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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CONTENTS

CONTENTS

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(8:33 a.m.)

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

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

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

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

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

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

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

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

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

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

The Comprehensive Plan we announced

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Thank you very much.

(Applause.)

MR. WALKER: Well, good morning to all

of you.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Thank you very much.

(Applause.)

MS. JOHNSON: Good morning, and thank you.

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

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

First of all, for over the next two

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

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

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

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

Jennifer, are you ready?

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

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

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

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

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

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

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

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

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

So now that you have a basic

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

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

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

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

Three, and SE report is not necessary.

And four, an exemption is otherwise appropriate.

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

It is grandfathered.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Second, the tobacco product is legally marketed.

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

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

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

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

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

correspondence.

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

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

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

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

Exemption requests will also be

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

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

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

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

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

be identified within the application.

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

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

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

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

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

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

Third, we have the notification phase.

And fourth, review and action phase.

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

The notification phase will include the following steps:

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

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

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

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

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

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

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

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

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

The product is in compliance with the Act.

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

The modifications are to a product that is commercially marketed.

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

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

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

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

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

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

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

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

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

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

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

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

FDA has gained additional experience with the submission and review of abbreviated reports. An appendix to the exempt order letter is provided with FDA's suggested format for the submission of the abbreviated report. Manufacturers may use the suggested format to certify that the tobacco product has met the requirements in Sections 905(j)(1)(A)(ii) and

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

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

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

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

Thank you.

(Applause.)

MS. STARK: Good morning.

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

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

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

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

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

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

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

As this pathway is based on a

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

threefold:

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

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

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

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

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

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

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

Now, once these steps have been

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

So, under the remove-from-review

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

So, in examining the types of

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

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

These changes in timelines were in

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

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

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

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

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

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

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

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

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

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

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

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

provided for the different subcategories.

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

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

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

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

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

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

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

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

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

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

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

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

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

inquiries email at "Ask CTP".

So, this concludes my presentation. Thank you.

(Applause.)

MS. JOHNSON: Thank you, Jennifer and Cristi.

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

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

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

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

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

Rosanna?

MS. BELTRE: Good morning.

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

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

All right. Well, I will start then.

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

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

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

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

experiences and kind of collectively put together some thoughts.

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

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

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

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

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

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

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

MR. LINDEGAARD: Good morning.

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

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

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

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

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

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

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

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

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

Thank you.

MR. MURPHY: Good morning, everyone.

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

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

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

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

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

(Laughter.)

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

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

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

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

I recognize that in many ways both the

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

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

(Laughter.)

Second, based on our experience and

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

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

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

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

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

in regards to provisional SE applications currently under review.

Thank you.

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

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

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

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

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

MS. JOHNSON: I read it as is.

MS. STARK: The PHI?

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

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

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

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

acids and bases.

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

Rosie, do you have anything to add?

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

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

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

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

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

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

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

MS. JOHNSON: Thank you.

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

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

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

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

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

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

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

foreign applicant? So, items such as that.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

I think that gets to the whole question?

MS. JOHNSON: Yes, yes.

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

So, I think, with the experience we

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

Have you discussed such an approach?

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

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

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

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

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

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

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

Did that get to some of your questions?

MR. LINDEGAARD: Yes and no.

(Laughter.)

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

But it would just be sort of a type of

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

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

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

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

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

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

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

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

for an SE report.

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

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

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

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

considered withdrawn. So, that's in regulation.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

MR. LINDEGAARD: Can I add one point?

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

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

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

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

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

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

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

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

provisional. I mean, it took a long time.

But I just wanted to clarify that point for you.

MR. LINDEGAARD: Thank you.

MS. BELTRE: You're welcome.

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

We're going to take a break.

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

(Applause.)

Thank you so much.

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

Thank you.

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

MS. RUDOLPH: Folks, before we move

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

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

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

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

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

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

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

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

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

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

Consideration for this is determined

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

submitted.

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

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

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

As of September 30th, 2018, CTP has

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Similar to other applications, MRTPAs

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

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

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

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

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

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

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

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

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

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

something that could be identified in the presubmissions meeting.

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

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

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

meet the filing requirements for an MRTPA.

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

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

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

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

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

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

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

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

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

order on consumer perception, behavior, and health.

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

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

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

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

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

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

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

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

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

numbers are reflective of such.

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

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

you so much for your time today.

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

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

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

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

transparency for the tobacco product application process.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

MS. RUDOLPH: Thank you. Jim?

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

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

it to FDA.

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

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

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

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

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

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

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

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

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

interesting.

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

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

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

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

MS. RUDOLPH: Thank you, Jim. Jeff?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

information, which is not as mandatory.

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

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

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

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

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

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

some of other sister centers from FDA.

MS. BELTRE: Sorry.

MS. RUDOLPH: That's all right.

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

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

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

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

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

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

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

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

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

MS. RUDOLPH: Okay, thank you. Jim?

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

course that addressed all of our concerns.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

product that could come through that exemption request pathway.

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

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

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

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

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

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

him his moment here.

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

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

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

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

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

MR. WALKER: Sure. Let me just

address the communication piece. Everything you said is correct. You will be told during the scientific review phase, it's still under review. But I think what I'd like to suggest would be more useful, is could we just have at some point in time, a little bit more detail on what is the decision making process like within, you know, the center? And also outside the center. Because I'm guessing that when a CTP makes a decision or has a scientific review completed, there are other things that have to happen next before a market order actually gets written.

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

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

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

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

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

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

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

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

MS. KOVACEVIC: If I may, with respect

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

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

MS. KOVACEVIC: Correct, correct, correct.

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

MS. KOVACEVIC: Yes, ma'am.

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

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

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

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

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

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

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

performance goal for the meeting's program.

MS. BANCHERO: We need a little technical support.

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

MS. BANCHERO: Okay.

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

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

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

submit prior to the meeting.

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

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

submitting your meeting request.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Here are some recommended items to be

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

discussion is needed at the subsequent meeting.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

MS. VICHENSONT: 1:15.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

CTP can then access and review the

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

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

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

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

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

Now Company A can submit a PMTA and

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

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

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

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

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

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

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

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

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

Electronic submission is generally available 24 hours a day, seven days a week. Therefore, it is encouraged to send TPMF submissions electronically through the CTP portal.

CTP also has a webinar on our website titled "Using a TPMF for Ingredient Listing Submissions" in September of 2018. This webinar reviews examples of ingredient-listing scenarios that a TPMF can address and how to cross reference TPMFs for ingredient submissions.

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

There is an establishment process, a stage where a request to establish a TPMF is received and submitted to CTP and CTP acknowledges the receipt.

There is also a scientific review process, the stage when a submission references the TPMF. At this point a TPMF scientific review

occurs and ends with a determination of adequate or inadequate.

Depending on the TPMF there may be multiple scientific reviews occurring at the same time if there are multiple submissions referencing the master file.

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

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

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

for example to grant or rescind a letter of authorization.

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

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

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

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

The admin information section contains

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

The second section, the content information section, should contain information that the owner wishes to be referenced. Currently there are no requirements for structure but CTP recommends the master file be organized in a logical manner.

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

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

reporting, and informed consent forms.

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

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

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

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

that references a master file.

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

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

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

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

receipt and establishment.

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

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

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

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

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

CTP.

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

If the TPMF were referenced to support ingredient listing CTP would focus on the review of ingredient requirements such as product identification, ingredient identification, part to which the ingredient is added, and the ingredient quantity.

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

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

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

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

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

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

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

When reviewing the master file CTP

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

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

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

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

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

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

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

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

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

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

PMTA letter, whichever is first, scientific review of the PMTA and amended TPMF will commence. CTP will then issue an appropriate letter consistent with the PMTA process.

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

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

If the TPMF owner does not respond or fails to provide documents necessary to support a pre-market order the order is likely to be denied.

We encourage the authorized party and

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

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

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

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

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

no longer review the content when referenced in a submission.

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

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

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

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

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

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

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

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

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

Secondly, the applicant or authorized

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

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

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

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

(Applause.)

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

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

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

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

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

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

I think that the process for

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

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

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

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

And I think like Jim said earlier we

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

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

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

I think those outputs could inform meetings and make applicants better prepared for those meetings. So applicants might have a chicken and egg issue, do you ask for a meeting

before you get more guidance from CTP, I think my preference would be to get more guidance from CTP before you conduct a meeting. So that would be a preference.

Other areas of potential improvement, maybe even shortening the time from the meeting request to the meeting. In some circumstances that would be very helpful.

More meetings. Somebody mentioned earlier it could be good to have more than one pre-submission meeting, particularly for a pre-market review program that from start to finish might be over the course of a few years.

You don't have all the answers in your first meetings. Things come up. And so some leeway in that regard would be good.

Meetings during the review process. I have detected a strong bias against that. I would like at times to have some relief from that bias.

I have seen that the communication process is less binary than it used to be. It

was kind of all or nothing either in writing or nothing else that it's become less binary.

I would like it to become even less binary. So in certain circumstances I think it could be very helpful to have meetings during the review process.

And then lastly I go back to my time as a litigator, you know, you write a brief, you can't put everything in a brief. Sometimes you'd like to talk to the judge about what you did and why you did it and I think you've spent three years getting something together it would be nice to sit in front of you guys and explain everything we have done, why we did it, and answer questions, and that might alleviate some of the potential for miscommunication during the review process.

I don't have much to say about master files, which is good because I think my time is short. We haven't spent much time submitting master files mainly because of my concern about submitting I guess what would be a partially

blindfolded submission that I can't see things that we are submitting and it's always been my concern that if something comes up in the review process because it's proprietary or CCI that you can't share it with me and then I don't know how to respond to it.

Fortunately I haven't had to do that. Maybe somebody could comment on how you deal with that. Thank you.

MS. P. MILLER: So, first of all, I want to thank CTP for having this workshop. I think it's a great opportunity for two-way communication and learning and I've already learned a lot of things today, so thank you for having it.

I'm Patricia Miller and I'm senior director in law and regulatory affairs in Altria. Altria, over the last several years, has had a bit of experience with meetings as well as TPMS.

I'm going to limit my comments to meetings, I'll let Russ deal with the TPMS. I would guess that we've had, over the last five

years, a little bit more than half a dozen, what I would consider, pre-submission meetings.

We think of pre-submission meetings as a tool to encourage innovation in reduced harm tobacco products, and that's a really important goal for us as I know it is for CTP.

As FTA and applicants are preparing their information to support authorization of innovative tobacco products, two key things are important. One is the need for clear foundational rules. And preferably by notice in comment rulemaking.

So to the extent that we have more guidance on what we're supposed to be doing, potentially there's less need to have meetings. And when we do have meetings, they could be more efficient and perhaps targeted. If we have those clear foundation rules.

When it comes to meetings, what we see is a need for meetings throughout the application process that allow for two-way communication. So when you talk about the opportunity for meetings,

if you look at a true pre-submission meeting.

So before you ever file anything you may want to have an introductory meeting to talk about a novel tobacco product and talk about the general parameters of your application. You may want to have meetings about particular studies that you're conducting, you may want to have meetings to conduct the, to discuss the structure in content of your application.

Even while an application is pending, and Bryan alluded to this, there may be opportunities for communication, in person, with FDA, that is more useful than responding to written questions in an A/I letter. Sometimes that two-way communication could be helpful.

And even post-authorization. I can see opportunities, for example, for an applicant to have a conversation with FDA about a supplement for modifications to an authorized tobacco product. So, we see the need for communication throughout the application process.

What I'm having difficulty with is,

I've heard a bit of that today from CTP, which I think is helpful, but when I look, for example, at guidance documents that CTP has. The current guidance document, which was the one that was issued in 2012 and updated in 2016, really talks about meetings to discuss scientific research. And particularly meetings with Office of Science.

Now, it's encouraging to have heard here, encouragement about having pre-PMTA meetings and pre-MRTP meetings. But what appears that we have is kind of a one size fits all type of meeting in terms of asking for that meeting and the construct of that meeting, that goes with that 2016 guidance which is more about research.

Our experience has been, well, I'll just say, what's worked for us in the meeting process so far, when we have particular scientific questions, and particularly research studies that we want to discuss and we pose them to CTP in the way that's requested in the 2016 guidance, we have gotten the meetings.

We've had really helpfully meetings.

We've had good suggestions from CTP. And we've had documented results of those meetings through the minutes process, which is great.

What we still see is the need to kind of break out of that one size fits all meeting structure. It can sometimes be a burdensome.

You know, from the time that an applicant asks for a meeting to the time you actually have the meeting, is at least two months. And then the meeting process, at least as outlined in the one guidance, is a bit stilted or scripted.

In other words, you submit your request, you get a response back from FDA in 21 days, you submit a meeting information package, which can be pretty voluminous at times, and then your meeting is limited to the topics that you've raised there.

I will say too, part of that process is you get responses back from FDA two days before the meeting. And I don't know about others but that can be quite a scramble. When

you get responses back two days before and your digesting those responses, trying to understand them, trying to know what you still have clarifying questions on and being ready for a meeting in just two days, it can be difficult.

So, we would like to see a process that at times can adjust to the type of topic and where you are in the application process. That would be really helpful.

And I will note also, in CTP's PMTA guidance, there is a limit stated of one to two meetings per applicant that can really limit communication, particularly with innovative tobacco products.

So, I will summarize to say, it would be helpful to have clear foundational rules that may alleviate some meetings and we would love to see an array of types of meetings.

MS. RUDOLPH: Thank you. Russell.

MR. WOLZ: Yes, hi, I'm Russ Wolz, I am from Enthalpy Analytical in Richmond, Virginia. I'm here just to share some of our

experiences with the TPMFs.

As the name implies, Enthalpy Analytical, we do analytical work. All hundreds of different types of chemical analyses as well as toxicological analyses.

We do these as routine analyses and as part of PMTA submissions. The benefits, Sarah has described very well what the content of the TPMF can be.

In our case, in our case our TPMF includes our methods and the validations of those methods and our accreditations. So many of our methods are public but we include them in our master file.

We have established a master file. And we included our methods in the master file so that people who use our analytical services can reference those methods and validations of the methods in their PMTAs.

So, as Sarah has also very well stated, the master files are a benefit, both to the manufacturers who are submitting the PMTAs as

well as to the support mechanisms. So, it saves us time by not having to create multiple reports and send the same set of SOPs and validations to a lot of different clients, we can just send it all to central, very secure repository.

(Laughter.)

MR. WOLZ: Then we assign the right of reference to certain clients. And we're still learning this process.

Our first submission was actually a hard copy document. And we then later updated that to do electronic submissions, primarily in the form of PDF files.

So when we move to the electronic submission, so now I'm going to move on to some of the challenges we've encountered. Your first electronic submission, after you've established your, or been accepted to establish a master file, is done through a test site.

So we created our master file and submitted it through the test site. Then as it turned out, we thought we had submitted it as a

formal submission but it turned out not to be the case. And it wasn't for two or three months that we found out that, oh, we need to submit it through the real site.

So, again, that was just education for us and that's why I'm sharing these challenges we've experienced with you.

The other challenge is simply in organizing these files. We have hundreds of methods, like, 250 methods, to organize.

First of all, to create a document of that size is very challenging and then to organize it is the additional challenge. So we've very recently updated our master file in a new format, which is now a PDF format with hyperlinks to the various sections.

And within each section we actually have hyperlinks to the actual SOPs and corresponding validations.

The only thing that we would recommend, that might help, is instead of having one giant master file, like I said, we've

submitted only 31 of our more than 200 methods, we might recommend that there be separate files corresponding, organized in different ways.

So, for example, we could have a master file dedicated to e-liquid analysis, another one for combustibles, another one for smokeless tobacco. So we would have, rather than one gigantic file, which is hard to wade through, even with all the hyperlinks, we think it might be better organized to use instead of having one big file, to use the electronic depository as more of a folder instead of just a file.

So, like I said, Sarah did such a good job explaining all the other things, that's all I have for you today.

MS. RUDOLPH: Great, thank you. And colleagues from FDA, would you like to introduce yourselves?

MS. RANDAZZO: Hi, I'm Joanna Randazzo, I'm a lead science policy analyst in OS.

MS. DOLLING: Good afternoon, I'm

Marcella Dolling, I am a branch chief within the Office of Science, division for Regulatory Project Management.

MS. RUDOLPH: Great, thank you. Well, I guess before we get started with a few questions that have been submitted, I guess I'm going to look over to my FDA colleagues, and based on what you heard from the panelist who are sharing the table here with you, are there a few things that come to mind that you think might be of interest for you to address at this time?

MS. RANDAZZO: Yes, actually, I would like to comment on a couple of the recurring comments that we heard from both Bryan and Patricia.

And part of it was about the time it takes to get a meeting scheduled. And one way that industry could actually help them reduce some of their time to get a meeting on the books with FDA is to submit their meeting information package with the original meeting request.

Because we do prefer to have 45 days

minimum to prepare. We want to give you really good responses.

And I think that I've heard through several of the presenters, and Jim from Swedish Match is one of them, thank you, that we do try to give really good responses and we do try and think about our responses and give you the best feedback we can.

We do want a great submission from you, it makes it easier to review, so we do want to give you adequate and decent feedback on all of your questions, as specific as we can get. And so, so we don't want to short ourselves with time either in order to give you a good work product back.

And then one of the other items that I was going to comment on was, regarding the interest in possibly meeting with OS or CTP during the review of a scientific application, generally we try not to duplicate efforts that are being undergone by the review team.

That is, working on preparing the

written questions and we're anticipating a response back from the applicant. But there are opportunities for clarifying questions during this time and, I mean, you can work with your regulatory health project manager to see if there is anything specific that you are seeking feedback on that we may be able to clarify that wasn't as clear as we may have intended in that letter.

And also, there are times when there may be trends across where you're seeing that you have certain questions that have come up in multiple SE reports, for example, or across other submissions that, if your questions are general in nature and not related to a specific SE report, for example, I mean, we would consider granting a meeting for specific, or for general questions as far as the research and development plans for your tobacco product applications.

MS. DOLLING: Thank you, Joanna. I would like to comment on your recommendation to increase the time period from two business days

from receiving the preliminary response. Thank you for that feedback.

We look at the preliminary response as a way for applicants to understand our thinking with the questions that were presented in the meeting request. That's your time to review our comments, and then we encourage you, and to Bryan's comment regarding the one hour, to utilize that document as a way to scope your future meeting with us.

So for example, if you submitted ten questions during your application and you only need clarification of two items, we encourage you to focus that meeting on those two specific areas.

In addition to the meeting, that one hour, we found that many companies spend a majority of that time presenting their portfolio. It will be helpful for you to possibly consider cutting down the time that you plan to represent information that's already given to us in that meeting package and really utilize that

discussion time to focus on those areas in which need clarification.

With respect to meeting logistics, I do want to know, it probably wasn't mentioned here, that Office of Science, in the next few weeks, we will be relocating to Calverton, Maryland. So currently all meetings that are scheduled will take place at our White Oak Campus, however, future meetings there may be scheduled in that location.

It's about ten minutes from our White Oak Campus. So we encourage you to pay attention to that meeting grant it letter, which will provide you with the address of any meeting that may be held.

MS. RUDOLPH: Thank you. Based on what you heard from FDA, Patricia or Bryan, did you have anything else that you wanted to check back in on? Okay. No? Yes?

MS. P. MILLER: I think we're fine.

MS. RUDOLPH: Okay, great. So we'll take a question that got sent in to us. So, and

this, I think, may be for you, Marcella and Joanna.

If there are multiple manufacturing facilities or production sites under the same company, how many TPMFs should we submit, one for each site or a single TPMF that covers all sites?

MS. DOLLING: So, the decision to establish a master file belongs to the owner. So we encourage applicants, or TPMF owners, to look at what's your best interest.

For example, we would be open to establishing multiple master files. And that, for example, you may consider, do I want to establish one for one site, multiple sites, do I want to establish one for cigarette products, smokeless products for example.

However, we encourage you, when you do submit a request for multiple master files, that the information is presented in a logical manner. And that applicant considers, and Russ is looking at me --

(Laughter.)

MS. DOLLING: So, for example, Russ, for your master file you may want to consider would, for example, submitting my master files by analyte or by flavor, for example, could that be an alternative for me. So, it's something that's manageable on your end but also something that FDA could easily reference for future submissions.

MR. WOLZ: Right. And so my question to you then, I'm learning a lot today, would be, so, in the example I gave we have maybe one master file for e-liquids, combustibles, smokeless, would those have to be separate master files with separate applications or could they be considered as, for example, appendices to the main master file?

MS. DOLLING: So, you have a couple options there, Russ. So, you can submit one master file and you could have separate sections. For example, you may want to have Section A be for your flavors or you may have Section A be specific for e-liquids.

MR. WOLZ: But that doesn't have to be in the same document --

MS. DOLLING: That can be in either the same document or we'd be open to establish separate submission tracking numbers --

MR. WOLZ: Okay.

MS. DOLLING: -- for each one. For your consideration, each master file, now, there are different responsibilities for you as an owner, to manage those multiple submissions.

MR. WOLZ: Thank you.

MS. RUDOLPH: Great. So the next two questions are related and it deals with our regulatory health, RHPMs.

So, the question really can be tied together, these two. Before manufacturers submits the first pre-submission meeting request, is it possible to be assigned to an RHPM, and if so, what is the process?

And subsequent to this, there was a question related and it's, you know, when there isn't already somebody who is assigned, is there

another way to communicate with CTP other than the CTP mailbox, given the responsiveness sometimes is not as timely as the applicant might like it to be?

MS. DOLLING: Generally we assign RHPMs upon receipt of the submission to CTP. Currently that can be, for example, submitted when an applicant requests an IM account.

So currently, if you do have an IM account, you have already been assigned an RHPM. If you need that information, you may contact the Ask CTP and we'll be able to provide that to you.

When you receive an application acknowledgment letter, in that letter, towards the end, it will identify your project managers name and their contact information.

MS. RUDOLPH: Great.

MS. RANDAZZO: I can answer the second question --

MS. RUDOLPH: Sure.

MS. RANDAZZO: -- about additional ways to contact CTP. Actually, one of the last

slides of Sarah's presentation did mention that we have, yes, the Ask CTP email, but also the ombudsman, Office of Small Business and our call center. Those are all other ways to get in touch and the correspondence will be routed appropriately.

MS. RUDOLPH: Thank you.

MS. RANDAZZO: Yes.

MS. RUDOLPH: So we got just handed two more questions here. So the first one, is it possible to use a master file for product registration, for example, if the same product is used in 25 different brands?

MS. DOLLING: So currently we do not intend to use TPMFs to reference registration eliciting information.

MS. RUDOLPH: Thank you. Let's see here. So what criteria does CTP use to determine when a granted meeting is face-to-face versus conference call or written response?

MS. RANDAZZO: So, when CTP receives the meeting request we evaluate the scope of the

questions, and we take into consideration the applicant or the requestor's preference for the meeting, but we make the ultimate determination of the format.

And written responses are generally those where we do not anticipate extensive discussion or clarifications and back and forth.

And as far as face-to-face and telecom, I'm going to kind of lump those in together because they really, neither one of them are limiting as far as the amount of back and forth discussion, it's just a matter of if you're coming to FDA Campus or if we're on the phone.

And teleconferences can actually be a really nice way to meet with CTP because it alleviates the need for additional travel. And on the company's end you can have additional participants that you may not have been wanting to all travel together or get airfare for the meeting.

And also, it's kind of a nice opportunity that if there is a need for internal

deliberation on a question that either party can put each other on hold and make sure that you give the proper vetted answer. And so, it kind of has a couple of nice little features that face-to-face doesn't provide because we're all just sitting there looking at each other.

So, it really depends on the scope of the questions. And generally, the written is less back and forth, maybe anticipated.

MS. RUDOLPH: Thank you. So, I have one last question. If I have other questions on different topics that I can think of during the meeting, can I ask them and get more information?

What if I provide more information in my opening talk to FDA when we have the meeting, can FDA provide me comment on the new information?

MS. RANDAZZO: Generally FDA will limit the discussion in a meeting to what we are prepared to talk about, as outlined in the applicant's meeting request and meeting information package.

However, there may be some low hanging fruit, I'll say, that if you're asking very simple questions that we are able to answer without further internal discussion or additional scientific expertise that may not be in the room with us that day. It really depends on the nature of the question, but in general we tend to stick to the scope of what the meeting topic was as outlined in the request.

MS. DOLLING: And I will just piggyback on that. And if there are comments that we can vet after the meeting or there are action items, we do intend to communicate those in the meeting minutes.

MS. RUDOLPH: Thank you. And, Bryan, did you have one other thing?

MR. HAYNES: Just one quick comment because I'm aware of what's in the guidance around supplemental information that you might submit once the meeting has been granted and that might cause the meeting to be rescheduled. Which I'm always terrified about.

Inevitably you come up with things when you're preparing for a meeting but then I don't want the meeting to be rescheduled so I'm hesitant to submit it.

My solution might be, well, we'll submit it, please don't reschedule my meeting, comment on it if you can but please don't reschedule my meeting. Would that be a fair middle ground?

MS. RANDAZZO: I mean, that sounds, I mean, as long as the expectation is pretty clear that you submitted this late --

MR. HAYNES: Yes.

MS. RANDAZZO: -- and you're not expecting us to comment. But, I mean, it really depends on what outcome you're seeking.

MR. HAYNES: Yes.

MS. RANDAZZO: If you feel the information is really important for us to provide an answer to, it may just have to be that we reschedule or you can setup a separate meeting. Yes, I --

MR. HAYNES: Fair enough.

MS. RANDAZZO: Depends on what you want.

MR. HAYNES: Fair enough.

MS. RUDOLPH: Thank you. Any further comments for the panel? Okay, thank you so much.

So, we'll be transitioning into our Session 4. We'll have two presentations. The first one is from Sharyn Miller, information resources on application review programs.

And the second will be from Jeff Smith on CTP electronic submission standards and activities. And following that we'll have another panel.

(Off the record comments.)

MS. S. MILLER: Welcome to the presentation on information and resources across application review programs. My name is Sharyn Miller and I'm a regulatory health project manager in the Office of Science.

In response to industry feedback, FDA Center for Tobacco Products has provided

manufacturers with additional information and helpful tools to assist in understanding tobacco product regulatory requirements.

Navigating FDA's website, we will walk through some of these resources and explain how this information may benefit you. To accomplish this, we will first walk through FDA's website to see where guidance and regulation documents are located. In addition to documents currently available for public comment.

After that we will take a look at marketing orders for pre-market programs. In support of specific FDA actions, we will learn how to access TPL reviews, order letters and environmental assessments.

To further assist in addressing regulatory and CTP specific questions, it may be helpful to know that FDA offers webinars, presentations and public workshops. We will guide you through these online educational materials and discuss ways to stay abreast of ongoing CTP activities and initiatives.

Let's begin with locating regulatory information using FDA's website. On CTP webpage there is a gray box titled, navigate the tobacco product section.

As shown here in the picture, there are six options to choose from. Including products, guidance and regulations, compliance, enforcement and training, newsroom, public health education, science and research, and about CTP.

Each option provides a brief description on that topic. Selecting the first option titled, products, guidance and regulations, directs us to a web page that shows information on marketing pathways, statutory requirements and documents for public comment.

FDA offers direct access to all CTP regulations and guidance documents. Selecting rules and regulations from the navigation pane displays all advanced notice of proposed rulemakings, also referred to as ANPRMs, proposed rules and final rules.

The Administrative Procedures Act

establishes the basic requirement for notice and comment rulemaking. Notice of proposed rulemaking, also referred to as NPRMs, make the public aware of the agency's intentions for the specific rule, while potential ANPRMs solicit information to inform policy on future rulemaking.

In summary, proposed rules explain the agency's intent, provide CTP spaces for issuing regulations and solicit public comments.

Selecting guidance allows anyone to search for and download documents that represent FDAs current thinking on a wide range of tobacco related issues. These documents usually discuss more specific products or issues that relate to product design, production, labeling, promotion, manufacturing and submission of regulated products.

Guidance documents help industry understand and comply with all laws and applicable regulations. Unlike final rules, guidance documents are not binding.

What this means is that you may use an alternative approach if that approach satisfies applicable statutes and regulations. Typically for draft guidance documents, the agency designates a comment period, generally 60 to 90 days so that comments can be considered as the draft is finalized.

One important aspect in reviewing guidance is to consider whether FDA has made any revisions. Revised guidance demonstrates a change in FDA's current thinking on that topic.

For example, effective April 13, 2018, FDA issued a revised listing of ingredients in tobacco products guidance. The purpose of this revision was to assist manufacturers of deemed tobacco products with the required ingredient listings under Section 904(a)(1) of the Federal Food Drug and Cosmetic Act.

In this revised guidance, FDA announced the intent to enforce the ingredient listing requirements, only with respect to those components or parts, one, made or derived from

tobacco, or two, containing ingredients that are burned, aerosolized or ingested during tobacco product use.

When reviewing these regulatory documents, note that the date listed reflects the effective date. Regulatory documents may be available for public viewing prior to the effective date, to solicit public comments.

Your feedback plays a critical role in helping shape tobacco policy and regulation. Because FDA regulatory decisions are based on science and law, agency reviewers look for logic, good science and other evidence as they evaluate comments.

To be sure comments have the greatest possible impact, we suggest reviewing our tips for submitting effective comments beforehand. A few tips for submitting effective comments include, adequately explain the reasoning behind your position. This helps the agency formulate the best policy.

Identifying credentials and experience

that may distinguish your comments from others. If you are commenting in an area in which you have relevant personal or professional experience, say so.

When disagreeing with a proposed action, suggest an alternative. Including not regulating at all. And include an explanation and/or analysis of how the alternative might meet the same objective or be more effective.

On that same navigation pane, you will see a section to submit comments on certain tobacco related products. If a tobacco related document is available for public comment, it is shown here.

Currently, FDA is seeking public comment on the public meeting, on tobacco product application review and also requesting member nominations to serve on the tobacco products scientific advisory committee.

These links will direct you to the federal registrar website where you can find additional information on the submission process.

Also open for public comment are several modified risk tobacco product applications. Including Copenhagen snuff, fine cut smokeless tobacco product, six Camel Snus smokeless tobacco products and three iCO systems with corresponding heat sticks.

Similar to public comments on guidance and proposed regulations, application related comments are submitted through regulations.gov. Selecting any of the application links will automatically direct you to a web page where immediate feedback may be provided.

When considering resources that improve public understanding of the scientific principles involved in application review, it may be helpful to know that FDA also posts relevant documents to explain the basis for certain actions.

Let's navigate CTP's website to identify where these resources are located. On the products, guidance and regulations navigation pane, we can select review and evaluation

process.

When we select this item, several additional options are displayed, including questions and answers, misbranded and adulterated NSE products, tobacco product marketing orders and three CTP marketing pathways.

To view marketing order reporting numbers across CTP programs, select tobacco product marketing orders. This shows the number of marketing orders, refused-to-accept and withdrawals for pre-market product applications, substantial equivalence and exemption from a substantial equivalence programs to date.

In cases where CTP has issued an order for any of the three marketing pathways, we can access relevant documents to better understand the application review process. To view this information, select the specific CTP marketing program, followed by marketing orders.

Let's take a look at marketing order information for CTP's most active marketing pathway, substantial equivalence. Shown here is

the general representative sample for the types of SE marketing order information available.

More specifically, order letters, decision summaries, environmental assessments, also referred to as EA, and finding of no significant impact, also referred to as FONSI, are available for public viewing.

Clicking the product's name provides the SE, or NSE order letter, for that tobacco product. The order letter acknowledges scientific review completion, explains marketing order status and reminds applicants that the new tobacco product specified are subject to the requirements of Chapter 9 of the Federal Food, Drug and Cosmetic Act.

The decision summary, also referred as the TPL review, captures the regulatory compliance and scientific review conclusions from that tobacco product application. Reading TPL reviews may be useful to understanding the scope and depth of CTP's application review process.

In addition to the order letter in TPL

review, FDA provides the corresponding EA to address environmental impacts that may be caused from tobacco product manufacturing, use and disposal.

In support of the EA, a FONSI may be prepared. Which includes that the marketing order for this new tobacco product will not have a significant impact on the quality of the human environment.

For more information on EA, please refer to Dr. Chang's presentation this afternoon.

Prior to website posting, FDA redacts information from these documents to protect confidential and trade secret information. In accordance with applicable statutes and regulations.

Additionally, these documents are reviewed to ensure compliance with Section 508. Which requires that all website content be accessible to people with disabilities.

For these reasons, the review time for posting may vary, based on the content in each

document.

With a comprehensive approach, CTP uses a variety of platforms for information sharing and educational training. Let's explore some of the information and training resources available to you.

With the ingredient listing compliance date of November 8th, 2018 looming for small-scale manufacturers, CTP created a new ingredient listing web page to provide additional information and updated forms, to assist with electronic submissions.

The creation of this webpage was a result of a bolus in inquiries regarding the ingredient listing submission process. To address industry concerns, the webpage includes the April 2018 revised guidance for industry, criteria for submitting one listing that corresponds with multiple tobacco products and product specific ingredient listing spreadsheets. Which are available for direct download here in an eSubmitter.

More recently however, CTP developed three webinars to account for the following. Examples of ingredient listing spreadsheets by product category, using a tobacco product master file for ingredient listing submissions and using FDA tools to submit ingredient listings electronically.

As we continue to identify industry knowledge gaps, CTP updates this webpage on a regular basis to include general information on topics received through public inquiries. For additional CTP webinars, select compliance enforcement and training on the left navigation pane.

This webinar series provides compliance, education and training on a variety of topics so tobacco retailers, importers and manufacturers learn all the steps necessary to comply with the statutory requirements for the marketing and sale of all tobacco products.

FDA considers new webinar topics based on public inquiries and ideas. To share an idea

for a future webinar, please contact Ask CTP Help Desk.

For a list of CTP press releases, meetings and workshops, we encourage you to visit the CTP newsroom. The top of the webpage highlights featured stories on tobacco product application review, steps taken to address youth epidemic of e-cigarette use and a spotlight on science.

Scrolling down the webpage shows additional information sorted by date. Each item will direct you to a page where you can find more information on that topic.

For example, if we select the first item, a public meeting tobacco product application review, we see information on the meeting location, objective, audience and registration. Topics to be addressed in the meeting are also noted here.

To ensure the most up to date information, we recommend you monitor the CTP newsroom periodically. To broaden our reach with

important updates, CTP is also active on a variety of social media platforms, including Twitter, Facebook and YouTube. In addition, we offer the option to subscribe for email updates.

Whether you're a tobacco product manufacturer retailer looking for compliance information, a parent in need of resources to educate your child about the dangers about tobacco use, or a scientist interested in learning more about the latest tobacco product research, we have the information you're looking for.

By subscribing to receive email updates from us, you will stay informed about all things tobacco products. The four unique email lists include CTP News, CTP Connect, Spotlight on Science and Modified Risk Tobacco Product Application Updates.

Signing up for CTP News allows you to be among the first to receive news from the center, as it happens. Including information about regulations, guidance, enforcement actions

and other compliance related announcements.

With CTP Connect, you can expect to receive a regular newsletter that includes messages from CTP leadership, a regulatory news roundup, featured articles on current tobacco issues and educational resources.

To stay current on CTP tobacco regulatory science and research efforts, we recommend the Spotlight on Science. This email subscription provides tobacco science publications, study findings and CTP grants.

If you want to know when materials from any MRTP applications under review have been posted, sign up for the MRTP application updates email list. But, be sure to sign up for the email list that best interests you.

To evaluate the usefulness of our public facing materials and address issues raised, we want to hear from you. There are multiple ways to contact us.

For general questions, CTP encourages you to reach out to the call center phone lines.

Staff are readily available to assist between the hours of 9:00 a.m. and 4:00 p.m. Eastern Daylight time.

Callers should select Option 1 for general questions, such as questions related to marketing application pathways and compliant states or Option 2 for questions regarding eSubmitter and CTP Portal.

General questions can also be sent by emailing AskCTP. For specific inquiries, CTP has several help desks available to ensure inquiries are routed to the appropriate person who can get you the response you need.

To prevent duplicative help desk tickets, which may delay responses, we recommend submitting individual inquiries through one channel. For tobacco industry questions, such as application submission process and timelines, please contact Tobacco Industry Help Desk.

If you're considered a small-scale tobacco product business and seeking more information on the regulatory process, you may

send questions to Tobacco Industry Help Desk or the small business office.

CTP stakeholder relations office helps increase stakeholder awareness and understanding of the Tobacco Control Act, including regulatory, science, communication and enforcement initiatives.

For questions on stakeholder engagement and awareness, please contact CTP's stakeholder relations. All regulatory correspondence, including written and electronic submissions, are processed through CTP's document control center.

Note that delivery hours are from 8:00 a.m. to 4:00 p.m., and deliveries received after 4:00 p.m. will be date stamped the following business day. Please refer to Mr. Smith's presentation on electronic submissions and associated forms for more information on eSubmitter and CTP Portal.

This concludes the presentation regarding information and resources on

application review programs. Clarifying questions will be addressed during the panel discussion for this meeting session. Thank you.

(Applause.)

MR. SMITH: Thanks, Sharyn, and thanks for fixing this remote. Let me see if we can get moving here. I'll probably refer to some things that Sharyn mentioned, and as well, Barbara.

It's cozy in here and --- very cozy. And your sugar is probably diving after lunch so I'll try to amp it up a little bit.

My name is Jeff Smith, I'm with the Office of Science Division of Regulatory Science Informatics. I'll be presenting about some electronic submissions, issues and considerations.

And Deborah Sholtes, who's a branch chief, will be sitting on the panel to entertain questions. So, after I give my presentation I'll duck for cover.

I want to mention a few things about where we came from. Some of the challenges that

we had standing up a new center and dealing with a newly regulated entity. To put it in context.

And then highlight one of our more recent advances, which were really in response to the feedback we've received from industry and from you, to try to help in your submission submittal part and communications.

Then some technical considerations, lessons that we've learned, that we'd like to share. Many of those lessons we've actually now put out in documents.

You also get some of those lessons in those pre-submission meetings that Barbara spoke of as well. Then that's important for those people who, the technical people who are actually putting together these submissions to submit to us.

Okay. Then, I want to talk about where we're headed toward an existing electronic submission standard. And that's very important for, also those technical people as well, but also important for the commercial marketplace of

solutions that we'll be building and providing tools built around those standards.

So, the Tobacco Control Act was enacted in June of 2009, and within six months we had to be prepared to receive this. We were all challenged on both sides. You in assembling and submitting and us, we, on receiving.

And so we actually began receiving other kinds of submissions within three months, even before we were staffed very well. So we had to track those and whose, what the status of those. So we had to beg, borrow and steal pretty much, from across centers.

Government contracting can be slow. All contracting can be slow. And so that's why, and then developing only begins to occur after that.

So, eSubmitter was a good choice. I think it's really helped. It's been well received. eSubmitter is the TurboTax like tool that you can fill out questions and answers, who are you and what is this about. Then you can

begin to attach those files.

And it's been very well received and it's served us well for the creation part of the submission.

Next is the transmission part. The agency already had an electronic submission secured gateway. And we got a lot of feedback about that.

And Russell alluded to that issue. It requires a high technical capability and in a newly regulated industry, especially with a lot of small businesses that's not always available. So we heard you and we responded.

Internal systems and building what we could in-house so we could begin to track everything we began to receive. And then of course the FDA unified registration listing of which, soon thereafter, the tobacco TRLM module under that was established.

So, in response to concerns and questions and frustrations, we rolled out, in August of 2016, the CTP Portal. And it really

was a first for FDA.

It's more like your HMO where you go in, it's an environment that your company and all the users that your company assigns can share in that environment, in their interaction with Center for Tobacco.

And it allows you to easily click and upload. So you don't have to negotiate the ESG any longer, you simply click on a button and upload it.

That was well received also, but more than subjectively. When we rolled that out we were majority paper. More than 70 percent paper. After, just after a year, that had flipped. We were 70 percent electronic.

Companies and people who had never submitted electronically were submitting it. It was easier than mailing. So that is a real testament to that. And CTP loves data. So I had to tell you that.

In order to make this fly, because we appreciate the concerns about confidentiality of

company material, we did not want to put ourselves in a position of assigning all of the accounts within that company, knowing whose coming and going. So we created the concept of the industry account manager, and then put it in the hands of the companies. Put it in your hands, to manage who in your company can and cannot get access.

A little screenshot there. So, when you go into the home screen you'll see different areas. Pretty self-explanatory here.

It lets you see the actions, the letters that were issued. It doesn't let you see the content of the letters yet, but it does give you administrative information about the letters.

To the right you will see some notifications and the bottom you'll see the most recent files that your company has uploaded. So anybody with that account that that company is given will see these screens.

I've clicked on the submission screen, so across the top actually. You can't really see

it, I feel sorry for you folks in the back, but the submission screen across the top.

And what is good about this is not only you can easily upload whatever you have created with eSubmitter, but you can also see when it was assigned in STN. You can see that submission tracking number, STN.

If you click on that hyperlink, for the STN, it will drill down and give you more information about it. It won't tell you and show you the content, but it will show you the administrative information.

So you can say, yes, FDA received it, they assigned this STN to it. And you can even see what files you had uploaded, the files names that are associated with that STN. So there's no doubt.

When you're ready to upload, the pointer is not going to do me any good here, so to the upper right there's a little button, orange button. And you'll get a screen showing you the list of the files that your company has

so far uploaded. And if you're sharing this role with another person in your company you can say, oh, she hasn't uploaded it yet, so now I'm going to upload that submission.

And you click. And then you browse to your hard drive or your file share and you click and you upload it.

What are you uploading? What are you attaching within eSubmitter?

Now, I'm no fan of electronic. Actually I, going from molecules to electrons, I like my molecules, they serve me well. They're allowing me to stand right here. I'm sure you love your molecules too.

But it's really only when those data can be provided in a form and format that can be further utilized by computers. So we have to be able to open, we have to be able process, read, archive.

It's great if it provides more capability than paper because then, now the electrons have more capability than paper. So,

if they're searchable.

So, here are some of the most common file types, the extensions for PDF is an excellent, I think, standard everybody is aware of. It's an open format.

Great for the narrative body, for telling your story, for guiding a reviewer through. And then of course you may refer them to associated data which there are formats appropriate for those SAS transport, unopened SAS format. Excellent for data, comma separated values.

Excel if you have to. But anything but PDF because, believe it or not, we do get some of those still with paginations and we're taking our time pulling the data out rather than reviewing, and that serves nobody any good.

So, also nonproprietary. When we get submissions in SAS, that's proprietary format. We prefer SAS transport. That's what the Center for Drugs, Biologics and Devices have been receiving for years. We're simply following

their lead.

Naming the files is important. You wouldn't believe how difficult it can be just knowing the entry point for the reviewer of where to go and dive in and begin reviewing. And these files number in the hundreds. It's just a swimming pool of files.

And so, naming it explicitly, MainTOC or MainBody, MainTOC would be good, has your table of contents, your main body from there. It can link to other pieces of your submission and reference.

So, we've had much difficulty with special characters and foreign characters. And when we start to have to rename files, that can break your links.

You may be referencing the files somewhere deep in your submission, now we cannot find the file because we renamed the file. We don't want to be in the business of doing that so that could slow things down and we'll have to get back with you about possibly resubmitting a

portion or more of the submission.

We're a Windows shop right now, we're hoping to change that, but there's a limit to the kind of files we can read and the length of the file names and the overall path. The overall path is folder, folder, subfolder, subfolder, subfolder/file name.

And when it goes too long we can see it, you can try this at home if you have a Linux machine and open it on Windows, you can see it but you can't get a handle on that file, Windows won't let you open it, it says, file cannot be found, but I'm looking right at it.

So, that's been a problem for us and we've had to work around those problems. So, keep it down to 180 characters in total. It's consistent with the other centers.

We're actually offering you more characters than the other centers. We think we can do that based on the way we're managing our files.

I'll refer you to some documents in a

couple of slides that detail some of this much better.

When you do create your submission file, your main body, it's helpful to you, and it saves time to generate it directly from the source rather than print it out and scan it in. It provides what's called a functional PDF.

It's searchable, but the great thing about PDFs you generate from the source is, you can zoom up, see letters and they don't pixelate, it just, so they don't become fuzzy. Sometimes things are scanned at low dots per inch and it's unclear and then when you zoom in it's just bigger but it's still unclear.

So, minimally, if you do scan it 300 dots per inch at least. And then OCR it because, again, that makes use out of those electrons.

It gives an advantage over paper then, and that's to all our benefit. And even in the company, if they have to search for the submission themselves and find information, which they often have to do too.

Table of contents is very important in that you reference every file throughout. We cannot presume the intention of a particular data set or file, we really need you to tell us why it's there and how it supports your claim. We cannot presume what you intended with the file.

So, everything has to be referenced in some way. Hyperlinks and bookmarks, I've heard mentioned here several times they're very helpful.

Existing templates. A minute ago, Sharyn talked about some resources available. One of those is the ingredients template.

Ingredients template, use that when you submit your ingredient submissions. But, that template is available on the CTP manufacturer website. You can find a lot of this on the CTP manufacturer website so I don't need to give you all these little links. You can find it there.

And that spreadsheet could also be used in support of your MRTP or your SE. It's an

ingredients template. Use it for your other application pathways. It benefits everyone.

Please test also. Often, well, not often, a few times we have had to open a submission, we've had difficulty. And the company discovered they could not open it either. Because people have third parties create some of these things and submit, so it's helpful if the company knows it can be opened as well.

And virus scan also, as regulated. We're also regulated. The federal government has information security, regulations and laws. And that's good for you because your data is secure.

And we do scan everything as it comes in, but we also require that, and the agency has made this a requirement, so CTP has to follow suit, that you scan and indicate what you used to scan it with if you're sending physical media in. If we do receive something that is virus contaminated, it is going to create a problem receiving anything further from that company until we can work this out.

And no need to encrypt or password protect. The portal encrypts at the point of origin. It goes over the wire encrypted, and when it's received it's decrypted. It uses secure socket layer.

Also, FDA has a long history of maintaining confidentiality. Okay.

So, here is some references, I'm not going to get into them, but they're references of what I've been talking about. And also, the pre-application meetings are important for that purpose.

But when you're ready, you can download eSubmitter, learn it. When you get ready to submit you'll need a portal account. It takes some lead time, ten to 14 days.

You'll need to submit a letter from the company, on company letterhead, appointing an industry account manager, and rules of behavior. And then you're ready to go. Open up the portal, browse to where your file is and upload it.

So now I'm going to try to speed this

up because now we're looking toward the future. Toward a structured electronic submission that can even stage us for more benefits.

And there's generally four areas of standards. One is a laboratory standards test, protocols and such, ISO and Caressa (phonetic) and so forth.

There is a submission content, which is how the data is arrayed and coded. You'll hear acronyms like CDISC, STTM, HL7.

Analysis standards, statistical standards, statistical assays. But what I want to comment here on is the container. The actual submission. The electronic submission itself that breaks a part a submission, assemblies it, packages it and send it to us so everything you've attached is sent to us.

FDA does try to make use of standards whenever possible. 21 CFR 10.95 requires us to participate, and utilize when possible and appropriate, and we do. And the eCTD, the electronic common technical document, is one such

standard that has been in use for almost 15 years.

The regulated product submission builds upon that standard but it still uses eCTD as the underlying code.

Now, we're going to have to modify this slightly to avoid confusing and angering people in eCTD. We're calling it the electronic tobacco technical document.

The eCTD breaks a submission into several discrete units. Not just theoretically, several separate files by area, by discipline, administrative area, clinical, quality, which would be CMC manufacturing and so on.

Going into each of these modules, it breaks it down even further. And for our purpose, we may have to remove some. Pediatric does apply here but we might need some behavioral studies, population health studies and we'll have to modify what we can without messing too much of the standard up and getting people angry at us.

The RPS builds on this, so not just an

individual submission standard, but all the submissions pertain to a product lifecycle. So it has a file cabinet or a dossier, where all the information pertaining to the life of that product would be stored.

So you had drawers for different application types. If SE applied you'd have SE here. In this case it probably would be SE exemption if there's a PMTA.

Then, a folder as a submission unit. The first one to come in might create that PMTA. An amendment would be another submission unit folder. Documents within it are the content. And so, it's fully metadata driven and so there's no need for folders.

The good thing about this is, the companies know where to put stuff, irregardless of the application pathway, and we know where to find stuff. And we can avail ourselves of more automation and tools to do that.

We can actually reference one piece within a submission to another piece within

another submission. And this is valuable instead of just referencing one application to another.

The most important thing, take home message is that, by subscribing to this type of standard, we both avail ourselves of a whole commercial marketplace of tools and solutions to create, submit and review and analyze these data. And it has served other parts of FDA well.

Just an example, how you have your documents and then you have your metadata file. So, a metadata file is simply saying, hey document, here's stuff, here's how to use it, this supersedes the previous one we sent and now when you look at your application you'll see this one and what it's to be used for.

A little bit of code here, and I'm almost done, a little bit of code just to show you some code. But actually, your email looks a lot like this if you were to look under the hood.

Computer communication is like this for financial data and medical data. And we're currently working on several technical documents,

highly technical documents, for those software firms and for the technical folks.

And I list them out here. And some sample files. Which is what was done for eCTD. And we're building in-house the databases and architecture to receive it.

We've actually completed a successful receipt of an eCTD from pilot participants in a software industry that support the pharmaceutical industry with these tools. They were able to figure out, from our technical specification, how to build an electronic eCTD and submit it to us. And we were able to receive that.

And then of course, we will go to the standard part of the good guidance process and make these documents available for public comment. But Dr. Holman wanted us to put our ducks in a row and validate this before we did that, and that's what we've done.

So, I think I'm two minutes over but thank you very much for your time. And I think this is going to benefit, as it has with CDER and

CBER, both sides and all parties, in the end. So thank you very much.

(Applause.)

MS. RUDOLPH: Before we head into our panel we're going to take a ten minute break. So if everybody could come back at about 3:05 that would be great.

(Whereupon, the above-entitled matter went off the record at 2:53 p.m. and resumed at 3:07 p.m.)

MS. RUDOLPH: So welcome back everyone. We're coming to the end of Session No. 4 with our distinguished panel and we will give -- as we have previously -- each person who's an outside representative five minutes to introduce him or herself -- actually herself in this case -- and to have an opportunity to kind of reflect on the session. And then we will move into questions from the audience, both in person and on the Web.

Paisley?

MS. CAMERON: Thanks. Paisley

Cameron. I'm with JTI USA. I've been working with this -- Matt and CTP for I guess since inception in 2009 now. So I wanted to thank both Matt and everyone here for having such a workshop. I think it's absolutely a great opportunity, and obviously we've come a long way since -- over the last eight years that we're now being able to collaborate on these items.

I'll just touch very briefly on both topics. The first one with the eSubmitter, and I'll qualify that by saying I don't really have the direct experience myself. Fortunately we have other people with better technical expertise than I do within our organization who handle these things. But my understanding is that we have used them for certain -- in certain instances. The ingredient submission for example, which Jeff had talked about earlier.

And there is a template that's there to be used, but in our case we found that the information -- how we, let's say, keep it in our systems, don't necessarily match with the way CTP

puts it in their template. So we then had to build like an interface and a mapping tool so that we could get it from our system into a template or into an Excel format that could then be easily uploaded in to the eSubmitter format. So it takes a little bit of time to do that, but in our case it made it easier for the long run. And also even just setting up the eSubmitter gateway in the first instance took a little bit of time as well.

And I think I heard a number of times sort of the technical expertise -- there is a fairly high level of technical expertise that's required for this. So I would encourage people to have sort of dedicated people within their organization who can do this, especially -- it sounds like in the future it's going to be more complex and although more beneficial I think because that way you're not going to lose track and you can more easily, let's say, track where your submission is at and you can get your STN numbers more quickly. And so -- and it will make

it easier for both CTP and for industry.

The one thing I would recommend is that there is sort of this continued dialogue and to understand -- or at least for CTP and industry to make sure that the system allows for let's say some flexibility for different product types of categories and for different information that needs to be loaded through the system for these different products as they come up for either substantial equivalent or PMTA or MRTP.

On the web site, look, there is a significant amount of valuable information out on the web site, clearly. There is everything from submission data to webinars to product metrics. I mean, you name it, it's there. It's just not always easiest to find. I mean, if you looked at the categories, they're not always let's say intuitive of how you can find information, so it does take a little bit of hunt and peck at times to go through and find the right information that you're looking for.

So one of the suggestions we might

have is maybe some quick links so that you can find information much more easily, say for example, the NSE determination summary, which I think was addressed by Christi this morning, that they're going to look at that as far as -- I think they're now calling it Appendix of Common Deficiencies that will be submitted or out there.

But one of the things that's let's say maybe even lacking in the past is a versioning of that. What's the actual date? What's the most recent version of that information that's out there. It was hard to know is there anything new? Is there anything different? And then if there was, sort of you had to look and see what your old version said and compare it to your new one. So if there was some way that CTP could version those or give us dates so that we would know when things were updated, even sometimes when to go look for information.

We don't always -- like I said, because there's so much information out on the web site and a lot of it's, like I said, really

valuable information that can be used by the industry. When those things are updated it would be nice to get a flag or a notice somehow that, okay, there's new information out there. Maybe on the main page a list of what's been put up recently, and then an actual link to that information I think would be very helpful.

And just a note on those sort of deficiency lists, I think if we could get a little bit more substantive information on what exactly it is that CTP is looking for in each of those instances. A lot of times it would just say the information is deficient. But if we could get some insights onto exactly what was missing, what would have been the solution, what would maybe CTP be looking for in that particular instance, it would provide some more transparency and clarity to the industry so that they would have let's say more complete applications in the first instance, and it would be an easier, quicker review time for CTP. And I guess that's -- my time is up.

(Laughter.)

MS. CAMERON: My cue. Thank you.

MS. RUDOLPH: Leann?

MS. CAMPBELL: Good afternoon. My name is Leann Campbell. I'm from RAI Services Company. I'm a senior manager in the eSubmissions Group and the Scientific and Regulatory Affairs. I also want to thank CTP for giving us this workshop and this opportunity to talk to you.

So my comments are mostly confined to the areas of MRTP and PMTA, of which I have direct experience dating back to my time working on clinical studies as a bio-statistician through converting some old legacy data for use in one of these type of applications, and then the actual compilation of these applications.

And then as for what has been working well with both of those application types, the available tools that are from FDA we feel like more or less we've been able to successfully use them or adapt them. For example, the ECTD

structure. It wasn't put together necessarily for us, but it does lend itself very well to providing a structure for an application of this type, particularly the scientific studies sections.

Another area that I think we have been able to have a successful adaptation is translating the guidances into a submission format absent a standalone guidance that's specifically for the tobacco product applications and absent a common table of contents. So it's sort of left to us to -- or and to our own devices to devise a submission structure for these applications.

And then speaking to something that came up in Jeff's talk, he didn't -- I don't remember hearing him say the word "flat folder structure," but that is the environment that we are building our applications in now and I feel like even though the eCTD structure utilizes folders, you're able to take the logic from the eCTD and translate into a flat folder environment

and then add metadata on top of that so you have a nice -- he's giving me a thumbs up --

(Laughter.)

MS. CAMPBELL: -- so you have a nice organized way to present hundreds and hundreds of files that go into a product application of these types.

And then one area that we've been limited thus far is using eSubmitter for either of these types of applications. I don't personally have experience working with the HPHC reporting and the ingredient listings, and I know our company has been able to use eSubmitter for those. We have not been successfully using them for MRTPs or PMTAs.

MS. RUDOLPH: Anuschka?

MS. MERSON: Hi, I'm Anuschka Merson. I work for ITG Brands. First I'll start with the FDA website. I've set up a process where we track the FDA website on a daily basis -- it's the CTP to understand what has changed. And there is a date at the bottom of each page, but

sometimes it's really hard to understand what has changed. It's not always clear. So if we could have something like that says new and the section that's changed currently. We have a printout of each page, and we compare that to determine if like something small changed. And if it's no worry, to let your stakeholders know.

Also I have experience in the eSubmitter tool and the CTP Portal. We love the CTP Portal. The ESG we never used because we weren't confident in it. The eSubmitter, the forms are very easy to use, and it tells you when you've made a mistake and what you need to go fix. I think the only thing where we would like some more guidance on PDFs like the submission, like a general format of how to submit an SE submission, for instance. Do you want it in smaller documents? Just a general format I think would be very helpful. Thank you.

MS. RUDOLPH: Thank you very much. And you heard from Sharyn, but would you like to introduce yourself?

MS. MILLER: Hi, everyone. Sharyn Miller, Regulatory Health Project Manager in the Division of Regulatory Project Management within the Office of Science.

MS. RUDOLPH: Thank you. Deborah?

MS. SHOLTES: I'm Deborah Sholtes. I'm a Branch Chief with the Division of Regulatory Science Informatics in the Office of Science.

MS. RUDOLPH: Fantastic. So before we get into -- and in case you all have not had a chance to write down your question, write it down now because we have got a little bit of room. We have one question so far submitted. So if you have anything, send it on over to your folks here on the ends of the rows.

But before we get into this one question that we do have, or others that may come, Deborah, as you were listening to the panelists talk, the other folks, do you have any comments or thoughts about what you heard them say?

MS. SHOLTES: I do. There are a couple of things that people tend to get confused because their names are so very similar. One is the Electronic Submission Gateway -- it's also called the ESG. And that's a very technical piece of the infrastructure, and that is very different from the eSubmitter tool. And the reason it gets confused is not just because the names are similar, but they're used in the same process of submitting an electronic submission to FDA.

So our portal actually is a simplified way of accessing the ESG, the Electronic Submission Gateway. It keeps you from having to have that really high technical expertise in house and makes it the simple point and click, attach your files. The type of files to attach are files you've created using the eSubmitter tool. So the names are very similar; the tools are quite different.

MS. RUDOLPH: Very helpful. Thank you.

And Sharyn, do you have anything to comment on from what you heard from the other folks at this point?

MS. MILLER: Yes, I think I'll piggyback on what Deborah was saying. And just to clarify with the holidays quickly approaching I think that it's easy for us to put into perspective eSubmitter, ESG and CTP Portal in terms of packaging gifts. So I'm going to do that for you.

If you want to think about eSubmitter as packaging that gift for the holiday season and then ESG and the CTP Portal as a way to get that gift to your designated recipient, I think that's just an alternative way to consider and think about those two different --

(Simultaneous speaking.)

MS. SHOLTES: So the portal is Santa's sleigh. Is that what you're saying?

(Laughter.)

MS. SHOLTES: I'll take that.

MS. MILLER: And to Paisley's point

that she mentioned the website not always being the easiest to find information, we certainly acknowledge that and want to continue having proactive discussions and collaborative efforts to ensure that our website enables for and allows intuitive navigation to find you the information and resources you need to complete the submission process and also to become more familiar with the regulatory items we have available.

That being said, I'd just encourage everyone to periodically check back with our web sites as we are continuously looking for areas to improve and continue quality enhancements to make that more intuitive.

One item that we've recently done and have in the past done -- Deborah can probably speak to previously -- is usability testing of some of our systems in place to see how manufacturers and industry are able to navigate through the information we have available and to use that as a resource and way to identify areas that further require improving. So continue to

check back.

I'll also say that in addition to having the date, the version date at the bottom left-hand side, in cases where we've updated recent forms, we will provide that version date right beside the form as just a quick reference and easy way to identify as opposed to scrolling to the bottom of that particular page.

So those are just a few of the more recent updates and things that we've done in the past to try and solicit feedback and really make this a collaborative effort to improve our processes.

MS. RUDOLPH: Thank you. So I have here now two questions: So the first one is actually from FDA. Can you speak about the IAM request process? What's the average time from request submitted to account creation?

MS. SHOLTES: Typically it's a couple of weeks if all of the information is correctly provided. We don't always get completely or completely correct submissions and then we have

to go back to the company and request resubmission. Some of the issues that we see sometimes is that the correct people have not signed in the right locations. The authorized party has to be able to sign for the -- the block for the authorized party. That would typically be an executive of the company. And the person who is going to be the IAM, the industry account manager for that company may very well likely not be the company executive. They may delegate that job to somebody who is more familiar with the submission process. And so it is the IAM themselves who must sign the Rules of Behavior form. So sometimes we get those two signatures backwards.

MS. RUDOLPH: So you addressed some of the next question, which is directed for both the folks who are outside representatives as well as for FDA, and that's what are some of the common reasons IMS gets held up? You were talking a little bit about the signatures, but maybe from both viewpoints, are there other issues that

folks from industry in setting it up have had difficulty with or things that you could identify there might be reasons why it gets held up? That's a question from our audience.

MS. SHOLTES: Not sending in the Rules of the signed Rules of Behavior is also an issue.

MS. RUDOLPH: Yes.

MS. SHOLTES: So we'll get the request, the letter without the signed Rules of Behavior. So it has to be complete.

MS. RUDOLPH: Okay. Any comments from other folks?

(No audible response.)

MS. RUDOLPH: No? And then there's one specific to Anuschka. When you had talked in your opening you had talked a little bit about not trusting ESG. Can you speak a little bit more about why it is that you don't trust ESG?

MS. MERSON: Sure. When you put the submission in, it doesn't tell you your submission is received. It just -- it's kind of out there. With the CTP Portal you can put in

your submission and it will say submission in progress and then it will say submission received. So it's just kind of a trust factor that you know you've met your deadline to the FDA and there's no proof that it went into the ESG. We just -- it was a trust factor. So we used to send it in on CDs --

MS. RUDOLPH: Okay.

MS. MERSON: -- with FedEx where we were able to track and ensure the FDA --

MS. RUDOLPH: So some kind of read receipt?

MS. MERSON: Correct. And it didn't have -- it doesn't have that capability when we -- the time we were using it.

MS. RUDOLPH: Okay. Okay.

MS. MERSON: Does that make sense?

MS. RUDOLPH: It absolutely does.

All right. Are there other things from the panel here? This has been a short time together, but welcome to take any thoughts that you all have amongst yourselves at this time.

Otherwise, we're a wrap.

(No audible response.)

MS. RUDOLPH: Looks that way. Then we are a wrap. Well, thank you very much.

(Applause.)

MS. CHANG: Hi. Good afternoon. Well, welcome to a very informative day and we're going close to the end, but I'm very excited talk to you about environmental assessment since it has been advertised at least five times during today's presentation.

(Laughter.)

MS. CHANG: All right. So all right. Let's start.

I'm Hoshing Chang, and I'm the Environmental Science Branch Chief in the Office of Science within the Center for Tobacco Products. I'm going to talk today about environmental assessments and claims of categorical exclusion for tobacco product application submitted to CTP.

I will briefly discuss the National

Environmental Policy Act and its purpose, the environmental assessment, or EA, outline for a product application, the probability availability of the EA, and how to handle confidential information, and the categorical exclusion, or CatEx outline for a product application. At the end of the presentation I will talk about available resources for the applicants and go over an example EA.

The National Environmental Policy Act, or NEPA, was sign into law on January 1st, 1970. To quote NEPA, it is "a national policy which will encourage productive and enjoyable harmony between man and its environment." To further quote NEPA, its purposes include "to promote efforts which will prevent or eliminate damage to the environment and biosphere and stimulate the health and welfare of man to enrich the understanding of ecological systems and natural resources important to the nation, to establish a Council on Environmental Quality."

Why is an EA needed? An EA is

required by law under NEPA for such things as: promulgation of new regulations, requests for actions such as product marketing orders.

Finally, the Code of Federal Regulations, under 21 C.F.R. 25.15(a), states: "All applications or petitions requesting agency action require the submission of an EA or a claim of categorical exclusion."

The useful information in the EA outline as the following elements: A cover page, a table of contents, the table of the EA, which I will discuss in more detail later, and any appendices.

The useful information in the EA includes a cover page with the following information: The title of the document; for example, Environmental Assessment for the Marketing Order for, your new product name and manufacture by, name of the applicant, the agency for which the EA was prepared; for example, prepared for the Center for Tobacco Products, U.S. Food and Drug Administration. And finally,

the date the EA was prepared.

The next section of the EA is a useful information in a table of contents. The table of contents includes EA section titles, EA subsection titles, appendices and confidential appendices. All office sections are listed with associated page numbers.

The body of the EA follows the table of contents and includes each EA section as described in the table of contents. I will go through the useful information in those sections now.

Section 1 titled "Applicant and Manufacture Information" includes the company or individual name of the applicant, the applicant's address, which includes the street address, the city, state and ZIP code, or the comparable information for a location outside of the United States, and the country when outside of the United States, the manufacturer's name and the address where the products are manufactured in the same format as used for the applicant's

address.

In Section 2, "Product Informations" describes useful information including the new product name, the name product -- the new product submission tracking number, STN, if available, and the predicate or original product name, if applicable. In addition product identification is provided include the product type, product subcategory, product package and product quantity per retail sale unit.

The next section is Section 3 titled "The Need for the Proposed Action." The useful information in this section identifies the proposed action and applicant marketing intent. For example, for the SE pathway, the applicant may state the proposed action requested by the applicant is for FDA to issue a marketing order, finding a new product substantial equivalent to the predicate products under the provisions of Section 19 in 905(j) of the Federal Food, Drug and Cosmetic Act, the applicant wishes to introduce the new tobacco product into interstate

commerce for commercial distribution in the United States.

Finally, if the application is for the SE pathway or an exemption request the useful information in this section identifies the status of the predicate and original product, respectively. Also this section gives a brief non-confidential description of how the new product differs from the predicate or original product. A detailed description of the differences are included in a confidential appendix which I will discuss later.

Section 4 is titled "Alternatives to the Proposed Action." This section discusses any identified alternatives to the proposed action. One such alternative is the no action alternative, meaning the action of not authorizing the new product. For that alternatives, the EA could state the no action alternative is -- FDA does not issue the marketing order for the new tobacco product in the United States.

Section 5 to 7 further address the potential environment impacts of the proposed action and alternatives. Section 5 includes the useful information to address impacts of manufacturing the new products. Section 6, use of the new product; and Section 7, disposal of the new product. These sections include several subsections which I will now go over.

The first sub-section is the affected environment. The useful information in this subsection describes the land use around the manufacturing facility and includes an aerial photograph showing the described area. It also describes the environment where the product will be used or disposed of.

The rest of the subsections described the evaluation of potential environmental impacts on the environmental resources where applicable. The useful information describes the environmental resources including air quality, water resources, land use and zoning, biological resources, geological features and soils,

socioeconomic conditions, solid waste and hazardous materials, flat plains, wetlands and coast zones and regulatory compliance. The analyses can be presented in a tabular form, however, the traditional paragraph form is appropriated for lengthy discussions.

One subsection is cumulative impacts. This subsection discussions the impacts on the environment which results from the described impacts of the proposed action when added to other past, present and foreseeable future actions. These subsections would also include any mitigation of the identified impacts.

Section 8 titled "List of Preparers." The useful information in this section is to identify the individuals who were primarily responsible for preparing and reviewing the EA. For each individual their name, title, organization, relevant education, relevant experience and relevant expertise is included.

Section 9 titled "Listing of Agency and Persons Consulted." The useful information

in this section is to identify agencies consulted and states what information this agency provided during the preparation of the EA, as well as the name, title and organization of the person contacted.

The EA concludes with sections of references and appendices, also useful information. Section 10 titled "References" provide any citation that were referenced in the EA.

The EA concludes with appendices where necessary. This also includes confidential appendices that contain information deemed business confidential. Examples of the information that would be appropriate for the confidential appendices include: Specific modifications or changes between a new and predicate product, calculation that were made base on confidential information about the new and predicate products or original products often related to the projected market share information, the identities of the suppliers when

they are not part of the company that submits the application and the location of any supplier manufacturing facility.

Here I would like to emphasize the EA is available to the public with the confidential information redacted. As noted in 21 C.F.R. 25.51(a) when confidential information is pertinent to the environmental review of a proposed action, that information should be submitted separately in a confidential section and summarized in the EA to the extent possible. 21 C.F.R. 25.51(b) notes that FONSIs and EAs will be available to the public in accordance with 40 C.F.R. 1506.6.

If an applicant believes they are marketing order request may qualify for a categorical exclusion, CatEx, they may submit a CatEx claim. The CatEx claim should identify the relevant CatEx by including a statement of compliance with the specific CatEx criteria. The applicant should also state to the best of their knowledge no actual ordinary circumstances exist.

Currently CTP has one class of actions relevant to tobacco product market applications. The criteria for that CatEx claim is that the new product is a provisional product and the criteria of the claim is listed in 21 C.F.R. 25.35(a) as described in the slide.

Shown here are resources for applicants for obtaining more information about a EA process. Examples of EA posted on the CTP web site in a webinar titled "Environmental Considerations of Tobacco Product Applications Submitted to CTP 2016."

Examples EA as described by previous speaker can be found on the web page of marketing orders for SE. When you click on the EA of your interest, you can read a redacted agency-prepared EA as shown in the next slides. These EAs have made -- have had any confidential information redacted from the public document. Using example of one of these redacted agency-prepared EA I will walk you through each section that I have previously discussed.

You see here the cover page and the table of contents. The cover page includes the title of the document, who prepared the EA and the date the EA was completed. When the EA is prepared by the applicant, the "prepared by" portion of the cover page will note the company name of the new product. The table of contents include a section of -- and associated page numbers.

As we move into the EA, you can see the first page contains the product name and other product information and the need for the proposed action. The next page begins the evaluation of impacts of manufacturing the product. The subsequent pages contain evaluations of impact of use and disposal of the product. And then as noted, the EA includes the list of preparers.

As noted previously, here is where the EA notes the government agency consorted. None for this document as it was prepared by the agency. This is followed in by the references

and appendices and then this EA concludes with a confidential appendix, which includes the confidential information important for the evaluation of the potential environmental impacts. As you can see here the potential -- the confidential information is redacted according to the mention regulation when posted on FDA's web page.

This concludes my presentation about the EA and CatEx for tobacco product applications submit to CTP. So you can visit us on the web site, you can call us, and you can email us. And I'd like to thank you for your attention.

(Applause.)

MS. CONEWAY: Good afternoon. My name is Renee Coneway and I'm a lead program analyst in CTP's Office of Science. Today I will be speaking about the transfer of ownership process for OS.

First, I will provide an overview of the transfer program and go over some key terms. Then I'll discuss the information we have

requested from applicants in order to complete a transfer of ownership, how to submit the request and finally the transfer acknowledgment.

In this section I will provide an overview of the Transfer of Ownership Program. Transfer of Ownership is a program with CTP in which an applicant transfers the rights and responsibilities for their applications to another company. An applicant typically transfers ownership of their applications if they're selling all or part of their company, merging with another company, or both. Currently there are no requirements to transfer ownership. Please note this process is independent from application review.

In OS, we commonly see two types of transfer requests: A one-to-one transfer where an applicant transfers all applications to a single applicant and a one-to-many transfer where an applicant may transfer different applications for their tobacco products to two or more applicants. Applicants subject -- applications

subject to transfer of ownership may include PMTAs, SEs, and EXs.

Here are some of the key terms to assist with the transfer of ownership process. The current applicant is the entity listed as the applicant of record. The current applicant is also the originator of the transfer request. The new applicant is the entity assuming ownership of the applications from the current applicant. And a treatment plan request is a signed letter from an authorized representative that contains sufficient information for CTP to start the transfer process.

In this section I will go over the process to complete a transfer request. Before getting into specific details, I would like to provide some examples of requests we receive that are not actual requests to transfer ownership.

We commonly receive requests notifying us of changes such as: a company name change, a notice of bankruptcy or sale statement, a change in legal representation and withdrawal requests;

however, these requests do not initiate the transfer process. For example, we receive inquiries from applicants who state I've already notified CTP that my company is bankrupt. Isn't that notification sufficient to transfer ownership? The answer is no because a notification of bankruptcy is not considered a transfer request. It is only a notification of bankruptcy.

If the applicant would like to transfer ownership, they should submit a request to CTP and include the party accepting responsibility for the transfer to be effective. Your RHPM can assist you with what it means to withdraw an application and the appropriate paperwork for that action, for that decision. They can also assist with updating authorized contacts and specific application-related questions.

Transfer of ownership is important to ensure accuracy of all records and the appropriate individuals are communicating with

FDA. Let me elaborate on this further. If applicant A were to submit an SE report and later selled that report under -- I'm sorry. If an applicant -- if applicant A were to submit an SE report and later sell that product under the report to applicant X and they do not update their files to show the transfer of ownership, applicant A will continue to receive all regulatory correspondence and decision making authority for that application.

It is important that CTP is made aware of the changes so the correct applicant may respond appropriately, which in this case -- which in this example is applicant X. In general, CTP follows a standard process for transfer of ownership.

Now let me walk you through the process. Prior to completing a transfer request it is helpful if the current applicant conducts an inventory and determines which specific applications will be included in the transfer. Currently there are no standard forms for a

transfer of ownership request. We generally have requested that the applicant -- that the current applicant submit a signed transfer request letter that clearly states the request is to transfer ownership to the new applicant.

We have also requested that the letter includes the specific applications and products -- product names by STN, a statement that all rights of the applications have been transferred to the new applicant, the point of contact information and the effective date of the transfer based on business transaction agreements. As a reminder, applications generally included in a transfer are PMTAs, SEs and EXs. If additional information is needed, we will communicate directly with the applicant.

Now I will go over the process for the new applicant. In processing the request we have requested a signed transfer acceptance letter that includes the specific applications and products being accepted, a commitment to all agreements, promises and conditions made by the

current applicant of record, a statement that the applicant has a complete copy of all applications or state they will request one, a statement that no modifications have been made to the transfer applications, and finally the effective date of the transfer.

So there are different options for submitting a transfer request. Applicants can submit electronically through the CTP Portal if they have an established account, via U.S. mail or through a courier service. Applicants can obtain the CTP mailing address, which is listed on the FDA web site at www.fda.gov/tobacco.

We will review the transfer request letters for completeness. If the letter is missing information, we may reach out to the applicant. Specifically when dealing with pre-market applications your RHPM will call to ask clarifying questions and verify if the request is truly for a transfer of ownership. If the request is not for a -- is not a transfer, for example, but a change in legal representation,

your RHPM can assist you with those updates. If the request is for a transfer of ownership, your RHPM will clarify if additional information will be helpful.

During the review phase we generally only communicate with the current applicant. The purpose is to protect the applicant's confidential commercial information. It is the responsibility of the current applicant to ensure that the new applicant has the sufficient information for their transfer acceptance letter.

Once the transfer request is complete and all items are present to support the request, we will update the official records to reflect the new applicant's information and issue a transfer acknowledgement letter to both parties. It is important to note that CTP's acknowledgement does not represent the agency's support with regard to a company's business plans or operations. We will continue to communicate with the current applicant until the acknowledgment letter is issued. Also, the new

applicant may be subject to other requirements such as registration.

With the issue of the acknowledgment letters this completes the transfer of ownership process. This means all records have been updated to reflect the new applicant and CTP is now communicating with the appropriate party for decisions on the transferred applications.

In my earlier example where applicant A sold their product to applicant X that had a pending SE report, both applicant A and applicant X had received transfer acknowledgment letters and CTP is now only communicating with applicant X, who is the new applicant of record.

This concludes my presentation on transfer of ownership. If you have any additional questions, I encourage you to ask during the next panel discussion or you can reach out to your RHPM, contact our call center or send an email to Ask -- to the Ask CTP mailbox. Thank you.

(Applause.)

MS. JOHNSON: Thank you again to our presenters. As she mentioned, we have our final panel. So if our panelists for Session 5 could make their way to the front, that would be great. Again, if you have any questions, please put those on the cards, the index cards. Raise your hand if you need one. Oh, there's one in back.

Okay.

(Off the record comments).

All right. So we'll have our industry panelists introduce themselves and make comments and statements on the presentations that we just witnessed, and we'll go on from there.

We'll start with you, Tony.

MR. ABBOUD: Thank you so much. Appreciate the opportunity. My name is Tony Abboud. I'm the Executive Director of the Vapor Technology Association.

The Vapor Technology Association is a membership organization. We are an advocacy organization. Our members include manufacturers, the largest manufacturers of devices and e-

liquids, the largest distributors of those products as well in the United States, and the largest number of flavoring companies and also vapor shops around the country. So we take a holistic and a unified view to the regulatory experience.

The focus of our advocacy is typically promoting a rational regulatory scheme that recognizes and truly embraces the lifesaving potential that ENDS products have. We also take the biggest issues of the industry to heart. In particular our focus on limiting youth access has been a priority of ours for the last two years, as well as the implementation of new requirements and new standards that relate to and can limit the access of those products.

Now I very much appreciate the detailed explanation and presentation that we just heard primarily on environmental assessments and categorical exclusions, however, I find when I frequently speak on these subjects I'm also reminding folks that we're kind of speaking from

a unique position, and in this particular case it's no different because ENDS products typically are not -- cannot access this particular aspect of the process. And first, as was noted, categorical exclusions are available only to provisional products that are submitted through an SE pathway. And of course ENDS products don't have that pathway available to them. The PMTA pathway is the single available pathway for our products.

So from that perspective I can't really comment on that process except to offer a couple of thoughts: The first thought I would offer is that the recent modifications that were made to the categorical exclusion and the environmental assessment rule in Part 25 was done before of course the deeming regulation was put into effect. And so companies that were in the vapor industry or manufacturers of ENDS didn't really have an opportunity to comment on that process.

The Vapor Technology Association took

an opportunity to comment on this aspect of it when we submitted comments to FDA in February of this year in response to their request for comments on the PMTA process. And we appreciate the opportunity to amplify those just briefly here.

Very shortly, the key issues from our perspective is that because we cannot make a CatEx claim, we need to consider whether or not it's appropriate for ENDS products to receive that same treatment. So we would suggest that a categorical exclusion is provided for for both devices as well as for e-liquids.

I think as Jeff Walker earlier noted that sometimes it's helpful to examine how FDA approaches these issues from a drug device or a combo perspective. I think that's -- it makes for an interesting analysis here. FDA would treat, would likely treat a device, an aerosolizing apparatus that is being sold and marketed with a cessation claim as a device or as a combo. And in that case it would probably

receive the broadest exclusions that are available to all drug products or drug devices. I mean, this is typically true that these categorical exclusions arise for pre-market approvals, for pre-market notifications, 510(k)'s, for investigative device exemptions, as well as humanitarian device exemptions.

So take just for example the medical device for asthma, a product which contains Freon 134a, I'm told. This is a product that has well-recognized environmental aspects, yet there is no environmental assessment required for that product. The same would be true with respect to lithium ion batteries that are included in medical devices. Again, functionally similar batteries in these products not subject to environmental assessment requirement.

So whether FDA is evaluating the product, evaluating the same device from the perspective of whether it should be treated as a medical device and whether it should be treated as a tobacco product by nature of the claim, then

an environmental assessment, if it's not necessary in the case of the former, should not be necessary in the case of the latter. So with that respect a categorical exclusion for ENDS products promotes consistency as well as avoids costly redundancy.

The last note I would quickly add, because I see my timer is coming to relieve me, is a similar analysis; and we won't belabor it, could be made for e-liquids where you have commonplace exclusions granted for a variety of drugs or biologics, the biohazards of which are not known or will not be known for many years because of the infancy of the process through which they are in. But at the end of the day the question is can FDA through the PMTA process use a technological -- the toxicological data that it will be collecting as well as the battery standards and any other sort of technological requirements to solve the issue that would otherwise be addressed by an environmental assessment so we can avoid redundancy?

MS. JOHNSON: Thank you, Tony.

Karen?

MS. COOK: Good afternoon. I'm Karen Cook with ITG Brands. I'm the Manager of Regulatory Affairs and I'm responsible for various regulatory submissions including grandfathering. My product experience is with cigarettes and cigars. Understandably, the grandfathering component to this discussion panel was canceled today. Hopefully CTP will provide another opportunity to discuss this important topic in the future.

I have just a couple of comments with regard to environmental assessments and transfer of ownership. With regards to the EA, a template would be great and some additional guidance, however, today's presentation did provide a lot of helpful information, so really appreciate that. Thank you.

With regard to the transfer of ownership, again a guidance document would be extremely helpful on this topic. ITG Brands did

experience a transfer of ownership. The process was very lengthy and not well-defined. It was as if the FDA was kind of learning the process along with us at the time when we were going through the transfer. So again, just a guidance document on this topic would be very helpful.

Just want to thank CTP for this opportunity today and for being here. Thank you.

MS. POWELL: Thank you. My name is Christie Powell and I'm a master scientist within the Submissions and Engagement Group and the Scientific and Regulatory Affairs Department of RAI Services Company.

My experience at RAIS involves the generation and submission of tobacco product applications including regular substantial equivalence filings, exemption requests, pre-market tobacco applications and modified risk tobacco applications, as well as their environmental assessments?

Now I know that there were three topics for today, so since my experience really

is primarily with environmental assessments, I'll keep my talking points to that, although I would like to make one note if it's okay regarding stand-alone grandfather submissions.

So RAIS has observed inconsistent review time frames for stand-alone submissions. So sometimes decisions are made in less than three months, which is great, and then we found that others can take a year or longer. And so we feel these are fairly straightforward submissions and so it's a little unclear why the review is so inconsistent. So this may be an area of opportunity for improvement.

So now back to the area of my expertise, EAs. So as highlighted today, the FDA has the authority to refuse to accept or file certain applications if the company's environmental assessments are found to be inadequate. And as mentioned a couple times, substantial equivalence is for provisional products, so the SE reports submitted between February 15th, 2007 and March 22nd, 2011 can

claim categorical exclusion, meaning that an EA is not required for these submissions.

This means that all other submissions including non-provisional SE reports, exemption requests, pre-market tobacco applications and modified risk tobacco product applications require an EA. Therefore, having a solid understanding of how to generate an environmental assessment is an important component of tobacco product applications.

So as someone who has been actively involved in the process of EAs at -- and the EA process at RAIS, I'd like to share a few learnings and observations on this topic.

First, there are quite a few guidance documents, there are some rules, there's the webinar that was mentioned today and there's examples that are provided by CTP, and I found those to all be very beneficial.

I do point anyone who is new to generating an EA to the Code of Federal Regulations Title 21, Section 25.40 on

environmental assessments. This is a good place to start. It just provides a high-level overview of what an environmental assessment is, outlines some information to include and some other considerations for your environmental assessment.

But I think more importantly are the publicly-available EAs on CTP's web site. Examples are extremely beneficial. They highlight the types of information that the agency evaluates in order to make a decision on environmental impact of the authorization of a tobacco marketing -- tobacco product marketing order, excuse me.

From these examples I've learned that it's important to take a holistic approach when evaluating a potential environmental impact of a product. By that I mean it is necessary to assess the environmental impact of the product through its life. So starting with the impact from manufacturing, the impact during product use and then its eventual disposal.

And then lastly I'll just note that

while the guidance and examples are extremely helpful, they also highlight the fact that there's no one-size-fits-all environmental assessment that can be applied across different product categories or applications. So different products may have different considerations that need to be made when it comes to their potential environmental impact.

And so right now there is no reference or guidance document currently available that breaks down on a product category level the types of information required for an environmental assessment. So it really is up to the manufacturer to determine what types of information need to be included in the environmental assessments in order to provide enough information for the agency to make a determination of the proposed action. Thank you.

MS. JOHNSON: That was perfect timing. Perfect timing. Thank you for that.

Would my FDA colleagues like to introduce themselves?

MS. BELTRE: Hi, Rosanna Beltre again here. Hi, I'm from the Office of Science, Division of Regulatory Project Management, if anyone has just entered the room.

I was being a smart aleck.

MS. BENSON: I'm Kimberly Benson and I'm the Director of the Division of Non-Clinical Science in the Office of Science.

MS. CHANG: Kim is my boss.

(Laughter.)

MS. CHANG: I'm the Branch Chief for the Environmental Science Branch in Division of Non-Clinical Science, Office of Science.

MS. JOHNSON: Thank you. So do you all have any reactions, any comments that you wanted to make after the statements by our industry colleagues? Any points you want to make?

MS. BENSON: Sure, I'll start off. First, I do appreciate that you all are appreciating seeing the agency written documents on our web site, and I'm glad they're helpful. That's been our goal to get them out there. And

hopefully you can see that they are also evolving, so as you point people towards them, I would point them to the most recent ones, because as we gain more experience and understand things better by evaluating them more, the template -- our documents are changing as well.

So I do appreciate the idea that it's not one-size-fits-all and a guidance that directs you to specific information dependent on the product or perhaps changes within a product guidances are hard to prioritize. There are, as we heard today, many, many topics that people would like to see a guidance on. And we would certainly like to pursue something like that ourselves, but where it fits on that chain I can't attest to.

I would recommend though you could contact us if you had a question, if you were working on an application for something that felt very different and you weren't sure what you should address, that you could reach out to us. And that's one of those meetings that could be

totally done via written comments.

So, and then to the second part about the CatEx and ENDS not actually being under our purview at the time that that rule was amended, certainly appreciate that. We couldn't foresee at the time, but I have to say even if we could, we would not have been able to make any additions to that for something we had no experience with.

So we work with the Center for Environmental Quality and they really stress the -- well, how much experience, how many times have you evaluated that, how many EAs have you received on that? So we would like to pursue options as well as we gain more knowledge to add to our CatEx role now that we could say that to CEQ, that we have certain experience with different changes that might be able to be CatEx'd.

We're always looking out for ways to address that. And that different centers might handle it different, that's also a difference of time. Those things were CatEx'd in other centers

15, 20 years ago. I don't know if they would be CatEx'd now. That's just my non-FDA opinion. That's just Kim Benson, standard scientist at home.

(Laughter.)

MS. BENSON: We function under our regs and with our knowledge and we pursue what we can with CEQ, and we will certainly continue to do that and to gain more experience and knowledge and a look towards amending that role in the future.

MS. CHANG: All right. So I would like to follow up on Kim, Tony and Christie's comments. Yes, as Christie mentioned that there's no one-size-fit-all EA, so whenever we prepare a EA, we always consider proposed action. So therefore, for CEDRs, their electronic cigarette approval, their proposed action is different from ours, so that therefore the environmental consideration would be the same. We don't have enough experience to say the direction to go. We don't have enough experience

to say that every product application authorization for electronic cigarettes, there's no significant impact. We don't know unless we see the application and the product itself.

But if I could follow up, Environmental Science Branch we have published a paper, and it that paper we identify the gap of -- research gap of environmental impacts related to electronic cigarettes. It's published in Tobacco Control. I think that document could be helpful. All right. Thank you.

MS. JOHNSON: Thank you.

MS. BELTRE: Okay. So I know everyone has talked about EAs, but I'm going to bring it back to transfer of ownership.

I have six points here that I would like to make sure that are clear since this is a relatively new topic that we haven't discussed necessarily in the past, and as you mentioned it was sort of convoluted, and we understand that and we hear you. I help processed that, so I know how painful that was. But a couple of things that

I think would go a long way when transferring.

One, plan for your transfer. You can't send a notice to the agency and disconnect your phones and expect us to be able to process your request. It's important for us to have accurate and updated information.

Ensure your files are up to date. Ensure that you work with the new owner to provide them that information that they need. If you need to provide them ingredient information, please do that in advance of the transfer. It may be that your ingredient submissions are bundled and contain information that is not being transferred, and that could be a challenge for the agency. So in terms of how long the process, as part of the -- it's sort of teasing out all the submissions that you have in house and ensuring that we are not transferring things that we shouldn't. So that's sort of the learning curve for I think both industry and the agency.

So continue to work with your current owner. If we send you a request for information

outlining information that is needed because the initial request comes from the current owner, make sure that you communicate any information that may be necessary or helpful to the new owner, because we're not communicating with them. So sort of making sure that there's an open communication in that process.

Clarify what you're requesting for. Like we mentioned, a notice of bankruptcy is not a transfer. If you're changing your company name and that is all that you're letting us know, please be clear. Please be clear that this not company A being called B, or now it's A who's selling to B. We can't read between the lines, so articulating that clearly will go a really long way.

Let's see. What else do I have here? I think that covers it. So hopefully that's enough information to help some people assemble their transfer requests and ensure that we have up-to-date information. I can speak a -- that was the sixth -- this is the sixth thing.

So some of the challenges that we've had are disconnected phone numbers, addresses, returned mail. That may not be the case for some of the larger companies, but these are some challenges. And again, the bundled submission and ensuring that you provide that opinion sort of outside of the process. The only thing the agency can sort of manage is the applications that we have in house, and trying to protect your information is obviously of most importance. And we hope that moving forward it's less painful. And we'll continue to take your feedback and try to make this program more widely known and easier moving forward.

MS. JOHNSON: Thank you.

Tony, did you have something to follow up?

MR. ABBOUD: (No audible response.)

MS. JOHNSON: Okay. So we did have a few questions. We had one about changes of ownership process, so I'm going to start with that.

Rosanna, since you were speaking on that. It's just one that asks what is the change ownership process where no marketing applications are involved such as only establishment's registrations, product listings, ingredient lists are being transferred?

MS. BELTRE: So what we presented here today I can only speak to transfer of ownership within the Office of Science and applications and submissions that are housed within the Office of Science. Unfortunately, there's nobody here from the Office of Compliance and Enforcement that can speak to what process they utilize for that, but obviously notifying the agency.

One thing that may not be very clear to everyone is that if a request is sent, whether it's to the Office of Science or to the Office of Compliance and Enforcement, the regulatory project manager will try to triage that information. So even if it was a transfer that came to us because a project manager may be sort of the only point of contact that a company has,

we will transfer that to the office, to the appropriate office to make sure that it's processed correctly.

MS. JOHNSON: Thank you.

Going back to EAs, we have a few questions on that. This question asks why are EAs needed at all for non-provisional products in the SD and SE exemption pathways? Shouldn't there be a CatEx for those products as there is for provisional products? And what is the justification for treating these two classes of products differently for EA purposes?

MS. CHANG: Well, there are a lot of questions.

MS. JOHNSON: Yes, we can finish the rest of the time on --

(Laughter.)

MS. CHANG: So all the federal -- all the decisions made by a Federal Government agency require a NEPA document. All the action. Every agency. So to allow a product to be on the market is an action, is a decision for the

agency, so therefore an EA -- at least an EA is needed. When I say "at least," that means maybe an environmental impact statement, but that's not in our regulation for -- in 21 C.F.R. 25.40 that we're talking today. So therefore, that's the reason every action, every decision made by any agency needs an EA.

MS. JOHNSON: Okay. So then it asks the justification for treating the two classes of products different for EA purposes. So that's --

MS. CHANG: Yes, mean EX and SE?

PARTICIPANT: No.

MS. CHANG: No?

PARTICIPANT: No, provisionals.

MS. CHANG: Oh, do you want to go?

MS. BENSON: Yes, so one of the reasons, as I had said, it as about having the experience with the products. So when we were working on this rule with the Center for environmental Quality, we proposed a number of things. And we had no experience with them, but they're just kind of instant and that we needed

to get more experience.

But the provisionals were on the market before the act, right? So we were able to write a strong justification to say that those could be categorically excluded. As is always the case when talking about the Office of Science, it's about a strong scientific justification. And in this case made towards the Center for Environmental Quality.

MS. CHANG: So if I could add on my boss' comment. So all the NEPA regulation needs to be cleared by Council on Environmental Quality. And what do they look for? They look for if the agency have -- that the agency has enough experience to say that their action has no significant impact. Currently under the regular SE program we don't have enough information to say that yet. So it's under evaluation.

MS. COOK: So you stated that you made the decision because these products were already on the market back in 2007, so with the newly-deemed products like cigars with the SEs not due

until 2020, will you consider that for that product portfolio?

MS. BENSON: It's certainly something we will evaluate with all the newly-deemed products to see if there are obvious strong cases for categorical exclusions in there. And I usually like to say why do they need an EA? You can blame Richard Nixon because that's his act.

MS. JOHNSON: Thank you. We have time for one more question. The question asks if the tobacco product was manufactured abroad, must we submit an EA discussing the environmental effects of a foreign factory?

MS. CHANG: That's correct. It's in our regulation. In 21 C.F.R. states that we need to evaluate the environmental impacts due to the federal actions as a result of FDA's actions. So if FDA allowed this product to be marketed in the United States, but it's manufactured abroad, then we do have to evaluate the impacts of that particular country.

MS. BENSON: This is something we hear

a lot of because everything else about the Tobacco Control Act is about in the United States. So even internally we would get, well, why were you talking about this? It's a foreign country. But since everything about that is governed by the National Environmental Policy Act and then FDA's regs that are tied to it, that's what's driving all of it. And it does address anything done in a foreign country as well.

MS. JOHNSON: Thank you. Any other comments from our panelists?

(No audible response.)

MS. JOHNSON: Okay. Give them a round of applause. Thank you so much for your time and your expertise.

(Applause.)

MS. JOHNSON: Matt? Matt, you going to send us home?

MR. HOLMAN: (No audible response.)

MS. JOHNSON: All right.

MR. HOLMAN: So I just want to say thank you to all my colleagues for their

hopefully --- (off the record comments).
--very helpful presentations. Hopefully there's a lot of good information that you all received today through those presentations.

I also want to give a big thanks to all of our panelists. I appreciate their willingness to come up here and tell us what things they've seen improvements on and other areas where there are still struggles, just a lack of transparency and consistency.

I've certainly taken a lot of notes today. I think there are a lot of good points being made that me and my colleagues will take back to the office. I look forward to continuing this same type of dialogue tomorrow. Today was more focused on process. Tomorrow is going to be more focused on the information contained within the applications. So I look forward to the same type of -- same level of conversation hopefully tomorrow as we had today.

I do want to make a couple of notes about tomorrow. We are going to be moved down

the hall to the Plaza Ballroom, so we won't be here tomorrow. We'll we just down the hall. There will be signs up like there was today, so you should be able to find it, no problem.

The other point I want to make is that our Session 8 at the end of the day tomorrow was focused on deemed products. That was going to be presented by our colleagues in the Office of Compliance and Enforcement. As Mitch mentioned this morning, they will not be participating in this meeting tomorrow.

However, we still want to have some discussion around deemed products, so our panelists are going to actually share their remarks, their perspective with us. And we're going to conduct that session a little differently than the other ones because we won't have a presentation and we won't have our colleagues from OCE here to present.

Instead what we're going to do during that last session is we're going to have microphones available so that those in the room

that have additional thoughts and perspective and want to share them, they have that opportunity. Certainly we are recording and transcribing this meeting. We are also taking notes. So we will certainly take back any input we hear, any of the feedback that's provided tomorrow during Session 8.

So just want to give people a heads up so you guys could be thinking it. If you do want to share your perspective on the deemed products and how you're dealing with those and meeting our regulatory requirements under the application review programs, that opportunity will be provided.

We will be starting tomorrow morning at 8:30 promptly as I said in the Plaza Ballroom.

So thanks again for everyone's participation today and I look forward to seeing you guys tomorrow morning.

(Applause.)

(Whereupon, the above-entitled matter went off the record at 4:26 p.m.)

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C E R T I F I C A T E

This is to certify that the foregoing transcript

In the matter of: Tobacco Product Application Review

Before: US FDA

Date: 10-22-18

Place: Rockville, MD

was duly recorded and accurately transcribed under my direction; further, that said transcript is a true and accurate record of the proceedings.

Neal R Gross

Court Reporter