Demo Transcripts for a Traditional ANADA A/A/OT

Welcome to the webinar for creating a traditional abbreviated new animal drug application (ANADA) in eSubmitter. This webinar will assist you in creating a traditional ANADA approval package in eSubmitter for the Division of Generic Animal Drugs. My name is Jennifer Kodak and I am a Consumer Safety Officer in the Division of Generic Animal Drugs.

Before we get started with the eSubmitter traditional ANADA demonstration there are a few details that have been discussed earlier today in the morning webinar sessions that will not be repeated in this demonstration. This demonstration is recorded and at the end of the demonstration there will be live question and answer session utilizing the chat box in WebEx. Please type your questions in the chat box at any time. If there are questions that are outside the scope of this demonstration, CVM would be happy to address your questions or concerns if you contact us directly.

Before we move to the eSubmitter template tools I would like for everyone to click and view the full screen.

A dummy file has been created to illustrate the eSubmitter template for traditional ANADA applications and does not include any proprietary information.

As mentioned before this webinar will not cover the following pieces of the eSubmitter template already covered in the webinar sessions earlier this morning. Under the CVM ONADE SUBMISSIONS tab sections that include the firm information, us agent information if applicable, responsible official information and submitter information. Along with the descripting in detail the Product Description Information tabs and folders and packaging the complete submission.

Let's start by revisiting how to move between tabs and folders. On the screen to look at each folder you double click. If you want to go between tabs click once and you can also use the arrows in the green circles above to go to next folder or previous folder.

Please note in the bottom right hand corner and throughout the template there are icons that are included such as the light bulb, a display hint or descriptive hint, blue circle indicating a required response and the red exclamation which is a required response but also critical in order to move forward in the template.

Let's take a look at the first folder document information you see appears under the CVM ONADE Submissions tab. You need to select the document type. For the purposes of this demonstration you would select the abbreviated new animal drug application from the drop down menu. The next question is "Is this submission for a currently established file or application?" Because this is a traditional ANADA template you would not have currently established file or application, select no.

Now we move to the Submission Type Selection tab. We know it is an ANADA, so what kind of submission is it? From the drop down select the only option, Original ANADA and that is because you selected ANADA as the document type. Then select the submission classification code from the drop down, the only option is Other; Unclassified (OT). Select the Review Division to which you are submitting this traditional ANADA. The only option available is the Division of Generic Animal Drugs or HFV-170.

The next tab is going to be a more detailed information requirement for an original traditional ANADA. Here in the general information folder under the original ANADA you have a request to attach a pdf document for AGDUFA user fee cover sheet. You can do that by clicking on the plus sign (select a file from your computer or desktop) or you can select from the submission list file manager. In which the process was discussed earlier in the morning. The most critical question here is "Is this an Administrative ANADA?" Because we are demonstrating a traditional ANADA we will select no. What that does is select specific nodes

and information to be highlighted and required to submit in each technical section. “Does the application contain safety or effectiveness data to support a hybrid generic approval?” For the purposes of this demonstration we will select no. If yes, what it does is highlight the ADUFA User Fee Cover Sheet. You will need to attach this cover sheet along with answering “Does the application contain new patents?” and if it does it is asking you to enter the patent numbers below in the memo field if applicable. For the purposes of this demonstration we do not have a hybrid generic approval and will select no. “Does the submission reference other documents (A)NADAs, (J)INADs, master files that contain information that support the application?” For the purposes of this demonstration we will select no. If you select yes, it will highlight 1.1 Associations Applications and Files. Here you will select new to begin your process, asking specific information about your application or file type, the number, what technical sections they support, do you own the associated application or file and attach the right of reference document. For the purposes of this demonstration we selected no. “Is the application requesting approval of generic Type A Medicated Article for use in the manufacture of Type B or C Medicated Feeds?” For the purposes of this demonstration we selected no. But if we select yes, the node under labeling will be activated under Labeling Technical Section for animal feed labeling. Lastly, briefly describe the application**.** This can be done by selecting the memo field and entering the text or click on the notepad and pencil icon to the right and you will get a free form dialog box where you would enter the text.

Next, we need to provide the referenced listed product information such as the document number, proprietary name and established name of the reference listed product.

As mentioned before we will not cover the product description but for the purposes of this demonstration I have selected a dosage form of gel, topical, and provided the common animal name swine.

Now we come to our Technical Sections in support of our ANADA application. For the purposes of this demonstration I selected bioequivalence, chemistry, manufacturing and controls, patent certification and marketing exclusivity, environmental impact, labeling and human food safety because I selected a food producing animal of swine. Once they have been selected, the nodes will be activated for each specific technical section allowing us to provide information as needed. You will notice under each technical section, the request “Do you have a technical section complete letter?” can be found. This is because you can start your approval process under a generic investigation new animal drug file (JINAD) as part of the phase review process and can convert to a traditional ANADA application along with your technical section complete letters. For the purposes of this demonstration we will be selecting no to this question under each technical section and move to the next folder. If you do have a technical section complete letter you would select yes and attach a pdf file.

As part of the bioequivalence technical section we have studies. What data or information are you submitting in support of this bioequivalence technical section. For the purposes of this demonstration we will select Blood Level Bioequivalence study, dissolution study, and analytical methods. Under 3.1.1 Blood level bioequivalence study folder please provide a brief summary of the blood level bioequivalence study data and information in the memo field. Click on the memo field and enter the text. Further provide study reports and copies of raw data in pdf files, you can attach that here. Attach any data files, statistical analysis programs and documentation and summary tables as xml files and/or xpt files. As part of 3.1.5 Dissolution Study, it is asking for the same information that is required but specific to the dissolution study data information. Include all the summary in the memo field and attach any study reports, raw data, data files as xml, xpt and pdf files. Again, with the analytical methods, it looks very similar in that you need to provide a brief summary of your analytical methods data in the memo field below and attach any pdf, xml or xpt documents as an attachment. Now that we are almost done with the bioequivalence technical section, the last folder asks if “You are submitting Freedom of Information (FOI) Summary text?” For the purposes of this demonstration we will select no. But if you did select yes, you can select the memo field and enter the text as needed or include an attachment.

Now we are at the chemistry, manufacturing and controls technical section. For this technical section we have a pre-recording from the Division of Manufacturing Technologies. I will go ahead and get that started.

Good afternoon. My name is Kristen Anderson and I am a reviewer in the Division of Manufacturing Technologies. Today I will be talking to you today about the CMC sections of the ANADA-A template.

To start the submission, you must first indicate if you have a technical section incomplete letter for CMC. If you do not have a technical section complete letter, and are submitting CMC information, you will now move on to Section 1.0 General Information. This set of questions will allow you to select Phase II of a two-phased submission, identify incomplete submissions, or start a traditional ANADA, which could include either the submission of a complete application to support the approval of an abbreviated new animal drug or a response to an incomplete letter received under a JINAD P technical section. Please note that the first two questions on the screen must be answered to provide the correct template. The first question asks if you are submitting a two phased submission. If you select yes to this question, you must select Phase II for the next question. Remember that Phase I may only be submitted under a JINAD P technical section. If you select phased submission, all of the CMC questions will be optional. This will allow you to answer only the questions that remain unanswered from the Phase I submission. For additional information on the submission of two phased submissions, please see Guidance for Industry #227: Two Phased Chemistry, Manufacturing and Controls Technical Sections. The next question asks if the submission references any master files. You should select yes if you have any master files to reference. If you select yes three additional questions will become available asking you to indicate if you have the Type II, Type V, or any other type of master file. Other types of master files would include Type III for packaging or Type IV master files for novel excipients.

Screen 1.1 Submitted Information

The questions that will be available on this next screen will be based on the answers you have provided to the question on the previous screen regarding phased submissions. If you select Phase II submission, the next question that will be available is “Is this in response to a previous CVM technical section incomplete letter?”. As you can see from this screen the only possible response is yes. Remember that the Phase I submission must be submitted under the JINAD as a CMC P technical section. The next option is whether you will be submitting an abbreviated response or a complete QbR response. An abbreviated response means you will only be asked to upload a PDF of the responses to the incomplete items. In most cases an abbreviated response is not an appropriate selection if you are completing Phase II. Once you have selected complete QBR response you will then be asked to select which sections you are updating in response to CVM’s incomplete letter. The possible selections are drug substance, drug product, feed method trial, and sterility. You should select all of the sections that apply. In most cases, the Phase I submission will only include the drug substance information. In this case you should be selecting a minimum of one section to be updated: the drug product. Depending on the dosage form you may also need to select feed method trial or sterility. If you had significant deficiencies in the drug substance information, you may also need to revisit the section of questions to address the incomplete comments. You will notice as the sections are selected additional questions further in the template will become active. Finally, if you respond no to “Are you submitting a two phased submission”, you will then be asked “Is this in response to a previous CVM technical section incomplete letter?”. Unlike the previous set of questions that we have discussed, you have the option to answer either yes or no. If this is the first time you are submitting CMC information, you should select no. You will have three selections available to you: CMC technical section, feed method trial with data only, or CMC technical section including a feed method trial study. You should select the item that corresponds to the dosage form that you are describing. If you answer yes to the question is this in response to a previous CVM technical section

incomplete letter, you will be asked if the complete QbR response will be completed or will an abbreviated response be submitted. If you only have a small number of incomplete comments to address, it may be appropriate to select an abbreviated response and upload the PDF as described above. If you had major deficiencies, or if there have been significant changes in the information submitted previously, the complete QBR response may be a more appropriate selection.

Because I selected yes to each of the types of available master files you can see that a new node has become active for each type of master file. Because the same types of information are required for each of the types of master files I will only describe the information required for the Type II master file table. For each applicable master file, you should select the green + to start a new entry. The first question asks you to select the file type: either VMF or DMF. You should then enter the file number - you do not need to include leading zeros. The next question asks for a brief description of the information covered in this master file. This could include items such as drug substance manufacturing information, analytical controls, sterilization information etc. For Type II master files, the description should include the name of the active pharmaceutical ingredient. The next question asks if you own the master file. If you have a DMF, you must include a letter of authorization regardless of whether you own the master file or not. If you have a VMF, you only need to include a letter of authorization if you do not own the master file. To attach the letter of authorization, press the green + and select the appropriate PDF file. You should repeat these procedures for each applicable master file.

For generic products, Screen 1.5 collects information regarding the reference listed product or RLNAD. You first must enter the (A)NADA document number for the RLNAD. For the proprietary name, be sure that you have included the entire name including copyright, trademark or registered symbols. You may do this by copying and pasting the proprietary name from another document such as a Word document (Proprietary1™). For feed or drinking water combinations, the proprietary names for each drug product and the combination should be included. Next, enter the firm name for the (A)NADA holder. Finally you are asked to identify the RLNAD product established name. Your product established name should match the RLNAD product established name.

The next screen is 2.0 Product Description. The first question asks if the drug product has a USP monograph. The next two pieces of information are the product established name and the proposed proprietary name. For the established name for a new product, you should enter the title of the monograph if one is available. If the drug product does not have a USP monograph, and the drug is already approved, then enter the approved product established name. If this is a new or novel drug product, where a USP monograph does not exist, the drug product established name should follow the USP nomenclature naming convention as described in USP <1121> Nomenclature. As a general rule, the titles for drug product established names shall appear in the following format:

[active moiety] [route of administration] [dosage form]

Remember that for generic products, your product established name should match the RLNAD product established name. If a USP monograph exists, but the RLNAD does not conform to that monograph title, you should use the RLAND established name. In this case, CVM will work with the RLNAD holder to revise the established name to match the USP monograph title. The generic company would then be asked to revise their established name. For the proprietary name, be sure that you have included the entire name including copyright, trademark or registered symbols. You may do this by copying and pasting the proprietary name from another document such as a Word document or by clicking the symbol button on the right hand side. This will allow you to select the appropriate symbol for insertion into your proprietary name. For feed or drinking water combinations, the proprietary names for each drug product and the combination should be included.

Due to the time constraints, the remaining portion of the CMC template will not be covered here. You may reference the recording for the Chemistry, Manufacturing, and Controls 1 session for the JINAD-P-MC template.

After our chemistry, manufacturing and controls technical section comes the patent certification and marketing exclusivity technical section. Here we selected no we do not have a technical section complete letter. Are there any relevant patents for the reference listed product claiming the drug substance, drug product, or method of use? For the purposes of this demonstration we have selected no. It takes me to 3.3.1 in which you need to check the box to certify that no relevant patents exist for the reference listed product claiming the drug substance, drug product, or method of use. The other option is to select yes to the any relevant patents question. Choose Paragraph I certification, then check the box to certify that relevant patents exist, and no patent information has been submitted to FDA. Or select Paragraph II certification, check the box to certify that relevant patents exist and have expired. Or select Paragraph III certification, check the box to certify that relevant patents exist and will expire within 5 years. Or select Paragraph IV, check the box to certify that relevant patents exist and are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the generic new animal drug for which the application is filed. You are making a commitment to provide this patent certification when FDA accepts this ANADA for filing. Let's go back and select no to any relevant patents. Then it comes to the folder 3.3.7 Marketing exclusivity. "Are there any unexpired marketing exclusivities?" If yes, it will highlight the memo field to enter the text indicating what was protected by the marketing exclusivity and the corresponding expiration dates.

Now we come to our environmental technical section. Here we do not have a technical section complete letter. Then we select the type of submission. Claim of categorical exclusion, environmental assessment with original study reports or environmental assessment without original study reports. So, the content on the Environmental Impact technical section screens in the ANADA template will be updated to be consistent with the template that you would fill out when you electronically submit this technical section as a JINAD P-submission. Typically, generic new animal drugs will qualify for a categorical exclusion under 21 CFR 25.33(a)(1), which is for drugs to be marketed under the same conditions of approval as a previously approved animal drug. But there are always exceptions. If you have any questions on how to fill out this portion of the template, you can view the P/NV webinar from this series or contact the Leader of the Environmental Safety Team. On the screen we have chosen claim of categorical exclusion. Once we move forward it wants us to select the specific section of the CFR under which the categorical exclusion is claimed which is 21 CFR 25.33(a) Action does not increase the use of the animal drugs. Then select one of the reasons why you are claiming a categorical exclusion, animal drug to be markete under the same conditions of approval as a previously approved animal drug. Also, briefly describe the drug use, dosage, species and indications that apply to this action. You can do this in the memo field as text. Last, certify to the best of your knowledge are there any extraordinary circumstances associated with the proposed action that may significantly affect the quality of the human environment.

Our next technical section is the labeling technical section. I do not have a technical section complete letter. What type of labeling are you submitting?" Is it final printed labeling-FPL, Facsimile labeling, or Combination of both final printed labeling and facsimile? And "Is the drug used in a Medicated Animal Feed?" For the purposes of this demonstration we selected no. If you selected yes, it will activate the node for labeling technical section under the Animal Feed labeling.

We come to 3.5.2 Other labeling which pertains to your generic labeling you are submitting in support of the technical section. I selected the immediate container labeling and package insert. Along with what reference listed other labeling is included in this submission. I selected the immediate container labeling and package insert. So now once you have determined what labeling components you are submitting, then you will need to attach that labeling. Here it is asking you to attach your immediate container label file. You can attach it by selecting the plus symbol or your submission list file manager. Because I selected package inert I need to attach that package insert file. Similarly, the reference listed product labeling you are to attach the immediate container label file and the package insert for the reference listed product that you selected previously.

Now we come to the human food safety technical section. I do not have a technical section complete letter. Select the type of submission number and select all that apply. For the purposes of this demonstration I have selected residue chemistry because all the nodes for each type of submission have the same questions, but requesting different information for toxicology, residue chemistry and microbial food safety. Briefly describe the residue chemistry data/information being submitted in support of this application. You can that in the memo field as text up to 250 characters or in the pad/pencil free form text dialog box. Provide CVM with residue chemistry data/information that should be attached below as a pdf. Further provide study reports and copies of raw data as pdf files along with any data files, statistical analysis programs and documentation and summary tables as xml files and/or xpt files.

Are you submitting freedom of information summary text? For the purposes of this demonstration we select no.

We have come to our last folder which is comments. If you have additional comments to include in this submission for CVM to review you add them as a single pdf document or type the text in the memo field as appropriate.

Before we finish and package your eSubmitter template, you want to see if your eSubmitter template is complete. There are two ways to determine if your eSubmitter template is complete. One way is to take a look at the folders under each tab. Each folder will have a green check mark that indicates the information is complete in that folder. If there is a folder with a question mark it means that your information is missing and incomplete. Here you can click on the folder and determine what information was missing. The second way would be to go to the top tab output tab at the top, click missing data/validation issues report, select ok in the output dialog. You will receive a missing data/validation issue report. What that does is provide you with the section, the sub section or folder where the information is missing. It tells you exactly where and what is missing. Here it says I didn't check the box to certify that no relevant patents exist. So, let's take a look. I indeed did not check the box. Let's see if we are complete and we are because there is a green check mark on the folder.

Let's go to our chat box and take some questions.

No questions? If you think of any additional questions or issues can be sent to cvmesubmitter@fda.hhs.gov

Thank you all for joining me today.