OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

CREATING AND MAINTAINING A REFERENCE COPY OF THE CURRENTLY APPROVED LABELING FOR AN APPLICATION (VOLUME 0)

I.   PURPOSE

This document establishes the procedures to create and maintain a reference to the currently approved labeling for an application (Volume 0) that is easily accessible within the administrative file. Other documents describe the review process to determine the appropriate content of approved labeling that is referenced in Volume 0 (see P&Ps 1243.6020 and 1243.6030).

II. BACKGROUND

In many applications, it is difficult to determine what is the currently approved labeling. The reasons for this can be many (e.g., the length of time since the original approval, the number of supplemental approvals over time resulting in components of the labeling being submitted at different times and within numerous volumes of information within the application, etc.). Thus, the Office of New Animal Drug Evaluation's (ONADE) business process includes establishment and maintenance of a Volume 0 file for each (abbreviated) new animal drug application ((A)NADA), and veterinary master file (VMF)[1], when applicable, that identifies the currently approved labeling components for that (A)NADA.

III. DESCRIPTION OF VOLUME 0

The Volume 0 is a listing of the submission(s) containing each of the components of the currently approved labeling for the application. Ultimately, a complete Volume 0 contains a reference to all of the labeling components for each approved product within a file.[2] A Volume 0 may consist of both paper and electronic labeling components. If a Volume 0 contains paper copies of labeling (i.e., if it was created prior to July 2011 and no new labeling has been approved since that time), it will be in the administrative record in the Document Control Unit (DCU) and will always be the first volume (Volume 0) in sequence for the application. Paper Volume 0 jackets can be identified by their purple colored

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[1] Although the approval of labeling occurs under an (A)NADA, an entity other than the (A)NADA drug sponsor may maintain ownership of approved labeling that is considered confidential or proprietary (e.g., a proprietary medicated feed formulation). In such cases, the approved labeling is maintained in a VMF that is owned by the VMF holder (e.g., feed manufacturer) while the labeling approval letter is maintained in the (A)NADA that is owned by the sponsor.

[2] It is important to note that reviewers must not presume the Volume 0 is complete and contains up-to-date copies of all labeling components for the approved product. For example, some products (particularly older products) may have additional sizes approved that are not currently marketed and have inadvertently not been added to the Volume 0. Such labels should be added to the Volume 0 when they are identified.

jacket. All Volume 0s created or updated after July 2011 are available electronically on the ONADE Volume 0 SharePoint site.[3]

IV.   PREPARER RESPONSIBILITIES

A. Determine Whether a Volume 0 Exists

All electronic Volume 0 Excel files are stored in a SharePoint folder for that specific file. To determine whether a Volume 0 (electronic or paper) has been created for an approved application, check the Document Overview screen in Submission Tracking and Reporting System (STARS) to see if the Volume 0 indicator is checked. If there is no existing Volume 0 (either paper or electronic) for an approved application, an electronic Volume 0 is created at the subsequent supplemental approval in which the target animal division (TAD) approves a change to the labeling. For new approvals, the TAD creates a Volume 0 at the time of the original approval. Follow this document as necessary to create, or to reference all revisions to, the approved labeling in the electronic Volume 0.

B. Creation of Electronic Volume 0 If No Volume 0 Exists

If a Volume 0 does not exist for an application, follow the steps in this section to create an electronic Volume 0. If a Volume 0 exists, proceed to Section C for instructions to update an existing file. For instructions on adding new electronic Volume 0 files or checking out an existing Volume 0 file for editing, refer to the Volume 0 User Guide posted on SharePoint.

If no electronic Volume 0 has been created, prepare a complete electronic Volume 0 to replace the entire paper Volume 0. If all components of labeling have not been updated in the current submission, you may need to examine the administrative file to identify all the approved components of labeling. For (A)NADAs that are Type A medicated articles, there should also be Type B (if applicable) and Type C medicated feed labeling (e.g., Blue Bird labeling) for each approved use (species/class, dosage/duration, and indication) on the Type A medicated article label. For VMFs with an approved Type A medicated article, there may be Type B and/or Type C medicated feed labeling for each proprietary formulation approved for use with the Type A medicated article.

TAD personnel perform the following steps.

1.   Use the Excel template on the SharePoint to create the electronic Volume 0 file. Save this edited template to your personal network drive using the file name "_Volume 0 (A/N/V)######".

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[3] URL for Volume 0 SharePoint: Internal information redacted.

2.   Complete the Table of Contents (TOC) Sheet.

The first tab in the template contains the TOC. At the top of the sheet, enter the file number, the trade name(s) (i.e., proprietary name(s)), the established name,[4] and the dosage form. For each component of labeling approved for that product, enter the type of labeling (e.g., vial label, package insert) on a separate line. On the next line, enter the name of each specific component of labeling (e.g., 100 mL presentation). For a medicated feed, the heading might be Type C medicated feed and the specific name "Drug X Finishing Swine Feed" (i.e., the name of the Type B or Type C Blue Bird label). If there are multiple components of labeling under a particular heading, enter each name on a separate line. List all components of approved labeling in the TOC, even if updated labeling is not present in the current submission. For labeling components not provided in the current submission, perform a search of the STARS and the paper administrative file located in the DCU to determine the location of the approved labeling.

Column D of the TOC sheet is entitled "**New "Approved by FDA under…" statement added? Mark "Y" if yes or "NA" if not applicable**". Use this column to identify labeling components to which the "Approved by FDA under A/NADA # XXX-XXX" statement has been added. This statement is required on labeling (except representative (Blue Bird) labeling) of approved new animal drugs by Section 502(w)(3)[5] of the Federal Food, Drug and Cosmetic Act (FD&C Act). See the ONADE Office Policy "Addition of Approved by FDA Statements to Labeling of Approved New Animal Drugs and Abbreviated (Generic) New Animal Drugs" for more details. Place a "Y" in column D to the right of each labeling component that has been approved with the statement – including any representative Blue Bird labeling or Veterinary Feed Directives (VFDs) in which a sponsor voluntarily added or updated the statement. If a labeling component is not required to add/update the statement (e.g., Blue Bird labeling, VFDs) and the sponsor did not add/update the statement to these components, place "NA" in the column. For certain labeling components exempted from the requirement per the ONADE Office Policy, place an "NA" in Column D and document the basis for not including the statement on the labeling component in the "Notes" sheet.

3.   Complete the Log of Labeling Component Changes (LLCC) sheet(s)

Complete a LLCC sheet for each labeling component specific to the application. This includes any labeling in the current submission as well as any previously approved labeling components. At the top of the sheet, enter the name of the labeling component. In the table below, enter the submission number for the submission containing the approved labeling and its submission date. If labeling was approved in a reactivation in which the labeling was not resubmitted, use the submission number and submission date for the submission the labeling was submitted under in the "Submission Number" and

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[4] For a VMF Volume 0, the established name should be followed by a description of the drug product (e.g., trade name) approved for use in the proprietary formulation and its associated (A)NADA number (the application under which the approval letter is maintained). For example: "(chlortetracycline Type C free-choice medicated feed); supplied by Aureomycin, NADA 048-761".

[5] 21 U.S.C. 352(w)(3)

"Date Submitted" columns. The "Date Approved/Closed Out" column should then list the approval date and submission number for the reactivation the labeling was approved under (e.g., 03/14/2011 (R-0011)). If completing the LLCC sheet(s) in a VMF Volume 0, then the "date Approved/Closed Out" column should list the approval date and the full (A)NADA submission number under which the approval occurred (e.g., 3/14/2011 (N-123456-G-0123). The "Date Approved/Closed Out" column may contain either the approved date or the file no reply (FNR) date (for final printed labeling (FPL)) as listed in STARS. Under Type, select FPL, Facsimile, or Representative (Blue Bird labels only). Under format, select Paper for any labeling that exists only in paper format or Electronic for both scanned and eSubmitter labeling. Complete with the Date Updated and Responsible Individual (preparer of the Volume 0).

4. Use your judgment on how best to organize the Volume 0 TOC/LLCC file. Strict adherence to the template is not necessary; however, consistency between similar products is desired. If less than all of the approved product's labeling components are used to create Volume 0, indicate this in the Notes section of the template.

5. For VMF Volume 0s, also update the referenced (A)NADA Volume 0.

   If the approval of labeling maintained in a VMF is completed under an (A)NADA, then the TOC of the referenced (A)NADA Volume 0 should reference the VMF number. Follow the instructions in Section D for how to update an existing electronic Volume 0. If one does not already exist, include a new product type entry for proprietary labeling maintained under a VMF at the bottom of the TOC sheet. On the next available line, enter the VMF file number(s) that include approved labeling that reference the (A)NADA.

6. Complete and submit the Volume 0 Notification form located on the SharePoint site to notify DCU that the Volume 0 flag needs to be activated for the file(s).

   After the submission has been closed out, upload the completed electronic Volume 0 file(s) to the appropriate library folder on the Volume 0 SharePoint site. For instructions on how to add new Volume 0 files in SharePoint, refer to the Volume 0 User Guide posted on SharePoint. Delete the template from your personal network drive.

C. Update That Converts a Paper Volume 0 to an Electronic Volume 0

To update an existing paper Volume 0 and convert to an electronic Volume 0 for the application, the preparer performs the following steps.

1. Request the paper Volume 0 jacket for the application.

   If Volume 0 is already out on loan, ask the Records and Information Management (RIM) Team to assist you in locating it. If there are multiple pending submissions requiring Volume 0, then coordinate the competing needs for Volume 0 during the final action and clearance process for the submissions containing labeling.

2. Use the provided Microsoft Excel template located on the SharePoint site to create the electronic Volume 0 file. Save this edited template to your personal network drive using the file name "_Volume 0 (A/N)######".

3. Complete the TOC Sheet.

   The first tab in the template contains the TOC. At the top of the sheet, enter the file number, the trade name(s) (i.e., proprietary name(s)), the established name, and the dosage form. For each component of labeling approved for that product, enter the type of labeling (e.g., vial label, package insert) on a separate line. On the next line, enter the name of each specific component of labeling (e.g., 100 mL presentation). For a medicated feed, the heading might be Type C medicated feed and the specific name "Drug X Finishing Swine Feed" (i.e., the name of the Blue Bird label). If there are multiple components of labeling under a particular heading, enter each name on a separate line. List all components of approved labeling in the TOC, even if updated labeling is not present in the current submission. For labeling components not provided in the current submission, search STARS and the paper administrative file located in the DCU to determine the location of the approved labeling.

   Column D of the TOC sheet is entitled "**New "Approved by FDA under…" statement added? Mark "Y" if yes or "NA" if not applicable**". Use this column to identify labeling components to which the "Approved by FDA under A/NADA # XXX-XXX" statement has been added. This statement is required on animal drug labeling (except representative (Blue Bird) labeling) of approved new animal drugs by Section 502(w)(3)[6] of the FD&C Act. See the ONADE Office Policy "Addition of Approved by FDA Statements to Labeling of Approved New Animal Drugs and Abbreviated (Generic) New Animal Drugs" for more details on this requirement. Place a "Y" in column D to the right of each labeling component that has been approved with the statement – including any representative Blue Bird labeling or VFDs in which a sponsor voluntarily added or updated the statement. If a labeling component is not required to add/update the statement (e.g., Blue Bird labeling, VFDs) and the sponsor did not add/update the statement to these components, place "NA" in the column. For certain labeling components exempted from the requirement per the ONADE Office Policy, place an "NA" in Column D and document the basis for not including the statement on the labeling component in the "Notes" sheet.

4. Complete the LLCC sheet(s)

   Complete a LLCC sheet for each labeling component specific to the application. This includes any labeling in the current submission as well as any previously approved labeling components. At the top of the sheet, enter the name of the labeling component. In the table below, enter the submission number for the submission containing the approved labeling and its submission date. If labeling was approved in a reactivation in which the labeling was not resubmitted, use the submission number and submission date for the submission the labeling was submitted under in the "Submission Number" and "Date Submitted" columns. The "Date Approved/Closed Out" column should then list the approval

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[6] 21 U.S.C. 352(w)(3)

date and submission number for the reactivation the labeling was approved under (e.g., 03/14/2011 (R-0011)). If completing the LLCC sheet(s) in a VMF Volume 0, then the "Date Approved/Closed Out" column should list the approval date and full (A)NADA submission number under which the approval occurred (e.g., 3/14/2011 (N-123456-G0123). The "Date Approved/Closed Out" column may contain either the approved date or the FNR date (for FPL) as listed in STARS. Under Type, select FPL, Facsimile, or Representative (Blue Bird labels only). Under format, select Paper for any labeling that exists only in paper format or Electronic for both scanned and eSubmitter labeling. Complete with the Date Updated and Responsible Individual (preparer of the Volume 0).

5. Use your judgment on how best to organize the Volume 0 TOC/LLCC file. Strict adherence to the template is not necessary; however, consistency between similar products is desired. If less than all of the approved product's labeling components are used to create Volume 0, indicate this in the Notes section of the template.

6. For VMF Volume 0s, also confirm that the VMF number is identified in the TOC of the referenced (A)NADA Volume 0.

    If the VMF number is not included, then the (A)NADA Volume 0 should be checked out and saved to your network drive using the existing file name ("_Volume 0 (A/N)######") (see section D for additional instruction on updating an existing electronic Volume 0). If necessary, update the TOC of the (A)NADA Volume 0 by including a new product type entry for the proprietary labeling maintained under a VMF at the bottom of the TOC sheet. Under the appropriate product type, enter the VMF file number(s) that include approved labeling associated with the (A)NADA on the next available line.

7. Update paper LLCC documents.

    As paper labeling is replaced with electronic versions, the preparer adds a note on the paper LLCC documents located in the paper Volume 0. Mark through any remaining open lines on each LLCC document and add the note "Future updates located in electronic Volume 0".

8. Ensure the outdated labeling components are destroyed

    Only paper labeling not currently available in an electronic format resides in the Volume 0. Paper versions of labeling components are destroyed as updated electronic versions are received. The preparer collects and binds the outdated labeling components replaced by the current approval, marks them as outdated, and attaches them to the front of the jacket with a completed Volume 0 Notification form so that DCU knows which documents to destroy. Return the paper jacket when you are notified that the approval package has been signed.

9. Close out the submission following Office policies

    After the submission has been closed out, upload the Volume 0 spreadsheet(s) to the appropriate library folder on the Volume 0 SharePoint site. For instructions on how to add new Volume 0 files in SharePoint, refer to the

Volume 0 user guide posted on the SharePoint site. Delete the template from your personal network drive after the submission is closed out.

D. Update an Existing Electronic Volume 0

To update the existing electronic Volume 0 for the application, the preparer performs the following steps.

1. Locate the Volume 0 spreadsheet file for the application or VMF located on the SharePoint site. Check out the file and save it to your personal network drive using the existing file name ("_Volume 0 (A/N)######"). For instructions on how to check out existing files in SharePoint, refer to the Volume 0 user guide posted on the SharePoint site.

2. Update the electronic LLCC sheet for each labeling component revised or create new a LLCC sheet(s) for any new labeling component(s) added in the current approval submission. Do not delete any entries in the existing LLCC sheets. Move to the next line in the sheet to add the updated labeling information.

3. Update the TOC if necessary.

   If not already added, insert a new "column D" to the TOC page entitled "New "Approved by FDA under…" statement added? Mark "Y" if yes or "NA" if not applicable". Be sure to "wrap text" so that the entire title is visible and add the bold lower border. Use this column to identify labeling components to which the "Approved by FDA under A/NADA # XXX-XXX" statement has been added. This statement is required on labeling (except representative (Blue Bird) labeling) of approved new animal drugs by Section 502(w)(3)[7] of the FD&C Act. See the ONADE Office Policy "Addition of Approved by FDA Statements to Labeling of Approved New Animal Drugs and Abbreviated (Generic) New Animal Drugs" for more details on this requirement. Place a "Y" in column D to the right of each labeling component in the submission that has been approved with the statement – including any Blue Bird labeling or VFDs in which a sponsor voluntarily added or updated the statement. If a labeling component is not required to add/update the statement (e.g., Blue Bird labeling, VFDs) and the sponsor did not add/update the statement to these components, place "NA" in the column. For certain labeling components exempted from the requirement per the ONADE Office Policy, place an "NA" in Column D and document the basis for not including the statement on the labeling component in the "Notes" sheet.

4. For VMF Volume 0s, also confirm that the VMF number is identified in the TOC of the referenced (A)NADA Volume 0.

   If the VMF number is not included, then the (A)NADA Volume 0 should also be checked out and saved to your network drive using the existing file name ({_Volume 0 (A/N)######"). If necessary, update the TOC of the (A)NADA Volume 0 by including a new product type entry for proprietary labeling maintained under a VMF at the bottom of the TOC sheet. Under the appropriate

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[7] 21 U.S.C. 352(w)(3)

product type, enter the VMF file number(s) that include approved labeling associated with the (A)NADA on the next available line.

5. Close out the submission following Office policies

   Upload the updated electronic Volume 0 file(s) to the Volume 0 SharePoint site and check it back in. For instructions on how to check in the existing file in SharePoint, refer to the Volume 0 user guide posted on the SharePoint site. Delete the file from your personal network drive after the submission is closed out.

V. REFERENCES

CVM Program Policy and Procedures Manual – ONADE Reviewer's Chapter

1243.3800 – Reviewing, Preparing, and Routing Approval Packages for Certain Abbreviated and New Animal Drug Applications

1243.6020 - Review of New Animal Drug Application and Abbreviated New Animal Drug Application Labeling Supplements (NL Subclass)

1243.6030 - Review of Labeling Changes in Manufacturing Supplements

ONADE Office Policy Page

Addition of Approved by FDA Statements to Labeling of Approved New Animal Drugs and Abbreviated (Generic) New Animal Drugs

VI. VERSION HISTORY

August 23, 2007 – Original version

October 7, 2011 – Updated to remove all references to paper copies of labeling and update for electronic labeling procedures.

February 10, 2012 – Updated to incorporate the Volume 0 Notification form.

April 8, 2014 – Updated to include the SharePoint site and remove references to the ONADE Records network drive.

July 8, 2016 – minor formatting revisions and redaction of internal information for the FDA.gov version.

April 4, 2019 – Updated to remove information about updating the Volume 0 tracking sheet on SharePoint site, because we are no longer doing that and add instructions for completing Column D of the electronic Volume 0 TOC sheet.

June 29, 2020 - Updated all internal links for SharePoint sites because FDA has migrated this information to a new version of SharePoint.

January 26, 2022 – Quality system review conducted of the document and no updates or revisions were necessary at this time.

July 15, 2022 – Quality systems review for minor formatting updates.

September 30, 2023 - Sections IV.B.2, C.3, and D.3 updated for changes associated with the law requiring the "Approved by FDA" labeling statement taking effect. To bring all office quality system documentation into compliance with the FDA Visual Identity Program approved fonts, ONADE has adopted Arial 11-point font. The font of this document was changed from Verdana 10-point font to Arial 11-point font.

September 11, 2024 – Updated the document to include information on the creation of a Volume 0 for VMFs and for identifying the VMF number in a referenced (A)NADA Volume 0.