V-A-OT Transcript

Hi, my name is Laura Moussa and I'm a reviewer on the Animal Bioengineering and Cellular Therapies (ABCT) Team. I am going to demo how to establish a Type VII Veterinary Master File (VMF) in eSubmitter. Before we get started, I wanted to say that if you have any broad questions (e.g., what type of submissions are needed for your product), then you can send your inquiries to AskCVM@fda.hhs.gov. That will be routed to the appropriate person within the Center. You can also reach out to our project management team. If you have any issues with eSubmitter itself and require technical help, then email CVMeSubmitter@fda.hhs.gov. If you have any questions during the presentation, please put them into the chat box and I will be answering them at the end.

Once you open eSubmitter, to open a new submission, you want to click on the left-hand side of the screen under Menu Options: the button called "Create New Submissions". For traditional products, we have used the "ONADE Submissions" template set. For any product that is designed to go to the ABCT Team, we have our own set of templates. You will need to select the "ONADE Animal Bioengineering and Cellular Therapies Submissions" set of templates. There is a description that shows what types of products are appropriate for these templates. Then you click next, input a descriptive name and a file name, and click "Create".

For this demonstration, we will be working in the eSubmitter test environment because our ABCT templates are still under development. This means that they will not be available on the eSubmitter on your computers after this demonstration. They should be available on October 1, 2018. To access the template, I'm now switching over to our test environment.

On the first screen, you will need to identify the "Document Type" as VMF (V) and you will specify which type of VMF you are opening: research or pre-investigational development. The type of VMF selected does not change the templates or the questions. You will need to identify the product category; there are four checkboxes that you can simultaneously click, but usually only one product category will apply [intentionally genetically altered (IGA) animals, cell-based products (including stem cells), gene therapy products, or other; other products could be combination products, new types of products, or anything that doesn't fit into one of the first three categories]. After you've designated the product category, we ask you to describe the product and to identify whether or not the animal comes from a food-producing species. If you say "Yes", you will be prompted to tell us whether or not the animal or its products is intended to enter the food supply. If you say "No", there is no subsequent question. The final question will ask "Is this submission for a currently established file or application?". Since this submission is to establish file, you will click "No".

The next screens are for administrative information. On Screen 2.0, you are requested to input information about who owns the file, whether it's a US institution, and then contact information. On Screen 3.0, you are requested to identify the Responsible Official and choose their role (institution/company representative or regulatory agent) as well as input contact information for that person. On Screen 4.0, you will input information regarding who is putting the information into eSubmitter, including contact information.

On Screen 5.0, you will select "Original Type VII VMF (A)" as the submission type; it's the only option in the drop-down menu because of what was selected in the first screen. You will select "Other; Unclassified" as the submission classification code. Next you will select the review division; it should be coming into the ABCT Team. The final question is grayed out because the questions is asking whether this submission is intended to amend a

pending submission. Wince you have indicated that this submission is intended to establish the file, no amendments are possible.

In the Original Type VII VMF template, there is an outline of all the screens in the template on the left-hand side. They are currently all activated because I selected all four product categories for demonstration purposes; anything that does not apply to your product will be grayed out. On Screen 1, you will provide a summary of the information provided in the submission. If you click on the notepad icon, then you can see the maximum number of characters allowed in the field. You are also allowed to attach a cover letter; you can see by the absence of the blue dot that a cover letter is not required. It is often helpful for a reviewer to have one though.

Screen 2 is the Referenced File Node. If you're using information that's in another file to support the information in this file, then you will be prompted to input that information here and provide the submission number(s). As you can see in the help text, the information that you input here must begin with a character (V for VMF, I for INAD, or G for General Correspondence) followed by six digits in order to be validated by the system. If you say that there's no information provided in referenced files, then the sub-questions will go away.

Screen 3 is the project summary. You are allowed to include multiple projects under one VMF. This section is divided based on the product type entered on the first screen when we designated the product category. Each product type has its own questions.

For IGA animal projects, you will click the green plus on Screen 3.A and provide the project objectives, a description of the construct, designation of the species and class, a schematic design of the intended genomic change, and a description of the genome editing method(s). There is a catchall "any additional information" question at the end that is optional.

For cell-based projects, you will click the green plus on Screen 3.B and provide the project objectives; product description; unique product ID; designation of the species, class, dose, and route of administration; a description of the donor animals and cell/tissue source; statement of the relationship between the donor and recipient; and the formulation (including the concentration of the drug and excipients). You will designate whether the product is combined with another article; if you answer yes, then you will be prompted to describe the other article(s). If you answer no, then that sub-question goes away. We conclude with the catchall "any additional information" question.

For gene therapy products, you will click the green plus on Screen 3.C and provide the project objectives; product description; unique product ID; statement of the species, class, indication, dose, and route of administration; descriptions of the rDNA construct, the technology, the formulation, and the target cells. You will also describe the assessment of potential shedding of the viral vectors. You will provide information for potential off-target effects (this question is optional). We conclude with the catchall "any additional information" question.

For other products, there are less specific questions. You will click the green plus on Screen 3.D and provide the project objectives; product description; and designation of the species, class, indication, dose, and route of administration (if dose and route of administration are applicable for the product). For each product type, you are able to

view a list of all projects. We conclude with the catchall "any additional information" question.

In Screen 4, you will describe any completed studies (text or file attachments) and state whether you have any studies that utilize client- or producer-owned animals or laboratory animals. If you click "Yes" to either question, then you can see in the template outline that the Study Description section will activate. If you click "No" to both questions, then those questions will gray out. You will certify that the investigational animals will not enter the human or animal food supply by checking the box. If you want to introduce animals into the food supply, that should be done under an INAD Food Use Authorization. We conclude with the catchall "any additional information" question.

If you have selected that there are studies to report, then in Screen 5 you will input the study title and ID and describe the study purpose. You will designate whether the study is proposed or ongoing; if you select "Proposed", then you will be prompted to enter the estimated study start date. Next, you will select the type of model used in the study. For client/producer-owned animals, you should attach the owner consent form(s); for lab animals, that sub-question will go away. Then you will input the study information regarding the species and class, number of animals, the product and product ID, dose, indication (if available), route of administration, and the study design (summarize as text or attach the protocol). We conclude with the catchall "any additional information" question.

In Screen 5.A, you will use the green plus to add information for all investigators involved in the study (name and contact information).

In Screen 5.b, you will state whether any part of the study is contracted out to another organization. If you select "Yes", then the questions for the contact information and description of transferred obligations become required. If you say "No", then they are grayed out.

In Screen 6, you will state whether there are or will be live animals that contain genetic alterations covered by this file. If you select yes, then Screens 6.A and 6.B will activate. If you select no, they will be grayed out.

Screen 6.A requests information about the animal management practices and conditions. You will click the green plus sign to add every facility that is involved with any animal management or shipping. First you will input facility information, including name, contact information. Then you will be asked whether oversight is needed. If you say "Yes", then the type of oversight question will activate; if you select "Other", then a second question will activate asking you to describe it. If you say "No", you will be asked for justification. You will be asked to describe the animal husbandry practices, containment, identification procedures, animal and animal waste disposal, and record keeping. You are able to view a list of all facilities. We conclude with the catchall "any additional information" question.

In Screen 6.B, you will state whether any live animals will be shipped under this file. If you say "Yes", then the sequent questions will activate. If you say "No", then there are no further questions. If you intend to ship animals under the file, you will provide the shipping conditions, transportation recordkeeping procedures, and a copy of the shipping label. We conclude with the catchall "any additional information" question.

In Screen 6.B.1, you will state where animals will be shipped and from whom. You will use the green plus to select the "To" and "From" locations (populated from the list in Screen 6.A) and the estimated number of animals shipped yearly.

Audience question: What is the definition of a regulatory agent?

Answer: A regulatory agent is a person or company that acts on behalf of the file owner. You can designate a regulatory agent by providing us with a letter of authorization for that person or company to act on your behalf.