I-P-EF Technical Section

Good afternoon, the next session is gonna be the I /P / EF module. I will go ahead and get it started and we'll do all of the questions in the chat pod if possible. If you have any problems hearing please go ahead and put that in the chat pod and I'll try to adjust from this end.

Click the next button which brings you to Submission Type screen. The first question, please select the INAD submission type. We're choosing major technical section P.

The next drop down allows you to choose the appropriate Submission Classification code. We're going to choose effectiveness. Then you please select the appropriate review division to which you are submitting. I am going to pick 110. Then the final question on this screen is 'Is this information intended to amend a submission currently pending and under review by CVM'; choosing 'no'. If you have questions about the amendment process, please refer to the amendment webinar.

Then you click the next button which brings you to General Information regarding the entire submission. The first question, 'Please select the final action letter you are requesting from CVM. The two options are Submitted Information Acceptable; Technical Section Incomplete or Technical Section Complete. I am going to choose Technical Section Complete, but your answer to this question does not change the template at all moving forward.

The next question is 'Is this in response to a previous CVM Technical Section Incomplete Letter?' I am going choose 'no' for our first run through the template. After we run through the template in its entirety one time I am going to circle back and I am going to choose 'yes' and I will show you how choosing 'yes' will change the template.

The next question is 'To provide a brief summary of the information in this submission'. I am to put in one field study, two lab studies. And there is a hint to the right here that provides a good example: For example, "Five lab studies and one field study to support treatment of flea infestation'.

The next area is a multiple file attachment question. This section is for introductory document such a Submission Summary, Cover Letter, Table of Contents. Some firms write Technical Section Summary. Whatever you consider an introductory document you attach via the plus sign. You choose your appropriate pdf and attach them here. Once you finish attaching your pdf, you click the next button which brings you the Product Description Screen. Product Description is covered in a separate webinar and will not be covered here.

So you click…I am going to click the next button and it brings you the Effectiveness Data Information. One of the major changes of the new template is you are going to submit each study separately. So in order to submit each study separately we are going to choose the plus sign and we are going to choose what type of study we are submitting. Earlier I said that I am

submitting one field study and two lab studies. I am going to choose field study. I am going to enter the study number and provide a brief description. And this hint over to right also provides a very good example of multi-study randomized field studies to support the indication for the treatment for flea infestation. And then you are going to enter the last question, 'Was an Electronic Data Capture (EDC) system used to collect data for this study?' I am going to choose 'yes' which also illuminates this question over to the left, the 3.6 button. If you choose 'no', you will not have to answer this question as you move through the template. So I am going to choose the plus sign again cause I also have two laboratory studies. So I have lab studies; I enter the study number. I write a brief description. And I did use electronic data capture. And I choose the plus sign again. I have another laboratory study. I enter my study number. I enter a brief description. And I say that electronic data capture was used to collect data for this study.

And after you have finished entering all the types of studies, you are going to include in your Effectiveness Technical Section, you click the list. And it will provide a list. This could be a really short list if your Effectiveness Technical Section is just a field study it would be Field Study listed here. But if you have a bunch of lab studies, it will be all of your laboratory studies and then all of your study numbers.

So let's click Field Study moving forward. I double click Field Study. I click the next arrow and it brings us to uploading just the field study information and you can tell by right up here at the top it says Field Study and the study number. So this first part is the Final study report upload. So you are going to click the plus sign, click pdf and attach it here. This is a single file attachment section. In some cases there is an amended final study report, so what we want is in quotations, the 'final' final study report. Any previous versions of the study report can be put in 3 dot 12 which is Other Study Related Information. If you have amendments to the Final Study Report, that are not attached to the Final Study Report, you can put them in either 3.12, Other Study Related Information, or if they would qualify as a Contributing Scientist Report, you can put them there.

So after you've uploaded or attached your final study report, you click the Next button and it brings you to the Protocol questions. The first question is 'Did you previously receive concurrence by CVM for your protocol?' If you choose 'no', that's the end of the question. If you choose 'yes', you are asked to you received concurrence by CVM on your protocol. If you say no, that's the end. If you say yes, you are asked to provide the submission number. My protocol was E-12 where you received concurrence on the protocol.

The next set of questions is 'Did you include a final study…a signed protocol in the final study report?' If you pick 'no', you can attach the signed protocol here. You click the plus button, choose your pdf and you attach the protocol here. Or, you can tell us where in the submission your signed protocol is. If you list the name of the pdf file and the page number where you…where the protocol is located. If you choose 'yes', 'I did include a signed protocol in the final study report?', you just add the page number of where that signed protocol begins.

Then you can click the next button which brings you to Test and Control Article Characterization. So to enter your test article and control article you click the plus button and you click either control or test article from the drop down menu. We'll start with test article. And it asks to provide an identifier that you used during the study, or was reflected in the final study report. And sometimes you use the actual proprietary name or established names. A lot of times it's a combination of letters and numbers. You are going to enter that there. Then you are going to provide us with a few extra details regarding the test article. So you are going to choose one of these four options. The proposed final formulation. You are going to provide the lot numbers. And then you are going to provide us with a location of the Certificate of Analysis in the actual submission. Providing these details here help us towards the end of the approval-or toward the end of the approval process when we have to go back and double check all the lot number having these lot numbers...having the information here would make that process or makes that process faster for us at the end of the approval process.

The second option is Currently Marked Approved formulation. You are just asked to provide the lot numbers. Any sort of change from the currently marketed approved formulation you are going to provide the lot numbers and you are also going to provide the, the, where the location of the Certificate of Analysis are in the submission.

If it's Other, like you used a pilot formulation and part of your effective technical section is bridging to a final market formulation you are going to provide the composition of the formulation in this free form text box and then you are going to provide the lot number of the test article.

To add your control article, you are going to click Control Article. You are going to provide the article identifier. Let's say, for example, you used a 'Vehicle', you are going to provide the lot numbers. And you are going to provide the lot numbers and the location of the Certificate of Analysis in the actual submission. However, sometimes control articles are water which, you know, would not have lot numbers or certificate of analysis in which case you can write Not Applicable.

Then you are going to press list button and it will provide a list of your test articles, control articles. You add as many as you need to reflect, accurately reflect what was used in your field study. For example, like a non-interference study, you may have three control articles and one test article, so you would enter all of those here.'

Click the next button and come to the Protocol Amendments and Deviation section. The first question is about protocol amendments: 'Were protocol amendments implemented in this study?' If you say 'no', that's the end of the question. If you say 'yes'; we ask that the protocol amendments are included in the final study report. If the amendments are included in the Final Study Report, you are just asked for the page number. If you say no, you can actually attach your protocol amendments here via the plus sign. You choose the appropriate pdf and attach it here or you can tell us the location of the protocol amendment in your submission.

The second one is Protocol Deviations which is identical to protocol amendments. 'Were protocol deviations implemented in the study?' 'No', then that's the end of the question. If you say 'yes', you are asked if the protocol deviations are included in the final study report. If you say 'yes', you are just asked for the page number. If you say 'no', then you are asked to either attach the deviations here or you can, in the free form text box, provide the location of the deviations in your submission.

You click the next button and provide… the next question is Standard of Conduct. Most field studies are GCP. You can also choose Other, then you would have to identify the quality standard used to conduct the study. We are going to choose GCP for the field study.

Next is Electronic Data Capture systems. So whatever the Electronic Data Capture systems used for the field study you are going click the plus sign. This information is going to be used under Data Files and in Section 3.8. So we are going to enter our Electronic Data Capture systems, our first one, that was used to collect clinical pathology. Our second EDC system was used to collect specifically physical examination, observations and the primary endpoint. And then our last Electronic Data Capture system was used to collect necropsy, histopathology, if needed, for a field study. And you click list and it will list all of your Electronic Data Capture systems and what they were used for.

The next screen is the Read Me file. The Read Me file is a single pdf attachment it contains information about the electronic data files and programming files in the submission. The file explains how the data sets are organized and describes how the programs are used for data set generation and data analysis. So you are going to click the plus sign, pick your Read Me file and attach it here. And that Read Me file is just for your field study.

You are going to click the Next button can come to the Data File. So we are going to start by entering and clicking the plus sign. We are going to describe the data collected within this data set. This is our clinical pathology data set. And it says, the next question 'Was an EDC system used to collect the information for the data files?' We are going to say 'yes'. And you are gonna have a drop down menu that you entered in 3.6. We are going to choose it was EDC 1 and then you are going to attach your data files here. Your data files are usually XML, XPT files or pdf. And you are going to click the plus button and attach your appropriate files here I don't have any XML or XPT files to to have an example with, but.

And then the next section of questions for the Data Files are the Audit Trail Files. The first question, 'Do audit trail files exist outside the date files?' So if your audit trail is actually contained within with your data files, in XML and XPT, you click 'no' and that is the end of that question. If your audit trail files are outside your data files, then the next question is 'Do you have non-proprietary XML or XPT file format audit trail files to attach?' You can say 'yes' and you can attach them here. If your say 'no', your audit data trail files are not XML or XPT, it asks if you have audit trail information in PDF. If you say 'yes' you are asked to attach the audit data

files here. If you say ‘no’ you are asked the reason why the audit trail information from electronically captured data cannot be submitted either via XML, XPT or PDF.

And so let’s go to the next section and we are going to demonstrate something kinda different about a field study. Let’s let’s go to, so, we, our second physical examination, observation and primary variable. We did use electronic data capture to gather that. It was EDC 2 and we are gonna attach all of the XPT, XML files here and answer the data audit file.

So now for a field study in particular, let’s say we have an owner diary which is collected by paper. And so ‘Was an EDC system used to collect the information for the data files to be included below?’ ‘No’ and you are asked to briefly describe how the data was collected when not using the EDC system. And say ‘dog owners recorded observations daily at home.’ And then you are going to click the plus button and pick your owner diary files and attach them here. And then you will see the audit trail files do not pop up. And so you are going to attach all of your data files in that fashion. And you can click List and it will show you all of your data set descriptions.

And so we are going to click Next and come to Program Files section. These programs are used to perform randomization, process the data, generate summaries and perform statistical analysis including the export files. They are generally in XML format. You do not need to submit staff output or log files. If CVM finds that we need to have one of these files, we will request an amendment. We also do not need electronic data files of calculated data, for example, average daily gain or summary statistics. So you will attach your program files. You click the plus sign and click your appropriate XML files, click Select and they will all come up here and it is a multiple file attachment area.

After you have attached all of your program files, you click Next and come to the Contributing Scientist Reports. If you have, so this series of questions will ask you where your Contributing Scientist Reports are, reside in the submission. So the first question, ‘Do you have any Contributing Scientist Reports associated with this study?’ If you say ‘no’, that’s the end of the question. If you say ‘yes’, then you are asked if the Contributing Scientist Reports are included in the final study report. If you say ‘no’, you are allowed to attach your contributing scientist report here. If you say ‘yes’, you can tell us where your Contributing Scientist Reports live. If you have Contributing Scientist Reports all over your final study report you can say that that one starts on page 68, the PK one starts on page 110. However, if all of your contributing scientist reports are sequential, you can say the report starts on page on 90.

Once you have provided that information you can click the next button and we come to Records of Communication. It asks ‘Do you have records of communication to attach for this study?’ If you say ‘no’, you are going to say where in the submission are your records of communication. And you can provide, again, the PDF name and the page number. Interesting for field studies sometimes the records of communication are broken up over multiple PDFs, so if you, if you have that situation you can provide more than one to let us know that there, there

is more than one. If you do have records of communication that are separate files you can choose ‘yes’ and click the plus one button and attach your appropriate pdf that has the records of communication in it. And records of communication are telephone calls, visits, emails, between sponsors, CROs and investigators.

Once you have answered these questions, you can click Next button and this is the Other Study Related Information. It is essentially a catch all area. It is not a required field. You are not required to attach files here. But if you have information that was not previously provided regarding this field study, you’re going to provide it here. Examples would be CVs, drug accountability records, training records, things of that nature. And you are going to click the plus sign, choose your appropriate CV or record… facility record and attach it here.

And you are going to click Next button, and you come to Labeling, Freedom of Information, Further Information. These have essentially remained the same from the previous input and asks if you are submitting labeling text information. If you say ‘no’, that’s the end of it. If you say ‘yes’ you are asked to attach the labeling text that you are going to submit with this P submission. It asks, ‘Are you submitting Freedom of Information text?’ If you say ‘no’, than that’s it. Please ‘yes’, you can attach your FOI summary here. If you have…Then it asks, ‘Do you have any further information to submit?’ If you click ‘no’, that’s the end of it. If you click ‘yes’, you can attach Further Information. And Further Information essentially used to be called All Other Information, and now we are referring to it as Further Information to differentiate it from the actual technical section. So anything that you would have submitted under All Other Information fora P you are going to submit it here; so those pilot studies, those drug reports or international reports, those things of that nature would all go, would all go in here.

And then you have a Comment section if you have any additional comments or instructions or anything that you find pertinent to this submission, you can provide it here. So let’s go backwards. And like I said I one field study and two laboratory studies. I am going to double click the laboratory studies. I am going to click the next button and you are going to start these questions all over, again. So let’s try to go backwards again. And we are going to run through ‘ Is this in response to a previous CVM Technical Section Incomplete Letter’? And we’ll say ‘yes’ and this will change the template moving forward. So this series of questions are specific to responding to a CVM technical section incomplete letter. And the first question is ‘Did CVM offer you a shortened review time with the resubmission of this Technical Section?’ If you say ‘no’, this queues our internal timelines. If you say ‘yes’, then this gives us a different timeline. And then it asks ‘Please provide the CVM Submission Number associated with the referenced Technical Section Incomplete Letter’. So my last technical section incomplete letter was number P-25; enter 25 here. Then it asks you, ‘Are there any additional CVM Submission Numbers associated with your CVM Technical Section Incomplete Letter?’ If I say ‘no’, then that is the end of it. If I say ‘yes’, then you are asked to provide the submission numbers; let’s say number 21. And so you include that here. So this technical section is in response to P-21 and P-25. If you

have more than the two, then you can click another one…and it was number 17. So it was, so I am responding to P-21, P-25 and P-17 technical section incomplete letters.

And then it asks you for a file attachment. You are asked about to provide a single PDF file that contains the description of the updates to your response to technical section incomplete letter. You click the plus sign. You click your pdf that summarizes your response to technical section incomplete letter and attach it here.

So let's move forward into…we'll choose lab study. So for the technical section incomplete letter, you will get this extra question: 'Have you submitted this study previously?' If you say 'no', you will notice on the left all the questions light up, if you say 'yes' 'I have submitted all of this study previously', then the left, the left side is all greyed out and you are asked to select a section that are to be updated in the study in response to the previous technical section incomplete letter. So let's say you had to add some data or rerun some data, and so you rewrote your final study report and we have new electronic data which means we had a ReadMe File, Data File and Program Files and that might mean we have a Contributing Scientist Report. And so you check those options here and then those options light up on the left here. So when you click through, you are asked to attach your new final study report and then it skips Protocol, Test Article Control Characterization and skips right to Electronic Data Capture system because we have new data there.

We have a new Read Me File, a new Data File, a new Program File, and, you know, maybe that new Contributing Scientist Report. And then you also look at Records of Communication and 3.12, which, personally, I would probably always pick 3.12, just in case, but you can always go backwards and say we forgot something that doesn't necessarily fit in all these sections so I go back and I click Other Study Related Information and now as I click through I can add a new CV or something along those lines. Let's go backwards one more time, I am going to say 'No, this is not in response to a technical section incomplete letter' and I am going to click on my lab study. So from this drop down there are lots of options, so how do you know to pick the correct one? So my personal recommendation would be to…, if you are uncertain you can always contact CVM or the appropriate review division to get feedback; so also reference presubmission conference. For example, if in your presubmission conference you were discussing what studies should make up your effectiveness technical section submission and you had, you know, one field study, one in vitro Study, one PK Study, and then your…, a dosage confirmation study. But that field study that you are going to conduct is supposed to stand for dosage confirmation study. In that case, when you have a field study and it is supposed to stand for dosage confirmation, according to your presubmission confirmation, I would choose Dosage Confirmation Study. If the In Vitro Study, which is also a Lab Study, if the in vitro study is supposed to stand for a lab study, I would click Lab Study but if you choose In Vitro Study, you are not going to be penalized. That is a true statement; it is an in vitro Study. So you're, this is just essentially to give us an idea of what's in a submission, like where we are starting and to give us an idea of where, of what kind of submission we are jumping into.

So let's go backward, one more time and then we are going to…I am going to show you a couple of differences in literature. So literature; if you choose literature, so you'll notice the left here, some of the areas are greyed out. So these are the sections, excuse me, we feel are needed when you have a literature effectiveness technical section. You will have a literature technical section, you'll have a Final Study Report, you'll have a Protocol, you may have Amendment Deviations. There would be a Standard of Conduct which I would recommend discussing with CVM or entering your presubmission conference. Oftentimes there are Electronic Data Capture System files, ReadMe files, Data files, Program files. So these are the areas you would need to answer for literature.

For Other, Unclassified, it's essentially just Other Study Related Information. Essentially you just put all of your information in that section. For Dosage Characterization you also notice that essentially everything is greyed out and it's just 3.12. And that is because dosage characterizations tend to vary widely so there wasn't a very good prescriptive template that we could make because dosage characterization is so different for each and every product.

So this concludes the INAD P Effectiveness template. If you have any questions, I am going to start going through the chat pod and try to answer all of the questions I can. If I am… if I don't answer your specific question during this webinar, I will answer it in the September webinar. Thank you and look forward to the questions.

Alright, let's go ahead and start through the chat pod, if you want to go ahead and enter some questions. I've got two which I will go ahead and start with. The first one is in Section 3.1: "If a final study report is more than a hundred megabytes and contains multiple files, where should we attach the files? It only allows for one attachment." So, your final study report containing multiple files, I guess my question is what would be the multiple files? 'Cause if they are a contributing scientist reports, possibly you could break that up and put them into Contributing Scientist Reports. So you just ask for the single attachment file to include the Final Study Report. For like your Lab Study, for your terminal study GLP, your file, like your Contributing Scientist Report has to be attached to the Final Study Report because of GLP regulations. So I guess my recommendation would be to kind of break it up in a logical manner so that that, not only can you for target animal safety, not only satisfy GLP but also kind of keep it all together as much as possible for the Final Study Report, Contributing Scientist Report, Protocol and still be within the one hundred megabytes.

Second question: "Please let me know what version, including release date of the eSubmitter I am using." I am not a hundred percent sure what version..I think it… I don't, as far as numbers. I know it was the version that was just released on August 15th.

So I will wait for (Second speaker: I have some)…Oh we have some more questions over here. Give me one second.

Alright, next: "Sometimes page numbers in the PDF do not correspond with page numbers in the Final Study Report. Which page numbers does CVM prefer we use for the amendment,

Certificate of Analysis?" My answer would be to provide the pdf page number would be my recommendation, but you are not going to be penalized if you provide the actual physical page number in the Final Study Report, either.

Next question, "Can you please give more detail about what you need to identify the EDC system?" Let me click through and make sure I am going to answer properly. So I am guessing you are talking about 3.6 Identify the EDC System. It would essentially be the name of the EDC system, would be my recommendation.

Oh, the next one is an environmental question.

Second speaker: Going back to the version of the release date. Right now I believe the current version is 1.25 is the current version that we are on right now.

Second speaker: The next question: "Does the environmental P template allow one to say that they are responding to more than one P incomplete letter in a single submission?" Second speaker: Usually it's the most recent incomplete P. Typically, for example, if you had an environmental assessment submitted under P-30, and then you got an incomplete letter there and you're resubmitting, you would just respond, you would just say you are responding to the specific, to the most recent incomplete letter. So you would only have to reference one.

(First speaker) Okay, next one: "What should we mark if we are answering CVM's question in a Q & A attachment?" I'm sorry; I am going to ask a bit of a follow up question: Is that…does that mean the entire P submission is the Q&A? So if you're entire P submission is made up of basically a Q&A document, I would just do…let me click backwards…I would just do Other; Unclassified, which would just bring up the 3.12 section and it essentially you just, it's just essentially just PDF attachments. If you have like a, essentially a Field Study and you have Q&A attached to that field study, I would put that under the Field Study section but under the 3.12 Other Study Related Information. Feel free to ask a follow up if I didn't answer that properly.

I will wait for a couple more, any more questions.

So the question is, a two parter: "If we are providing a response to each CVM question, that we received an incomplete letter, and we have a stand-alone document with each question and its answer, may or may not involve additional attachments. Further, we are asked to say what section of the eSubmitter we are changing in the submission, new report etc., but if we are not changing anything just answering questions, is CVM asked

Okay, let's see, let me click backwards. So I just put up on the screen; I think that is probably how I would move forward. I would choose the appropriate study that you are responding to, if it's Field Study or Lab Study and then you have submitted, you have submitted the study previously, and say yes. And if it's just Q &A, there is no other actual like study, like Final Study Report, Protocol, it's just questions and answers or responses, I would click Other Study Related Information and attach the PDF there.

You're welcome. Any additional questions? And Kristen, did you want to demonstrate through the version number?

Second speaker: Yea, in this morning, you might have seen, I wasn't walking you through when I did this, but you know, this morning, they were talking about the importance of making sure your that eSubmitter is up to date with the latest version, that we will come out with all these updates. If you go to file in your Properties, and then go to the Additional Information, you can find your version your template is you're working on. So it's right here. This information is also at the start up. Also, this information is also at the Start Up, when when when you first open eSubmitter you'll see it initializing and the little blue bar going across the the screen, at that point it will tell you which version you're on. So I think that is where you can probably most figure that out.

First speaker: Okay I will give some time for some more questions to come in.

Okay, I don't see any more questions coming through. We'll hang on for probably like another five minutes and see if anybody has any more questions otherwise we will give everybody an extra hour or so in their day.