say that in addition to
3 having the date, the version date at the bottom
4 left-hand side, in cases where we've updated
5 recent forms, we will provide that version date
6 right beside the form as just a quick reference
7 and easy way to identify as opposed to scrolling
8 to the bottom of that particular page.

9 So those are just a few of the more
10 recent updates and things that we've done in the
11 past to try and solicit feedback and really make
12 this a collaborative effort to improve our
13 processes.

14 MS. RUDOLPH: Thank you. So I have
15 here now two questions: So the first one is
16 actually from FDA. Can you speak about the IAM
17 request process? What's the average time from
18 request submitted to account creation?

19 MS. SHOLTES: Typically it's a couple
20 of weeks if all of the information is correctly
21 provided. We don't always get completely or
22 completely correct submissions and then we have

1 to go back to the company and request
2 resubmission. Some of the issues that we see
3 sometimes is that the correct people have not
4 signed in the right locations. The authorized
5 party has to be able to sign for the -- the block
6 for the authorized party. That would typically
7 be an executive of the company. And the person
8 who is going to be the IAM, the industry account
9 manager for that company may very well likely not
10 be the company executive. They may delegate that
11 job to somebody who is more familiar with the
12 submission process. And so it is the IAM
13 themselves who must sign the Rules of Behavior
14 form. So sometimes we get those two signatures
15 backwards.

16 MS. RUDOLPH: So you addressed some of
17 the next question, which is directed for both the
18 folks who are outside representatives as well as
19 for FDA, and that's what are some of the common
20 reasons IMS gets held up? You were talking a
21 little bit about the signatures, but maybe from
22 both viewpoints, are there other issues that

1 folks from industry in setting it up have had
2 difficulty with or things that you could identify
3 there might be reasons why it gets held up?
4 That's a question from our audience.

5 MS. SHOLTES: Not sending in the Rules
6 of the signed Rules of Behavior is also an issue.

7 MS. RUDOLPH: Yes.

8 MS. SHOLTES: So we'll get the
9 request, the letter without the signed Rules of
10 Behavior. So it has to be complete.

11 MS. RUDOLPH: Okay. Any comments from
12 other folks?

13 (No audible response.)

14 MS. RUDOLPH: No? And then there's
15 one specific to Anuschka. When you had talked in
16 your opening you had talked a little bit about
17 not trusting ESG. Can you speak a little bit
18 more about why it is that you don't trust ESG?

19 MS. MERSON: Sure. When you put the
20 submission in, it doesn't tell you your
21 submission is received. It just -- it's kind of
22 out there. With the CTP Portal you can put in

1 your submission and it will say submission in
2 progress and then it will say submission
3 received. So it's just kind of a trust factor
4 that you know you've met your deadline to the FDA
5 and there's no proof that it went into the ESG.
6 We just -- it was a trust factor. So we used to
7 send it in on CDs --

8 MS. RUDOLPH: Okay.

9 MS. MERSON: -- with FedEx where we
10 were able to track and ensure the FDA --

11 MS. RUDOLPH: So some kind of read
12 receipt?

13 MS. MERSON: Correct. And it didn't
14 have -- it doesn't have that capability when we
15 -- the time we were using it.

16 MS. RUDOLPH: Okay. Okay.

17 MS. MERSON: Does that make sense?

18 MS. RUDOLPH: It absolutely does.

19 All right. Are there other things
20 from the panel here? This has been a short time
21 together, but welcome to take any thoughts that
22 you all have amongst yourselves at this time.

1 Otherwise, we're a wrap.

2 (No audible response.)

3 MS. RUDOLPH: Looks that way. Then we
4 are a wrap. Well, thank you very much.

5 (Applause.)

6 MS. CHANG: Hi. Good afternoon.

7 Well, welcome to a very informative day and we're
8 going close to the end, but I'm very excited talk
9 to you about environmental assessment since it
10 has been advertised at least five times during
11 today's presentation.

12 (Laughter.)

13 MS. CHANG: All right. So all right.
14 Let's start.

15 I'm Hoshing Chang, and I'm the
16 Environmental Science Branch Chief in the Office
17 of Science within the Center for Tobacco
18 Products. I'm going to talk today about
19 environmental assessments and claims of
20 categorical exclusion for tobacco product
21 application submitted to CTP.

22 I will briefly discuss the National

1 Environmental Policy Act and its purpose, the
2 environmental assessment, or EA, outline for a
3 product application, the probability availability
4 of the EA, and how to handle confidential
5 information, and the categorical exclusion, or
6 CatEx outline for a product application. At the
7 end of the presentation I will talk about
8 available resources for the applicants and go
9 over an example EA.

10 The National Environmental Policy Act,
11 or NEPA, was sign into law on January 1st, 1970.
12 To quote NEPA, it is "a national policy which
13 will encourage productive and enjoyable harmony
14 between man and its environment." To further
15 quote NEPA, its purposes include "to promote
16 efforts which will prevent or eliminate damage to
17 the environment and biosphere and stimulate the
18 health and welfare of man to enrich the
19 understanding of ecological systems and natural
20 resources important to the nation, to establish a
21 Council on Environmental Quality."

22 Why is an EA needed? An EA is

1 required by law under NEPA for such things as:
2 promulgation of new regulations, requests for
3 actions such as product marketing orders.

4 Finally, the Code of Federal
5 Regulations, under 21 C.F.R. 25.15(a), states:
6 "All applications or petitions requesting agency
7 action require the submission of an EA or a claim
8 of categorical exclusion."

9 The useful information in the EA
10 outline as the following elements: A cover page,
11 a table of contents, the table of the EA, which I
12 will discuss in more detail later, and any
13 appendices.

14 The useful information in the EA
15 includes a cover page with the following
16 information: The title of the document; for
17 example, Environmental Assessment for the
18 Marketing Order for, your new product name and
19 manufacture by, name of the applicant, the agency
20 for which the EA was prepared; for example,
21 prepared for the Center for Tobacco Products,
22 U.S. Food and Drug Administration. And finally,

1 the date the EA was prepared.

2 The next section of the EA is a useful
3 information in a table of contents. The table of
4 contents includes EA section titles, EA
5 subsection titles, appendices and confidential
6 appendices. All office sections are listed with
7 associated page numbers.

8 The body of the EA follows the table
9 of contents and includes each EA section as
10 described in the table of contents. I will go
11 through the useful information in those sections
12 now.

13 Section 1 titled "Applicant and
14 Manufacture Information" includes the company or
15 individual name of the applicant, the applicant's
16 address, which includes the street address, the
17 city, state and ZIP code, or the comparable
18 information for a location outside of the United
19 States, and the country when outside of the
20 United States, the manufacturer's name and the
21 address where the products are manufactured in
22 the same format as used for the applicant's

1 address.

2 In Section 2, "Product Informations"
3 describes useful information including the new
4 product name, the name product -- the new product
5 submission tracking number, STN, if available,
6 and the predicate or original product name, if
7 applicable. In addition product identification
8 is provided include the product type, product
9 subcategory, product package and product quantity
10 per retail sale unit.

11 The next section is Section 3 titled
12 "The Need for the Proposed Action." The useful
13 information in this section identifies the
14 proposed action and applicant marketing intent.
15 For example, for the SE pathway, the applicant
16 may state the proposed action requested by the
17 applicant is for FDA to issue a marketing order,
18 finding a new product substantial equivalent to
19 the predicate products under the provisions of
20 Section 19 in 905(j) of the Federal Food, Drug
21 and Cosmetic Act, the applicant wishes to
22 introduce the new tobacco product into interstate

1 commerce for commercial distribution in the
2 United States.

3 Finally, if the application is for the
4 SE pathway or an exemption request the useful
5 information in this section identifies the status
6 of the predicate and original product,
7 respectively. Also this section gives a brief
8 non-confidential description of how the new
9 product differs from the predicate or original
10 product. A detailed description of the
11 differences are included in a confidential
12 appendix which I will discuss later.

13 Section 4 is titled "Alternatives to
14 the Proposed Action." This section discusses any
15 identified alternatives to the proposed action.
16 One such alternative is the no action
17 alternative, meaning the action of not
18 authorizing the new product. For that
19 alternatives, the EA could state the no action
20 alternative is -- FDA does not issue the
21 marketing order for the new tobacco product in
22 the United States.

1 Section 5 to 7 further address the
2 potential environment impacts of the proposed
3 action and alternatives. Section 5 includes the
4 useful information to address impacts of
5 manufacturing the new products. Section 6, use
6 of the new product; and Section 7, disposal of
7 the new product. These sections include several
8 subsections which I will now go over.

9 The first sub-section is the affected
10 environment. The useful information in this
11 subsection describes the land use around the
12 manufacturing facility and includes an aerial
13 photograph showing the described area. It also
14 describes the environment where the product will
15 be used or disposed of.

16 The rest of the subsections described
17 the evaluation of potential environmental impacts
18 on the environmental resources where applicable.
19 The useful information describes the
20 environmental resources including air quality,
21 water resources, land use and zoning, biological
22 resources, geological features and soils,

1 socioeconomic conditions, solid waste and
2 hazardous materials, flat plains, wetlands and
3 coast zones and regulatory compliance. The
4 analyses can be presented in a tabular form,
5 however, the traditional paragraph form is
6 appropriated for lengthy discussions.

7 One subsection is cumulative impacts.
8 This subsection discusses the impacts on the
9 environment which results from the described
10 impacts of the proposed action when added to
11 other past, present and foreseeable future
12 actions. These subsections would also include
13 any mitigation of the identified impacts.

14 Section 8 titled "List of Preparers."
15 The useful information in this section is to
16 identify the individuals who were primarily
17 responsible for preparing and reviewing the EA.
18 For each individual their name, title,
19 organization, relevant education, relevant
20 experience and relevant expertise is included.

21 Section 9 titled "Listing of Agency
22 and Persons Consulted." The useful information

1 in this section is to identify agencies consulted
2 and states what information this agency provided
3 during the preparation of the EA, as well as the
4 name, title and organization of the person
5 contacted.

6 The EA concludes with sections of
7 references and appendices, also useful
8 information. Section 10 titled "References"
9 provide any citation that were referenced in the
10 EA.

11 The EA concludes with appendices where
12 necessary. This also includes confidential
13 appendices that contain information deemed
14 business confidential. Examples of the
15 information that would be appropriate for the
16 confidential appendices include: Specific
17 modifications or changes between a new and
18 predicate product, calculation that were made
19 base on confidential information about the new
20 and predicate products or original products often
21 related to the projected market share
22 information, the identities of the suppliers when

1 they are not part of the company that submits the
2 application and the location of any supplier
3 manufacturing facility.

4 Here I would like to emphasize the EA
5 is available to the public with the confidential
6 information redacted. As noted in 21 C.F.R.
7 25.51(a) when confidential information is
8 pertinent to the environmental review of a
9 proposed action, that information should be
10 submitted separately in a confidential section
11 and summarized in the EA to the extent possible.
12 21 C.F.R. 25.51(b) notes that FONSI's and EAs will
13 be available to the public in accordance with 40
14 C.F.R. 1506.6.

15 If an applicant believes they are
16 marketing order request may qualify for a
17 categorical exclusion, CatEx, they may submit a
18 CatEx claim. The CatEx claim should identify the
19 relevant CatEx by including a statement of
20 compliance with the specific CatEx criteria. The
21 applicant should also state to the best of their
22 knowledge no actual ordinary circumstances exist.

1 Currently CTP has one class of actions relevant
2 to tobacco product market applications. The
3 criteria for that CatEx claim is that the new
4 product is a provisional product and the criteria
5 of the claim is listed in 21 C.F.R. 25.35(a) as
6 described in the slide.

7 Shown here are resources for
8 applicants for obtaining more information about a
9 EA process. Examples of EA posted on the CTP web
10 site in a webinar titled "Environmental
11 Considerations of Tobacco Product Applications
12 Submitted to CTP 2016."

13 Examples EA as described by previous
14 speaker can be found on the web page of marketing
15 orders for SE. When you click on the EA of your
16 interest, you can read a redacted agency-prepared
17 EA as shown in the next slides. These EAs have
18 made -- have had any confidential information
19 redacted from the public document. Using example
20 of one of these redacted agency-prepared EA I
21 will walk you through each section that I have
22 previously discussed.

1 You see here the cover page and the
2 table of contents. The cover page includes the
3 title of the document, who prepared the EA and
4 the date the EA was completed. When the EA is
5 prepared by the applicant, the "prepared by"
6 portion of the cover page will note the company
7 name of the new product. The table of contents
8 include a section of -- and associated page
9 numbers.

10 As we move into the EA, you can see
11 the first page contains the product name and
12 other product information and the need for the
13 proposed action. The next page begins the
14 evaluation of impacts of manufacturing the
15 product. The subsequent pages contain
16 evaluations of impact of use and disposal of the
17 product. And then as noted, the EA includes the
18 list of preparers.

19 As noted previously, here is where the
20 EA notes the government agency consorted. None
21 for this document as it was prepared by the
22 agency. This is followed in by the references

1 and appendices and then this EA concludes with a
2 confidential appendix, which includes the
3 confidential information important for the
4 evaluation of the potential environmental
5 impacts. As you can see here the potential --
6 the confidential information is redacted
7 according to the mention regulation when posted
8 on FDA's web page.

9 This concludes my presentation about
10 the EA and CatEx for tobacco product applications
11 submit to CTP. So you can visit us on the web
12 site, you can call us, and you can email us. And
13 I'd like to thank you for your attention.

14 (Applause.)

15 MS. CONEWAY: Good afternoon. My name
16 is Renee Coneway and I'm a lead program analyst
17 in CTP's Office of Science. Today I will be
18 speaking about the transfer of ownership process
19 for OS.

20 First, I will provide an overview of
21 the transfer program and go over some key terms.
22 Then I'll discuss the information we have

1 requested from applicants in order to complete a
2 transfer of ownership, how to submit the request
3 and finally the transfer acknowledgment.

4 In this section I will provide an
5 overview of the Transfer of Ownership Program.
6 Transfer of Ownership is a program with CTP in
7 which an applicant transfers the rights and
8 responsibilities for their applications to
9 another company. An applicant typically
10 transfers ownership of their applications if
11 they're selling all or part of their company,
12 merging with another company, or both. Currently
13 there are no requirements to transfer ownership.
14 Please note this process is independent from
15 application review.

16 In OS, we commonly see two types of
17 transfer requests: A one-to-one transfer where
18 an applicant transfers all applications to a
19 single applicant and a one-to-many transfer where
20 an applicant may transfer different applications
21 for their tobacco products to two or more
22 applicants. Applicants subject -- applications

1 subject to transfer of ownership may include
2 PMTAs, SEs, and EXs.

3 Here are some of the key terms to
4 assist with the transfer of ownership process.
5 The current applicant is the entity listed as the
6 applicant of record. The current applicant is
7 also the originator of the transfer request. The
8 new applicant is the entity assuming ownership of
9 the applications from the current applicant. And
10 a treatment plan request is a signed letter from
11 an authorized representative that contains
12 sufficient information for CTP to start the
13 transfer process.

14 In this section I will go over the
15 process to complete a transfer request. Before
16 getting into specific details, I would like to
17 provide some examples of requests we receive that
18 are not actual requests to transfer ownership.

19 We commonly receive requests notifying
20 us of changes such as: a company name change, a
21 notice of bankruptcy or sale statement, a change
22 in legal representation and withdrawal requests;

1 however, these requests do not initiate the
2 transfer process. For example, we receive
3 inquiries from applicants who state I've already
4 notified CTP that my company is bankrupt. Isn't
5 that notification sufficient to transfer
6 ownership? The answer is no because a
7 notification of bankruptcy is not considered a
8 transfer request. It is only a notification of
9 bankruptcy.

10 If the applicant would like to
11 transfer ownership, they should submit a request
12 to CTP and include the party accepting
13 responsibility for the transfer to be effective.
14 Your RHPM can assist you with what it means to
15 withdraw an application and the appropriate
16 paperwork for that action, for that decision.
17 They can also assist with updating authorized
18 contacts and specific application-related
19 questions.

20 Transfer of ownership is important to
21 ensure accuracy of all records and the
22 appropriate individuals are communicating with

1 FDA. Let me elaborate on this further. If
2 applicant A were to submit an SE report and later
3 sold that report under -- I'm sorry. If an
4 applicant -- if applicant A were to submit an SE
5 report and later sell that product under the
6 report to applicant X and they do not update
7 their files to show the transfer of ownership,
8 applicant A will continue to receive all
9 regulatory correspondence and decision making
10 authority for that application.

11 It is important that CTP is made aware
12 of the changes so the correct applicant may
13 respond appropriately, which in this case --
14 which in this example is applicant X. In
15 general, CTP follows a standard process for
16 transfer of ownership.

17 Now let me walk you through the
18 process. Prior to completing a transfer request
19 it is helpful if the current applicant conducts
20 an inventory and determines which specific
21 applications will be included in the transfer.
22 Currently there are no standard forms for a

1 transfer of ownership request. We generally have
2 requested that the applicant -- that the current
3 applicant submit a signed transfer request letter
4 that clearly states the request is to transfer
5 ownership to the new applicant.

6 We have also requested that the letter
7 includes the specific applications and products
8 -- product names by STN, a statement that all
9 rights of the applications have been transferred
10 to the new applicant, the point of contact
11 information and the effective date of the
12 transfer based on business transaction
13 agreements. As a reminder, applications
14 generally included in a transfer are PMTAs, SEs
15 and EXs. If additional information is needed, we
16 will communicate directly with the applicant.

17 Now I will go over the process for the
18 new applicant. In processing the request we have
19 requested a signed transfer acceptance letter
20 that includes the specific applications and
21 products being accepted, a commitment to all
22 agreements, promises and conditions made by the

1 current applicant of record, a statement that the
2 applicant has a complete copy of all applications
3 or state they will request one, a statement that
4 no modifications have been made to the transfer
5 applications, and finally the effective date of
6 the transfer.

7 So there are different options for
8 submitting a transfer request. Applicants can
9 submit electronically through the CTP Portal if
10 they have an established account, via U.S. mail
11 or through a courier service. Applicants can
12 obtain the CTP mailing address, which is listed
13 on the FDA web site at www.fda.gov/tobacco.

14 We will review the transfer request
15 letters for completeness. If the letter is
16 missing information, we may reach out to the
17 applicant. Specifically when dealing with pre-
18 market applications your RHPM will call to ask
19 clarifying questions and verify if the request is
20 truly for a transfer of ownership. If the
21 request is not for a -- is not a transfer, for
22 example, but a change in legal representation,

1 your RHPM can assist you with those updates. If
2 the request is for a transfer of ownership, your
3 RHPM will clarify if additional information will
4 be helpful.

5 During the review phase we generally
6 only communicate with the current applicant. The
7 purpose is to protect the applicant's
8 confidential commercial information. It is the
9 responsibility of the current applicant to ensure
10 that the new applicant has the sufficient
11 information for their transfer acceptance letter.

12 Once the transfer request is complete
13 and all items are present to support the request,
14 we will update the official records to reflect
15 the new applicant's information and issue a
16 transfer acknowledgement letter to both parties.
17 It is important to note that CTP's
18 acknowledgement does not represent the agency's
19 support with regard to a company's business plans
20 or operations. We will continue to communicate
21 with the current applicant until the
22 acknowledgment letter is issued. Also, the new

1 applicant may be subject to other requirements
2 such as registration.

3 With the issue of the acknowledgment
4 letters this completes the transfer of ownership
5 process. This means all records have been
6 updated to reflect the new applicant and CTP is
7 now communicating with the appropriate party for
8 decisions on the transferred applications.

9 In my earlier example where applicant
10 A sold their product to applicant X that had a
11 pending SE report, both applicant A and applicant
12 X had received transfer acknowledgment letters
13 and CTP is now only communicating with applicant
14 X, who is the new applicant of record.

15 This concludes my presentation on
16 transfer of ownership. If you have any
17 additional questions, I encourage you to ask
18 during the next panel discussion or you can reach
19 out to your RHPM, contact our call center or send
20 an email to Ask -- to the Ask CTP mailbox. Thank
21 you.

22 (Applause.)

1 MS. JOHNSON: Thank you again to our
2 presenters. As she mentioned, we have our final
3 panel. So if our panelists for Session 5 could
4 make their way to the front, that would be great.
5 Again, if you have any questions, please put
6 those on the cards, the index cards. Raise your
7 hand if you need one. Oh, there's one in back.

8 Okay.

9 (Off the record comments).

10 All right. So we'll have our industry
11 panelists introduce themselves and make comments
12 and statements on the presentations that we just
13 witnessed, and we'll go on from there.

14 We'll start with you, Tony.

15 MR. ABOUD: Thank you so much.

16 Appreciate the opportunity. My name is Tony
17 Abboud. I'm the Executive Director of the Vapor
18 Technology Association.

19 The Vapor Technology Association is a
20 membership organization. We are an advocacy
21 organization. Our members include manufacturers,
22 the largest manufacturers of devices and e-

1 liquids, the largest distributors of those
2 products as well in the United States, and the
3 largest number of flavoring companies and also
4 vapor shops around the country. So we take a
5 holistic and a unified view to the regulatory
6 experience.

7 The focus of our advocacy is typically
8 promoting a rational regulatory scheme that
9 recognizes and truly embraces the lifesaving
10 potential that ENDS products have. We also take
11 the biggest issues of the industry to heart. In
12 particular our focus on limiting youth access has
13 been a priority of ours for the last two years,
14 as well as the implementation of new requirements
15 and new standards that relate to and can limit
16 the access of those products.

17 Now I very much appreciate the
18 detailed explanation and presentation that we
19 just heard primarily on environmental assessments
20 and categorical exclusions, however, I find when
21 I frequently speak on these subjects I'm also
22 reminding folks that we're kind of speaking from

1 a unique position, and in this particular case
2 it's no different because ENDS products typically
3 are not -- cannot access this particular aspect
4 of the process. And first, as was noted,
5 categorical exclusions are available only to
6 provisional products that are submitted through
7 an SE pathway. And of course ENDS products don't
8 have that pathway available to them. The PMTA
9 pathway is the single available pathway for our
10 products.

11 So from that perspective I can't
12 really comment on that process except to offer a
13 couple of thoughts: The first thought I would
14 offer is that the recent modifications that were
15 made to the categorical exclusion and the
16 environmental assessment rule in Part 25 was done
17 before of course the deeming regulation was put
18 into effect. And so companies that were in the
19 vapor industry or manufacturers of ENDS didn't
20 really have an opportunity to comment on that
21 process.

22 The Vapor Technology Association took

1 an opportunity to comment on this aspect of it
2 when we submitted comments to FDA in February of
3 this year in response to their request for
4 comments on the PMTA process. And we appreciate
5 the opportunity to amplify those just briefly
6 here.

7 Very shortly, the key issues from our
8 perspective is that because we cannot make a
9 CatEx claim, we need to consider whether or not
10 it's appropriate for ENDS products to receive
11 that same treatment. So we would suggest that a
12 categorical exclusion is provided for for both
13 devices as well as for e-liquids.

14 I think as Jeff Walker earlier noted
15 that sometimes it's helpful to examine how FDA
16 approaches these issues from a drug device or a
17 combo perspective. I think that's -- it makes
18 for an interesting analysis here. FDA would
19 treat, would likely treat a device, an
20 aerosolizing apparatus that is being sold and
21 marketed with a cessation claim as a device or as
22 a combo. And in that case it would probably

1 receive the broadest exclusions that are
2 available to all drug products or drug devices.
3 I mean, this is typically true that these
4 categorical exclusions arise for pre-market
5 approvals, for pre-market notifications,
6 510(k)'s, for investigative device exemptions, as
7 well as humanitarian device exemptions.

8 So take just for example the medical
9 device for asthma, a product which contains Freon
10 134a, I'm told. This is a product that has well-
11 recognized environmental aspects, yet there is no
12 environmental assessment required for that
13 product. The same would be true with respect to
14 lithium ion batteries that are included in
15 medical devices. Again, functionally similar
16 batteries in these products not subject to
17 environmental assessment requirement.

18 So whether FDA is evaluating the
19 product, evaluating the same device from the
20 perspective of whether it should be treated as a
21 medical device and whether it should be treated
22 as a tobacco product by nature of the claim, then

1 an environmental assessment, if it's not
2 necessary in the case of the former, should not
3 be necessary in the case of the latter. So with
4 that respect a categorical exclusion for ENDS
5 products promotes consistency as well as avoids
6 costly redundancy.

7 The last note I would quickly add,
8 because I see my timer is coming to relieve me,
9 is a similar analysis; and we won't belabor it,
10 could be made for e-liquids where you have
11 commonplace exclusions granted for a variety of
12 drugs or biologics, the biohazards of which are
13 not known or will not be known for many years
14 because of the infancy of the process through
15 which they are in. But at the end of the day the
16 question is can FDA through the PMTA process use
17 a technological -- the toxicological data that it
18 will be collecting as well as the battery
19 standards and any other sort of technological
20 requirements to solve the issue that would
21 otherwise be addressed by an environmental
22 assessment so we can avoid redundancy?

1 MS. JOHNSON: Thank you, Tony.

2 Karen?

3 MS. COOK: Good afternoon. I'm Karen
4 Cook with ITG Brands. I'm the Manager of
5 Regulatory Affairs and I'm responsible for
6 various regulatory submissions including
7 grandfathering. My product experience is with
8 cigarettes and cigars. Understandably, the
9 grandfathering component to this discussion panel
10 was canceled today. Hopefully CTP will provide
11 another opportunity to discuss this important
12 topic in the future.

13 I have just a couple of comments with
14 regard to environmental assessments and transfer
15 of ownership. With regards to the EA, a template
16 would be great and some additional guidance,
17 however, today's presentation did provide a lot
18 of helpful information, so really appreciate
19 that. Thank you.

20 With regard to the transfer of
21 ownership, again a guidance document would be
22 extremely helpful on this topic. ITG Brands did

1 experience a transfer of ownership. The process
2 was very lengthy and not well-defined. It was as
3 if the FDA was kind of learning the process along
4 with us at the time when we were going through
5 the transfer. So again, just a guidance document
6 on this topic would be very helpful.

7 Just want to thank CTP for this
8 opportunity today and for being here. Thank you.

9 MS. POWELL: Thank you. My name is
10 Christie Powell and I'm a master scientist within
11 the Submissions and Engagement Group and the
12 Scientific and Regulatory Affairs Department of
13 RAI Services Company.

14 My experience at RAIS involves the
15 generation and submission of tobacco product
16 applications including regular substantial
17 equivalence filings, exemption requests, pre-
18 market tobacco applications and modified risk
19 tobacco applications, as well as their
20 environmental assessments?

21 Now I know that there were three
22 topics for today, so since my experience really

1 is primarily with environmental assessments, I'll
2 keep my talking points to that, although I would
3 like to make one note if it's okay regarding
4 stand-alone grandfather submissions.

5 So RAIS has observed inconsistent
6 review time frames for stand-alone submissions.
7 So sometimes decisions are made in less than
8 three months, which is great, and then we found
9 that others can take a year or longer. And so we
10 feel these are fairly straightforward submissions
11 and so it's a little unclear why the review is so
12 inconsistent. So this may be an area of
13 opportunity for improvement.

14 So now back to the area of my
15 expertise, EAs. So as highlighted today, the FDA
16 has the authority to refuse to accept or file
17 certain applications if the company's
18 environmental assessments are found to be
19 inadequate. And as mentioned a couple times,
20 substantial equivalence is for provisional
21 products, so the SE reports submitted between
22 February 15th, 2007 and March 22nd, 2011 can

1 claim categorical exclusion, meaning that an EA
2 is not required for these submissions.

3 This means that all other submissions
4 including non-provisional SE reports, exemption
5 requests, pre-market tobacco applications and
6 modified risk tobacco product applications
7 require an EA. Therefore, having a solid
8 understanding of how to generate an environmental
9 assessment is an important component of tobacco
10 product applications.

11 So as someone who has been actively
12 involved in the process of EAs at -- and the EA
13 process at RAIS, I'd like to share a few
14 learnings and observations on this topic.

15 First, there are quite a few guidance
16 documents, there are some rules, there's the
17 webinar that was mentioned today and there's
18 examples that are provided by CTP, and I found
19 those to all be very beneficial.

20 I do point anyone who is new to
21 generating an EA to the Code of Federal
22 Regulations Title 21, Section 25.40 on

1 environmental assessments. This is a good place
2 to start. It just provides a high-level overview
3 of what an environmental assessment is, outlines
4 some information to include and some other
5 considerations for your environmental assessment.

6 But I think more importantly are the
7 publicly-available EAs on CTP's web site.
8 Examples are extremely beneficial. They
9 highlight the types of information that the
10 agency evaluates in order to make a decision on
11 environmental impact of the authorization of a
12 tobacco marketing -- tobacco product marketing
13 order, excuse me.

14 From these examples I've learned that
15 it's important to take a holistic approach when
16 evaluating a potential environmental impact of a
17 product. By that I mean it is necessary to
18 assess the environmental impact of the product
19 through its life. So starting with the impact
20 from manufacturing, the impact during product use
21 and then its eventual disposal.

22 And then lastly I'll just note that

1 while the guidance and examples are extremely
2 helpful, they also highlight the fact that
3 there's no one-size-fits-all environmental
4 assessment that can be applied across different
5 product categories or applications. So different
6 products may have different considerations that
7 need to be made when it comes to their potential
8 environmental impact.

9 And so right now there is no reference
10 or guidance document currently available that
11 breaks down on a product category level the types
12 of information required for an environmental
13 assessment. So it really is up to the
14 manufacturer to determine what types of
15 information need to be included in the
16 environmental assessments in order to provide
17 enough information for the agency to make a
18 determination of the proposed action. Thank you.

19 MS. JOHNSON: That was perfect timing.
20 Perfect timing. Thank you for that.

21 Would my FDA colleagues like to
22 introduce themselves?

1 MS. BELTRE: Hi, Rosanna Beltre again
2 here. Hi, I'm from the Office of Science,
3 Division of Regulatory Project Management, if
4 anyone has just entered the room.

5 I was being a smart aleck.

6 MS. BENSON: I'm Kimberly Benson and
7 I'm the Director of the Division of Non-Clinical
8 Science in the Office of Science.

9 MS. CHANG: Kim is my boss.

10 (Laughter.)

11 MS. CHANG: I'm the Branch Chief for
12 the Environmental Science Branch in Division of
13 Non-Clinical Science, Office of Science.

14 MS. JOHNSON: Thank you. So do you
15 all have any reactions, any comments that you
16 wanted to make after the statements by our
17 industry colleagues? Any points you want to make?

18 MS. BENSON: Sure, I'll start off.
19 First, I do appreciate that you all are
20 appreciating seeing the agency written documents
21 on our web site, and I'm glad they're helpful.
22 That's been our goal to get them out there. And

1 hopefully you can see that they are also
2 evolving, so as you point people towards them, I
3 would point them to the most recent ones,
4 because as we gain more experience and understand
5 things better by evaluating them more, the
6 template -- our documents are changing as well.

7 So I do appreciate the idea that it's
8 not one-size-fits-all and a guidance that directs
9 you to specific information dependent on the
10 product or perhaps changes within a product
11 guidances are hard to prioritize. There are, as
12 we heard today, many, many topics that people
13 would like to see a guidance on. And we would
14 certainly like to pursue something like that
15 ourselves, but where it fits on that chain I
16 can't attest to.

17 I would recommend though you could
18 contact us if you had a question, if you were
19 working on an application for something that felt
20 very different and you weren't sure what you
21 should address, that you could reach out to us.
22 And that's one of those meetings that could be

1 totally done via written comments.

2 So, and then to the second part about
3 the CatEx and ENDS not actually being under our
4 purview at the time that that rule was amended,
5 certainly appreciate that. We couldn't foresee
6 at the time, but I have to say even if we could,
7 we would not have been able to make any additions
8 to that for something we had no experience with.

9 So we work with the Center for
10 Environmental Quality and they really stress the
11 -- well, how much experience, how many times have
12 you evaluated that, how many EAs have you
13 received on that? So we would like to pursue
14 options as well as we gain more knowledge to add
15 to our CatEx role now that we could say that to
16 CEQ, that we have certain experience with
17 different changes that might be able to be
18 CatEx'd.

19 We're always looking out for ways to
20 address that. And that different centers might
21 handle it different, that's also a difference of
22 time. Those things were CatEx'd in other centers

1 15, 20 years ago. I don't know if they would be
2 CatEx'd now. That's just my non-FDA opinion.
3 That's just Kim Benson, standard scientist at
4 home.

5 (Laughter.)

6 MS. BENSON: We function under our
7 regs and with our knowledge and we pursue what we
8 can with CEQ, and we will certainly continue to
9 do that and to gain more experience and knowledge
10 and a look towards amending that role in the
11 future.

12 MS. CHANG: All right. So I would
13 like to follow up on Kim, Tony and Christie's
14 comments. Yes, as Christie mentioned that
15 there's no one-size-fit-all EA, so whenever we
16 prepare a EA, we always consider proposed action.
17 So therefore, for CEDRs, their electronic
18 cigarette approval, their proposed action is
19 different from ours, so that therefore the
20 environmental consideration would be the same.
21 We don't have enough experience to say the
22 direction to go. We don't have enough experience

1 to say that every product application
2 authorization for electronic cigarettes, there's
3 no significant impact. We don't know unless we
4 see the application and the product itself.

5 But if I could follow up,
6 Environmental Science Branch we have published a
7 paper, and in that paper we identify the gap of
8 -- research gap of environmental impacts related
9 to electronic cigarettes. It's published in
10 Tobacco Control. I think that document could be
11 helpful. All right. Thank you.

12 MS. JOHNSON: Thank you.

13 MS. BELTRE: Okay. So I know everyone
14 has talked about EAs, but I'm going to bring it
15 back to transfer of ownership.

16 I have six points here that I would
17 like to make sure that are clear since this is a
18 relatively new topic that we haven't discussed
19 necessarily in the past, and as you mentioned it
20 was sort of convoluted, and we understand that
21 and we hear you. I help processed that, so I know
22 how painful that was. But a couple of things that

1 I think would go a long way when transferring.

2 One, plan for your transfer. You
3 can't send a notice to the agency and disconnect
4 your phones and expect us to be able to process
5 your request. It's important for us to have
6 accurate and updated information.

7 Ensure your files are up to date.
8 Ensure that you work with the new owner to
9 provide them that information that they need. If
10 you need to provide them ingredient information,
11 please do that in advance of the transfer. It
12 may be that your ingredient submissions are
13 bundled and contain information that is not being
14 transferred, and that could be a challenge for
15 the agency. So in terms of how long the process,
16 as part of the -- it's sort of teasing out all
17 the submissions that you have in house and
18 ensuring that we are not transferring things that
19 we shouldn't. So that's sort of the learning
20 curve for I think both industry and the agency.

21 So continue to work with your current
22 owner. If we send you a request for information

1 outlining information that is needed because the
2 initial request comes from the current owner,
3 make sure that you communicate any information
4 that may be necessary or helpful to the new
5 owner, because we're not communicating with them.
6 So sort of making sure that there's an open
7 communication in that process.

8 Clarify what you're requesting for.

9 Like we mentioned, a notice of bankruptcy is not
10 a transfer. If you're changing your company name
11 and that is all that you're letting us know,
12 please be clear. Please be clear that this not
13 company A being called B, or now it's A who's
14 selling to B. We can't read between the lines,
15 so articulating that clearly will go a really
16 long way.

17 Let's see. What else do I have here?

18 I think that covers it. So hopefully that's
19 enough information to help some people assemble
20 their transfer requests and ensure that we have
21 up-to-date information. I can speak a -- that
22 was the sixth -- this is the sixth thing.

1 So some of the challenges that we've
2 had are disconnected phone numbers, addresses,
3 returned mail. That may not be the case for some
4 of the larger companies, but these are some
5 challenges. And again, the bundled submission
6 and ensuring that you provide that opinion sort
7 of outside of the process. The only thing the
8 agency can sort of manage is the applications
9 that we have in house, and trying to protect your
10 information is obviously of most importance. And
11 we hope that moving forward it's less painful.
12 And we'll continue to take your feedback and try
13 to make this program more widely known and easier
14 moving forward.

15 MS. JOHNSON: Thank you.

16 Tony, did you have something to follow
17 up?

18 MR. ABOUD: (No audible response.)

19 MS. JOHNSON: Okay. So we did have a
20 few questions. We had one about changes of
21 ownership process, so I'm going to start with
22 that.

1 Rosanna, since you were speaking on
2 that. It's just one that asks what is the change
3 ownership process where no marketing applications
4 are involved such as only establishment's
5 registrations, product listings, ingredient lists
6 are being transferred?

7 MS. BELTRE: So what we presented here
8 today I can only speak to transfer of ownership
9 within the Office of Science and applications and
10 submissions that are housed within the Office of
11 Science. Unfortunately, there's nobody here from
12 the Office of Compliance and Enforcement that can
13 speak to what process they utilize for that, but
14 obviously notifying the agency.

15 One thing that may not be very clear
16 to everyone is that if a request is sent, whether
17 it's to the Office of Science or to the Office of
18 Compliance and Enforcement, the regulatory
19 project manager will try to triage that
20 information. So even if it was a transfer that
21 came to us because a project manager may be sort
22 of the only point of contact that a company has,

1 we will transfer that to the office, to the
2 appropriate office to make sure that it's
3 processed correctly.

4 MS. JOHNSON: Thank you.

5 Going back to EAs, we have a few
6 questions on that. This question asks why are
7 EAs needed at all for non-provisional products in
8 the SD and SE exemption pathways? Shouldn't
9 there be a CatEx for those products as there is
10 for provisional products? And what is the
11 justification for treating these two classes of
12 products differently for EA purposes?

13 MS. CHANG: Well, there are a lot of
14 questions.

15 MS. JOHNSON: Yes, we can finish the
16 rest of the time on --

17 (Laughter.)

18 MS. CHANG: So all the federal -- all
19 the decisions made by a Federal Government agency
20 require a NEPA document. All the action. Every
21 agency. So to allow a product to be on the
22 market is an action, is a decision for the

1 agency, so therefore an EA -- at least an EA is
2 needed. When I say "at least," that means maybe
3 an environmental impact statement, but that's not
4 in our regulation for -- in 21 C.F.R. 25.40 that
5 we're talking today. So therefore, that's the
6 reason every action, every decision made by any
7 agency needs an EA.

8 MS. JOHNSON: Okay. So then it asks
9 the justification for treating the two classes of
10 products different for EA purposes. So that's --

11 MS. CHANG: Yes, mean EX and SE?

12 PARTICIPANT: No.

13 MS. CHANG: No?

14 PARTICIPANT: No, provisionals.

15 MS. CHANG: Oh, do you want to go?

16 MS. BENSON: Yes, so one of the
17 reasons, as I had said, it as about having the
18 experience with the products. So when we were
19 working on this rule with the Center for
20 environmental Quality, we proposed a number of
21 things. And we had no experience with them, but
22 they're just kind of instant and that we needed

1 to get more experience.

2 But the provisionals were on the
3 market before the act, right? So we were able to
4 write a strong justification to say that those
5 could be categorically excluded. As is always
6 the case when talking about the Office of
7 Science, it's about a strong scientific
8 justification. And in this case made towards the
9 Center for Environmental Quality.

10 MS. CHANG: So if I could add on my
11 boss' comment. So all the NEPA regulation needs
12 to be cleared by Council on Environmental
13 Quality. And what do they look for? They look
14 for if the agency have -- that the agency has
15 enough experience to say that their action has no
16 significant impact. Currently under the regular
17 SE program we don't have enough information to
18 say that yet. So it's under evaluation.

19 MS. COOK: So you stated that you made
20 the decision because these products were already
21 on the market back in 2007, so with the newly-
22 deemed products like cigars with the SEs not due

1 until 2020, will you consider that for that
2 product portfolio?

3 MS. BENSON: It's certainly something
4 we will evaluate with all the newly-deemed
5 products to see if there are obvious strong cases
6 for categorical exclusions in there. And I
7 usually like to say why do they need an EA? You
8 can blame Richard Nixon because that's his act.

9 MS. JOHNSON: Thank you. We have time
10 for one more question. The question asks if the
11 tobacco product was manufactured abroad, must we
12 submit an EA discussing the environmental effects
13 of a foreign factory?

14 MS. CHANG: That's correct. It's in
15 our regulation. In 21 C.F.R. states that we need
16 to evaluate the environmental impacts due to the
17 federal actions as a result of FDA's actions. So
18 if FDA allowed this product to be marketed in the
19 United States, but it's manufactured abroad, then
20 we do have to evaluate the impacts of that
21 particular country.

22 MS. BENSON: This is something we hear

1 a lot of because everything else about the
2 Tobacco Control Act is about in the United
3 States. So even internally we would get, well,
4 why were you talking about this? It's a foreign
5 country. But since everything about that is
6 governed by the National Environmental Policy Act
7 and then FDA's regs that are tied to it, that's
8 what's driving all of it. And it does address
9 anything done in a foreign country as well.

10 MS. JOHNSON: Thank you. Any other
11 comments from our panelists?

12 (No audible response.)

13 MS. JOHNSON: Okay. Give them a round
14 of applause. Thank you so much for your time and
15 your expertise.

16 (Applause.)

17 MS. JOHNSON: Matt? Matt, you going
18 to send us home?

19 MR. HOLMAN: (No audible response.)

20 MS. JOHNSON: All right.

21 MR. HOLMAN: So I just want to say
22 thank you to all my colleagues for their

1 hopefully --- (off the record comments).
2 --very helpful presentations. Hopefully there's
3 a lot of good information that you all received
4 today through those presentations.

5 I also want to give a big thanks to
6 all of our panelists. I appreciate their
7 willingness to come up here and tell us what
8 things they've seen improvements on and other
9 areas where there are still struggles, just a
10 lack of transparency and consistency.

11 I've certainly taken a lot of notes
12 today. I think there are a lot of good points
13 being made that me and my colleagues will take
14 back to the office. I look forward to continuing
15 this same type of dialogue tomorrow. Today was
16 more focused on process. Tomorrow is going to be
17 more focused on the information contained within
18 the applications. So I look forward to the same
19 type of -- same level of conversation hopefully
20 tomorrow as we had today.

21 I do want to make a couple of notes
22 about tomorrow. We are going to be moved down

1 the hall to the Plaza Ballroom, so we won't be
2 here tomorrow. We'll we just down the hall.
3 There will be signs up like there was today, so
4 you should be able to find it, no problem.

5 The other point I want to make is that
6 our Session 8 at the end of the day tomorrow was
7 focused on deemed products. That was going to be
8 presented by our colleagues in the Office of
9 Compliance and Enforcement. As Mitch mentioned
10 this morning, they will not be participating in
11 this meeting tomorrow.

12 However, we still want to have some
13 discussion around deemed products, so our
14 panelists are going to actually share their
15 remarks, their perspective with us. And we're
16 going to conduct that session a little
17 differently than the other ones because we won't
18 have a presentation and we won't have our
19 colleagues from OCE here to present.

20 Instead what we're going to do during
21 that last session is we're going to have
22 microphones available so that those in the room

1 that have additional thoughts and perspective and
2 want to share them, they have that opportunity.
3 Certainly we are recording and transcribing this
4 meeting. We are also taking notes. So we will
5 certainly take back any input we hear, any of the
6 feedback that's provided tomorrow during Session
7 8.

8 So just want to give people a heads up
9 so you guys could be thinking it. If you do want
10 to share your perspective on the deemed products
11 and how you're dealing with those and meeting
12 our regulatory requirements under the application
13 review programs, that opportunity will be
14 provided.

15 We will be starting tomorrow morning
16 at 8:30 promptly as I said in the Plaza Ballroom.

17 So thanks again for everyone's
18 participation today and I look forward to seeing
19 you guys tomorrow morning.

20 (Applause.)

21 (Whereupon, the above-entitled matter
22 went off the record at 4:26 p.m.)

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Before: US FDA

Date: 10-22-18

Place: Rockville, MD

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