CVM ESUBMITTER WEBINAR 2: AFTERNOON BREAKOUT SESSION; PRIMARY REVIEW DIVISION 2

MS. AILA ALBRECHT: OK, good afternoon everyone. To give an overview of the session, we have four speakers who will demonstrate how to fill out the eSubmitter templates for a variety of meetings. I will provide an overview of the templates, and show how to request your first presubmission conference. Krystyna Reign will show how to request a mid-project presubmission conference to revisit the development plan; Josh Hayes will show how to request mid-project meetings to discuss a specific technical section and he'll demonstrate both the presubmission conference and other ONADE meeting options; and Jacob Bitterman will show how to request a method demonstration meeting.

To introduce myself, I'm Aila Albrecht, I'm the leader of Project Management Team 1 and, as I said, I'll be providing an overview of the meeting request template and demonstrating how to request a first presubmission conference.

I have my screen shared so you can see the eSubmitter tool and I am working in the test environment so I'm going to create a new submission for this meeting request. Choose the correct template version, name and create the file, and this brings me to the document information screen. My meeting that I am requesting is under an

existing INAD that I've already established so for document type, I'm choosing investigational new animal drug file which is an "I". Is this submission for a currently established file? Yes. And then enter my document number.

I'm going to skip through the next couple of screens, the firm information and the submitter information, because this was covered in the morning session and that brings me to the submission type code screen. I'm going to select my submission type which is a request for a meeting, or a "Z" submission. The submission classification code, I only have the one option, which is an ONADE meeting. And then the review division to which I'm submitting. I'm going to submit to the Division of Business Information Science and Management, HFV-180, to direct this request to the project management teams.

Is this information intended to amend a submission? No, it is not. And that brings me to the meeting specific templates. The first question I'm asked is to select the scope of my meeting request. I have a few options here and I have descriptions up above for what these mean. My particular meeting is to discuss the development plan for my product. I want to know what number and types of studies will be required to support approval so I'm going to choose that this is a presubmission conference.

For the type of meeting, I want this to be an in person conference. Then I'm asked do the firm participants include any foreign visitors and I have the note here that if someone is not a US citizen, they are considered a foreign visitor. It's very important to correctly identify when someone is a foreign visitor as CVM needs to

complete a clearance process for them to enter the building. In my particular case for this meeting, I do not have any foreign visitors so I'm going to select no.

Then I'm asked will the meeting include or involve discussions about additional documents. Saying yes to this question will result in a duplicate meeting request being created under the additional document or documents. For my case I really want to discuss just the one INAD I already entered so I'm going to say no. Then I'm asked will this meeting discuss the approval requirements for the product as an ADAA combination. For this case, no.

Then the last question on this screen is about early information. Early information can be submitted in several submission types including meeting requests. For any questions about early information and how best to submit it, please contact the project management team. For this particular case for my meeting today, I do not have early information to include so I'm going to select no.

I'm going to skip over this screen, the product description. This was something else that was covered this morning. And that brings me to my meeting and teleconference information. I am required to enter at least one proposed date and time so I'm going to request October 10, 2018 at nine in the morning. And my proposed duration in minutes, I'm going to request 120 minutes for a two hour meeting. I have the option to then propose two alternate dates and times and I'm going to go ahead and do that. My second choice would be October 11 at 9 and then my third choice, I'm going to go back to the tenth at 1. And then

do I have audio-visual requirements? I'm going to say yes and that I would like to have computer projection in the conference room.

Then my next screen is the firm participants. If you add participants, you click the plus sign here. Then you fill out the fields. My first firm participant is going to be Dr. Jane Doe and she is a regulatory affairs manager and her firm name is Animal Drugs Inc. And if I had additional participants, I just click the plus sign and run through the same fields for each of them.

Then I come to the requested CVM participants and I have a few options here. I can request by name, by program support area, or both. So if I request by name, it enables the first section here and I can click the plus sign and type in the name of the participant I'm requesting. If I choose program support area, then that section I was just in disables and it enables the bottom part of the screen. If I click on that plus sign I get a list of various divisions and teams and offices to choose from. I'm going to go down and request project management. And then if I request both, both sections of the screen are now enabled and so the choice that I made is still there and I can go back up to the participants by name section and request a specific person in addition to the team that I asked for.

Then I come to the Meeting Agenda and Supporting Materials. There's a note here on the screen saying that the template options from this point will change based on the meeting scope that I selected back in section 1 which was the general information. At that point I selected presubmission conference. If I realize at this point that I need to change that, I won't lose any of the information that I just

showed. The product description, the meeting date and time, and the participants will all remain but everything that I'm about to show from this point on will be impacted by the meeting scope. Again, I had selected presubmission conference so we're going to move forward through the presubmission conference screens.

The first thing I'm asked is what is the purpose of the meeting and/or the expected outcomes? There are some examples listed of the kinds of things CVM is looking for. I can either type in text or I can attach a file. In my case I'm going to type that we seek agreement on our development plan and the number and types of studies required to support approval. Then I'm asked if this is the first meeting to address the development plan for this approval effort and I'm going to say yes it is. I get the pop up note that based on my selections, this submission will be directed to the Project Management Team in HFV-180. This is the same group that I had selected back when I was choosing the recipient for the meeting request. If I had chosen someone different that would now be overridden by the selection that I just made. If there is an override, it will not affect any of the CVM participants that I had requested on the previous screen. The selection also activates template options that we'll see on the next screen. But before we get to those I have one final question on the screen which is the approval effort for the product to be used in a food or non-food animal? In my case, I have a food animal product.

Now I come to the technical section overview screen. There is some information at the top that I'll go through. I have a note first that I'm going to need to choose at least one technical section to

discuss at the current meeting. That is my first option here and each option is explained. To "discuss at current meeting" means that the technical section or component will be discussed at the meeting and CVM representatives for the element will be present at the meeting. The next option is "to discuss at a future meeting". That means that the technical section or component will not be discussed at this meeting and CVM will not provide any specific feedback either at the meeting or in the acknowledgement letter. CVM representative for the element will not be present at this meeting.

My third option is for "CVM to confirm but not for discussion". That means the technical section or component will not be discussed at the meeting but CVM will provide feedback in the acknowledgement letter. CVM representatives for the element will not be present at the meeting. "Already complete" means I believe the technical section or component has already been addressed. CVM will assess that selection and provide the assessment in the acknowledgement letter. CVM representatives for the element will not be present at the meeting. The final option is "not applicable" which means I believe the component does not apply to this approval effort and again CVM will assess that selection and provide the assessment in the acknowledgement letter. CVM representatives for the element will not be present at the meeting.

So just a couple notes: the first option, "to discuss at current meeting" is the only option that will result in CVM representatives for that section being represented at the meeting. It is also the only option that will result in discussion about that technical section or

component at the meeting. For the options for which CVM will transmit comments, those comments will be transmitted in the acknowledgement letter accompanying the memorandum of conference.

For my particular meeting, I have a number of technical sections that I do want to discuss but I'm going to choose some of these other options, too. So effectiveness and target animal safety I do want to discuss at the current meeting. For microbial food safety, I believe that is not applicable. Toxicology and residue chemistry I do want to discuss at the current meeting. For environmental impact, I would like CVM to confirm my plan but I won't need to discuss it. And then chemistry, manufacturing and controls, I do want to discuss but not yet. So I'm going to select that I want to discuss that at a future meeting.

Based on the selections I made here, we'll navigate through the remaining templates. It comes first to effectiveness. There are some notes at the top. For the specific questions here I can type the text directly in the field, I can attach documents that are specific to effectiveness, or I can refer to the location of the effectiveness proposal in a larger document. When I outline my effectiveness proposal, I need to include at least the number and types of studies that I intend to do. This would be the minimum information required. I can include additional details which would be discussed at a high level, so not at the level of a protocol review, and when I submit my proposal I should include my rationale for it.

The first question is asking me how I propose to establish effectiveness. In my case, I have a single document that addresses all

aspects of my development plan, do I'm going to refer CVM to a specific place in that document. I'm going to refer CVM to pages 3 through 10 of the development plan proposal. Then I'm asked what specific questions about effectiveness I want CVM to address. There are two and I'm going to refer to the questions on page 10 of the development plan proposal.

The next screen I come to is target animal safety. It looks very similar to effectiveness. I do have an additional question at the top which is asking whether I propose to use this product in breeding animals and in my case, yes I do. Then it asks how I propose to demonstrate safety in the target animal. And so again I'm going to refer CVM to the appropriate section of my document which is pages 11 to 16. And then my specific questions, I'm going to refer to the questions on page 16.

Microbial food safety, this is where I had selected earlier that I believe this is not applicable for my product. I'm asked to explain why I believe it's not applicable. In my case, my product is not an antimicrobial and does not have antimicrobial activity and I've explained that in my document so I'm going to refer CVM to page 17 of that document.

I then come to toxicology and you can see at the top of the screen we have a couple of references included: a guidance for industry and a guideline document. I'm asked how I propose to evaluate the oral toxicity of the drug residues. I'm going to refer CVM to pages 18 through 20 of my development plan proposal. And then I'm

asked what specific questions I have about toxicology so I'm going to refer here to the questions on page 20.

The next screen is residue chemistry and again we have some references at the top. I'm asked how I propose to evaluate the quantity and nature of residues in animal tissues? I'm going to refer CVM to pages 21 to 23 of my proposal and then my specific questions, refer to page 23.

Environmental impact – this is the one where I had selected that I wanted CVM to comment but I did not want to discuss in the current meeting. I'm asked whether I plan to request a categorical exclusion or to submit an environmental assessment. For this particular approval effort, I'm going to request a categorical exclusion. When I choose that, I'm asked which citation I'm going to cite and in my case I'm going to cite 25.33(d)(5) which is drugs intended for use under prescription or veterinary order for therapeutic use in terrestrial species and I've explained this in my development plan proposal so I'm going to refer CVM to page 24 of that document. And my specific questions for the environmental safety team are also on page 24.

Now I come to the screen where I can attach my agenda brief and/or other supporting materials. Through the previous templates I was referring to specific sections of my development plan proposal. This is the screen where I upload that proposal. So I'm going to click the plus sign and then I need to navigate to where I have my file. And here it is: development proposal plan dot PDF. I'm going to select it and it's now attached.

The last screen I come to is the screen where I can enter any additional comments that I may have. This concludes the demonstration of how to request the first presubmission conference and I will now turn it over to the next speaker.

KRYSTYNA REIGN: Hi, I'm Krystyna Reign, leader of Project Management Team 2, Division of Business Information Science and Management. In my scenario, a meeting request is done with the project and the intent is to revisit the development plan across all technical sections. For example, the first PSC for this project could have happened a year ago and now this meeting request is to discuss changes to the already-established development plan. In this example, I want to talk about changes to the wording in the indication and the number and types of studies needed for approval.

As Aila already reviewed the previous screens, I'm going to start with screen 6.0. Here, just as Aila showed you, the first question is the INAD submission type and we're going to select "Z" to request a meeting. The submission classification code is going to be OM which is the only choice and just like in the previous example, I'm going to select HFV-180 because I want to talk about the development plan across all technical sections. So for HFV-180, this is going to route the submission to the project management team.

The next question asks whether the intent is to amend a submission currently pending and under review by CVM. I'm going to say no in this case.

On the next screen, it will ask me again what type of meeting this is going to be and I'm going to say presubmission conference and

I'm going to select in person; there will be no foreign visitors; and I'm only going to talk about one INAD so the response to the question if I want to talk about additional documents is going to be no. This is not an ADAA combination and it's also not an early information meeting in this submission. Again, this screen is the same as Aila already showed you.

I'm going to skip through Screen 2 and 3 as they are exactly the same as Aila already shared. Four is also the same. Five is also the same to enter the CVM participants and now I come to screen 6 which will give you the same message that was in Aila's example.

Screen 6.2 is asking for the purpose of the meeting and expected outcomes. Here I already pre-populated that: "we seek agreement on changes to our development plan, previously discussed under Z-0050. We want feedback on our proposed changes to the wording of the indication, and agreement on the number and types of studies needed for approval."

The next question asks whether this is the first meeting to address the development plan for this approval effort and this is where the difference is. I'm going to select "no". That's because I already held a meeting under Z-0050 as stated in the previous response.

The next question is: does your proposal represent a change to aspects of the approval effort discussed in a previous meeting? I'm going to say yes which brings up another question. You are asked to briefly describe the nature of the change. I'm just going to say that

I want to talk about "changes to the indication and number and types of studies needed for approval."

In the next question, we are asked whether we want to revisit the development plan based on the changes above. I will say yes. A message will pop up saying that based on your response, the submission is going to be routed to the project management team and which are already pre-selected, which is in HFV-180.

In my example, we're going to talk about a non-food animal. Based on that response, you'll see what under technical sections overview, human food safety is not listed here.

For the effectiveness, target animal safety, environmental impact, and chemistry, manufacturing, and controls, you will have the same choices where you can select that you want to discuss at the current meeting, you want to discuss at a future meeting, or you want to confirm but not discuss it at the meeting. You also have an option to "already complete" or "not applicable".

I'm going to say that I want to talk about effectiveness at the current meeting, target animal safety, for environmental impact I just want to confirm but not discuss. And for chemistry, manufacturing, and controls, I'm going to say "already complete."

Based on these selections, screens for effectiveness, target animal safety, environmental impact, and CMC will pop up. These are the same screens as covered by Aila so in my example, I'm also going to refer to pages in an attached briefing document. So I'm just going to say to refer to page 3 of the briefing document. And my questions are in the briefing document as well so I'm going to refer to page 5.

I'm going to do the same for target animal safety. I'm going to say no, this is not a breeding animal. And when it asks for my rationale for my proposal, I'm going to refer again to my briefing document. And again, my questions are in the document as well so I'm going to say refer to page 9.

For environmental impact, I selected that I want confirmation from CVM but I do not want to talk about it at the meeting. I am going to say that I want a categorical exclusion and then I will refer to page 12. And for my questions asking to confirm my selections.

For CMC, I stated that it is complete and the screen will ask for the rationale for why the technical section is complete or the component is complete and I'm going to refer to my briefing document as well. And here you can basically state that it was approved per an earlier technical section and that you're not making any changes about what your rationale is.

The next screen again asks for an agenda or brief just like Aila showed you. You can attach a briefing document and the last screen is the comments, also covered by Aila.

So now I want to go back to a previous screen, this is screen 6, and actually change one of my answers.

On this screen the last question here asks if the information intended to amend a submission currently pending and under review by CVM? If I select "yes" because I already submitted my meeting request, but I didn't attach something that I want to refer to, and I say yes, on the next screen it will ask me for my submission number so I will just put 90 here. And I'll say that no, this is not an amendment to

change or direct the response to a different webtrader account. The next question is is this an amendment requested by CVM. If I select "no", a message should pop up stating that CVM will reschedule the meeting based on the amendment being submitted; therefore, we recommend that you always contact CVM prior to submitting an unsolicited amendment to a meeting request.

Now I will turn it over to Josh Hayes.

JOSH HAYES: Hi there, this is Josh Hayes, I'm a reviewer and I'm walking you through an example here of a down the road meeting request after you've had your larger development plan meeting. So in this case, I want to talk only about one of the technical sections. But it is a meeting request in which I want to talk about things that would normally cause it to become part of a presubmission conference.

So as you've seen before, make the appropriate selections about the type of meeting, and foreign visitors, the discussions about additional documents, and whether or not it's an ADAA combination, and early information.

And as discussed earlier, the product description we'll continue past, as well as the meeting/teleconference information, firm participants, and requested CVM participants. And so we're at this screen where again you are prompted for entering in the purpose of the meeting and expected outcomes and in this case I'm seeking CVM's feedback on aspects of the revised protocol to satisfy the effectiveness technical section. And as Krystyna mentioned, I'm prompted to answer the question: is this the first meeting? And in my case, it is not. And does this proposal represent a change and in my

case, it does not. I'm coming back for further information, further detail.

In this scenario, I'm talking about the approval effort for use in a food animal.

Continuing on, I want to talk about effectiveness, so I select it. And continue. And here I'm prompted with the question of have I proposed a plan to address the effectiveness section in a previous meeting request? In this case, yes I did. And what specific questions do I want CVM to address? I direct CVM to pages 2 through 5 of the briefing document.

Continuing, I can enter here my slide set as well as my briefing documents. Now, if I were to jump back to an earlier node, scroll through, if I did not, previously, as you saw with the different options, if I wanted to talk about effectiveness in a future meeting, here I am now, I want to talk about effectiveness and I did not previously discuss effectiveness in my previous meeting request. So I select "no" and this screen should look familiar. This is the screen you would normally fill out when you are asked to address how you're going to propose to establish effectiveness and so I will again direct CVM to the appropriate place in my document. And in this case, my questions specifically are only on page 5. And then we continue as normal.

Let's switch to a different scenario. Technical difficulties here, one second. So this is a scenario in which I have already discussed technical section requirements and now I have some questions that are not related to specific numbers and types of studies that are

needed for approval. Instead I have some follow up questions in this case related to the protocol. So I'm going to choose an ONADE other meeting, subclass "OO", with the appropriate selections. Continue past the screens you've seen and in this case, I have the option to provide an agenda, either as text, an attachment, or both. I've selected both and put in the box here that the intent is to get CVM's input on inclusion and exclusion criteria and additional protocol elements for a study and I direct CVM to the attached slides and draft protocol language and then attach the documents as you've seen before.

As with all the templates, you have the space to put additional comments if you need them. And with that, I'll turn it over to our next presenter.

JACOB BITTERMAN: Hi, my name is Jacob Bitterman and I'm a reviewer on the Residue Chemistry Team in the Division of Human Food Safety and I'm here to talk about doing a request for a method demonstration meeting.

For a little background on what a method demonstration meeting is, for a new drug intended for use in a food-producing animal, where a tolerance will be established for residue monitoring, an official method is required that can accurately identify the marker residue at the tolerance concentration in the target tissue.

The method demonstration is a step in this process where the sponsor's reference laboratory demonstrates performance of the official method at CVM's Office of Research to prepare for the inter-laboratory method transfer trial.

As the others have, I'm going to start on this screen. We're doing a request for a meeting and select ONADE meeting which is the only option and this method demonstration request would always go to the Division of Human Food Safety, or HFV-150.

When you get to the meeting request template, the first question is on the scope of the meeting so for the method demonstration, you're going to select "method demonstration" as the scope of your meeting request. You'll note that this now pops up a new request for information in a box just below the scope of the meeting that reads: "please provide the CVM submission number associated with the Z, H, or P submission where CVM agreed that the analytical method may proceed to the method trial."

If you click the help lightbulb here it gives you a little hint on how to answer this question. For methods undergoing the full method trial, enter the number for the Z submission of the 3-hour meeting where the proposed analytical method was discussed. For methods where CVM has agreed that the method can undergo a single laboratory validation, enter the number for the H or P submission containing method validation information for the proposed analytical method.

So the number you will put in this box here is the 4-digit number of the submission number so I'm just going to say 0110. Also note that this defaults the type of meeting to an in person conference because this is always an in person meeting.

For the foreign visitors question I'm going to put "no" but as Aila discussed, it's very important that you select "yes" if you do have foreign visitors so that we can complete the clearance process.

We will not be discussing any additional documents, this is not an ADAA combination, and this is not an early information meeting.

I'm going to skip the product description. For screen 3, I'm selecting the date and time. When you're requesting a method demonstration meeting, hopefully you'll have discussed previously with CVM the scheduling of the meeting so that we can get our laboratory personnel ready so we ask that you request the date that we've already discussed by email. In this case, I'm going to put October 31, 2018. We're going to start at 9 am and it's all day, so I'm going to select 480 minutes. Usually you will want to have computer projection for the meeting.

The firm participants, I'll just go through quickly because Aila already covered it. Dr. John Doe from Regulatory Affairs will be attending. For requesting CVM participants, you should request from "program support area" and select the residue chemistry team, HFV-151.

Then for section six you'll get this warning about selecting the appropriate scope of the meeting and then you can move onto 6.1 where you can attach an agenda or supportive materials. We ask that you always attach the method SOP for the analytical method and a protocol for the method trial so I'm going to attach those here. I have my method SOP and my method trial protocol.

Then at the last screen, I have an opportunity to put in any additional comments or documents that you have not covered previously. And that covers the request for a method demonstration meeting.

ANNA O'BRIEN: So that concludes our demonstration on the different meeting requests eSubmitter templates. Like I said at the

beginning of this module, if attendees have any questions, please type them out in the chat pod here in the Webex screen. I'll put myself on mute for a minute or so to give you a chance to think of any questions that you might have. [extended silence] OK. Seeing that there are no questions in the chat pod, we can conclude this module. Thank you very much for your attendance and have a good rest of your afternoon. Thank you.