OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

REVIEWING, PREPARING AND ROUTING APPROVAL PACKAGES FOR CERTAIN ABBREVIATED AND NEW ANIMAL DRUG APPLICATIONS

I. PURPOSE

This documents how to review, prepare, and route approval packages for:

- original new animal drug applications (NADAs);
- original abbreviated new animal drug applications (ANADAs);
- conditional new animal drug applications (CNADAs);
- B1 supplemental (A)NADAs;[1] and
- ANADA non-fee (NF) supplements, except for proprietary name change NFs.

The processes for preparing approval packages for other supplements (NF, non-fee labeling (NL), and manufacturing supplements[2]) are described in other P&Ps.[3]

II. PROCESS OVERVIEW

(A)NADAs are classified as either administrative or non-administrative; the process to prepare an approval package is similar for both. When CVM receives an (A)NADA that results in an original or supplemental approval, the division assigned the application is responsible for preparing the approval package. Applications are assigned to either the division responsible for review of the Target Animal Safety and Effectiveness sections or the Division of Generic Animal Drugs. The division assigns the application to the person(s) responsible for preparing and reviewing the approval package. The approval

[1] B1 supplemental ANADAs are rare.
[2] Manufacturing (Chemistry, Manufacturing and Controls (CMC)) supplemental approvals are prepared by the Division of Manufacturing Technologies (DMT) and approved at the division level.
[3] For more information, see P&Ps 1243.6020 and 1243.6030 for supplements and the applicable P&Ps/templates for preparing NL approval packages; and P&P 1243.6040 for information on NF supplements.

package replaces the standard "final action package" for most Submission Tracking and Reporting System (STARS) submissions.

Designated division personnel perform the initial review needed to determine that the application is approvable (described in section III). Division personnel then prepare the documents for the approval package (described in section IV), route the draft and final packages (described in sections V and VI, respectively) and follow the post-approval steps (described in sections VII, VIII, and IX).[4]

III. INITIAL STEPS IN REVIEWING THE (A)NADA SUBMISSION

A. Ensure the Accuracy of STARS

Administrative and non-administrative (A)NADAs have different STARS due dates. If the preparer determines that the sponsor chose the wrong type of application, use the "Review Time Change" workflow in Appian to change the due date (per the Appian User Guide).

If an application has been received in paper and accepted and there are other errors in the coding (e.g., OT subclass vs. B1 subclass), send an email to the EDSR Mailbox.[5] The subject of the email should be STARS Correction Request and request the paper submission be recoded. (For information on voiding submissions, see P&P 1243.3011. For information on handling paper submissions, see P&P 1243.3002.) The ONADE Business Informatics Team manages the mailbox. When the change in STARS has been made, the requestor will get a notification email from the EDSR Mailbox.

B. Technical Section (TS) Verification

Prior to final approval of the application, verify that the previously issued TS complete (TSC) letters are still valid.

C. Review of the Application

Review the application to ensure that it, as a whole, meets the requirements for approval in the Federal Food, Drug, and Cosmetic Act (FD&C Act) and applicable regulations. For information on refuse to file, see P&Ps 1243.2050 and 1243.3100.

1. The application should include:[6]

    - a copy of each TSC letter or memorandum of conference from a pre-submission conference documenting what TS(s) are considered complete;
    - information to address any TS that is not considered complete (non-administrative (A)NADAs only);
    - complete facsimile or electronic final printed labeling; and

[4] For purposes of this document, designated division personnel refers to a reviewer, consumer safety officer, or other individual from the division responsible for preparing and reviewing the application approval package.

[5] Internal information redacted.

[6] In addition to these items, paper applications should also include a cover letter, a signed FDA Form 356V, a table of contents, and a summary.

- CVM acknowledgement letter for the FOI Summary (administrative (A)NADAs only),

2. If an administrative (A)NADA contains minor errors or is missing one of the above components, CVM may request an amendment. See Appendix 1 for information about processing deficient administrative (A)NADAs. For non-administrative (A)NADAs, request amendments as needed per P&P 1243.3026.

3. If needed, send consulting review requests within the appropriate timeframe for the application (per P&P 1243.3200).

4. Sponsors are required by law to submit patent information for NADAs as part of the application.[7] As part of the review, confirm that patent information has been submitted or that the sponsor has provided a statement that no patents exist. If necessary, contact the sponsor to request they provide an amendment with either the patent information or a statement that there is no patent information to include with the application.

5. Section 502(w)(3)[8] of the FD&C Act requires the statement "Approved by FDA under NADA # XXX-XXX" or "Approved by FDA under ANADA # XXX-XXX" to be included on labeling (except representative (Blue Bird) labeling) of approved new animal drugs and generic new animal drugs, respectively, or else the drug will be considered misbranded. We encourage sponsors to add the statement to Blue Bird labeling, but this is voluntary on their part. Refer to the ONADE Policy "Addition of Approved by FDA Statements to Labeling of Approved New Animal Drugs and Abbreviated (Generic) New Animal Drugs" (on the ONADE Policy SharePoint) for additional information. If any labeling components in the application, other than Blue Bird labeling, Veterinary Feed Directives (VFDs), or exemptions identified in the ONADE Policy do not include the applicable labeling statement, the application must be amended with updated labeling including the statement before the application can be approved.

6. For administrative (A)NADAs, we generally do not prepare a review or a submission summary; instead, document that the application is approvable in the Memorandum Recommending Approval (MRA), per P&P 1243.5741. To document relevant information too extensive to be described in the MRA (e.g., sponsor emails or clarification of information in the application), prepare a brief review document (e.g., review, submission summary, or memo to file (MTF)) per P&P 1243.3009 and the applicable ONADE template. For non-administrative (A)NADAs, prepare a review per P&P 1243.3009 and the ONADE template.

7. If the application is a non-administrative NADA[9] and it

   1) is for use in a food-producing animal and

[7] Under FD&C Act, section 512(b)(1), sponsors are required to submit this information. Under section 512(d)(1)(G), we cannot approve a NADA if the application fails to contain the patent information prescribed by section 512(b)(1).
[8] 21 U.S.C. 352(w)(3)
[9] For administrative NADAs, the antimicrobial email alert is sent by the project manager during the end game.

2) contains either an antimicrobial drug (regardless of medical importance)[10] or a drug intended as an alternative to traditional antimicrobials,

prepare the antimicrobial email alert using the ONADE Antimicrobial Alert email template and send it to the ONADE Director (OD) and Deputy OD[11] within 30 days of receipt of the application. A copy of the email is not included in the approval package.

IV. PREPARING THE DRAFT APPROVAL PACKAGE

A. Request the Draft FEDERAL REGISTER (FR) Documents

If the approval requires a change/addition to the regulations, complete the ONADE "Request for Federal Register Notice" email template and send it to the Policy and Regulations Staff (PRS, HFV-6). Attach the following documents to the email:

- draft MRA or draft Freedom of Information (FOI) Summary, and
- labeling, or other informative labeling (e.g., representative Type C (Bluebird) labeling).

The PRS will provide a draft FR document to the preparer by email with entries for inclusion in the quarterly final rule for application-associated actions. The response will include:

- preamble text containing basic approval information (file number, sponsor name and address, product name, conditions of use, other approval actions (e.g., establishment or change of a tolerance), and CFR sections affected) in a tabular format for incorporation into the table in the preamble of the final rule, and
- regulatory text (containing authority citations and amendatory instructions for the CFR sections affected), and
- the pre- and post-change versions of the affected regulations.

NOTE: The pre- and post-change regulation may not be needed for certain approvals (e.g., for first codification of a product, changes to tolerances, or labeling of medicated feeds). Discuss these situations with PRS as they arise.

Both the PRS and ONADE reviewer will check all parts of the draft FR package to ensure the information is accurate and complete (e.g., that it also includes changes to the sections related to tolerances and combination medicated feeds, if applicable).

For NADA approvals intended for use in food-producing species, email the marked-up copy of the draft FR document to the Division of Human Food Safety (DHFS) for comment.[12] When all comments have been received on the draft FR package, work with the CVM Policy and Regulations Team to make any revisions. Convert the email from DHFS into a PDF and include it in the approval package.

[10] Except ionophores. It is not necessary to notify the ONADE Office Director prior to approval of ionophores.
[11] Also include the HFV-157 TL, the TAD reviewer's TL, the TAD reviewer's DD, and the project manager in the cc: line.
[12] May also be required for certain ANADAs. Consult your team leader for additional information.

B. Obtain the Environmental Documents

If a categorical exclusion (CE) was granted for the (A)NADA, then there are no environmental documents. If a CE was not granted, then the approval package contains the Finding of No Significant Impact (FONSI) and Environmental Assessment (EA). If the approval package contains an EA and FONSI, the preparer notifies the Environmental Safety Team (EST) team leader (TL) and requests that they confirm the environmental documents still support the approval. Document the EST's confirmation in the MRA. If confirmation from EST is required, include a PDF copy of the confirmation email in the approval package.

In the MRA, document the location of the environmental safety reviews, TS complete letters (if applicable), environmental safety information in the end-game meeting memo (if applicable), any other environmental safety review documents (e.g., FONSI), and the confirmation email. Refer to the MRA template for details.

Include the electronic files for the signed EA and FONSI in the approval package (they are uploaded into Appian). The original signed EA and FONSI, which is used to support the approval, can be found in the investigational new animal drug (INAD) file (generally with the Environmental Impact TS complete letter). On rare occasions, an Environmental Impact Statement (EIS) and Record of Decision (ROD) may replace the EA and FONSI. For the approval package, the procedures are the same for EIS and ROD as for the EA and FONSI.

C. Request a Good Manufacturing Practices (cGMP) Status Check, if Needed

GMP status checks are required for original and supplemental (A)NADAs except for Animal Drug Availability Act (ADAA) feed combination NADAs and medicated feed combination ANADAs (see P&P 1243.8500). Use Appian to request a consult from the relevant team in DMT (per P&P 1243.3200). For all (A)NADAs, initiate the cGMP Status Check immediately when beginning to assemble the approval package for all applications. For non-administrative (A)NADAs, a status check may not be required if a CMC consult is requested for that submission. If the package will be approved within 60 days of the return of a CMC consulting review containing GMP status check results, a new status check does not need to be requested.

D. Request a Bioresearch Monitoring (BIMO) Status Check

BIMO status checks are required for original and supplemental (A)NADAs except for ADAA feed combination NADAs (see P&P 1243.8220) and ANADAs granted a waiver from the requirement to conduct *in vivo* bioequivalence studies. Use the BIMO Status Check Form on the ONADE Forms SharePoint to request the BIMO status check. Convert the email and inspectional report into a PDF and include it in the approval package. If multiple PDFs are included as part of the BIMO status check, combine them into a single PDF before including it in the draft approval package.

E. Perform a Drug Experience Report (DER) Status Check

DER status checks are required for original ANADAs, supplemental (A)NADAs, and original and supplemental ADAA feed combination NADAs. DER status checks are not required for original NADAs. For ANADAs, the primary reviewer (PR) does a DER

status check of the reference listed new animal drug to determine marketing status. Both procedures below are acceptable to perform the DER status check.[13]

1. Email the Marketed Product Information Team (HFV-244) TL to request a DER status check. Include the (A)NADA number, proprietary and drug product established names, and, for supplemental approvals, the effect of the supplement. Request that the status check be completed within five (5) days.

2. Print a DER History report from the Corporate Database Portal DER module. Conduct an initial review of the report (per 1243.130.002). If there are concerns, check with the Division of Veterinary Product Safety (HFV-240), Office of Surveillance and Compliance (OSC) for input.

Perform the DER status check just prior to forwarding the draft package. Convert the DER status check email or history report to a PDF for inclusion in the package.

F. Prepare and Send the Notice of Pending Approval Email

Any original or supplemental (A)NADA approval with a letter signed by the Center Director (CD) is a possible candidate for media interest. Prepare a notification email using the "Notice of Pending Approval for (A)NADA" email template on the ONADE Templates SharePoint. The email is sent to HFV-6 and the Strategic Communication Staff. The email includes instructions for HFV-6 to verify that there are no pending citizen petitions that could impact the approval. The notification email is not needed for supplemental NADA approvals signed by the Office Director (OD). For example, an HFV-6 citizen petition check is not performed for NADA packages signed by the OD. It is needed for supplemental ANADA NF approvals signed by the OD. HFV-6 provides a response regarding citizen petitions. The preparer includes the response from HFV-6 in the approval package. The Strategic Communication Staff will contact the PR to let them know whether or not external communication is required. The email the Strategic Communication Staff sends the PR is not included in the approval package.

G. Prepare the MRA

The MRA briefs the individual signing the approval (i.e., the CD or OD) on the basis for our recommendation to approve an (A)NADA. Prepare an MRA for all original and supplemental (A)NADAs per P&P 1243.5741 and the appropriate ONADE template.

H. Prepare the FOI Summary

The FOI Summary summarizes the data and information used as a basis for the approval (e.g., safety and effectiveness data, bioequivalence studies). Use P&P 1243.5761 (NADA) or 1243.5762 (ADAA Feed Combination Drug NADA) and the appropriate ONADE template.

I. Prepare the Approval Letter

Use the ONADE Approval Letter template appropriate for the type of (A)NADA application. Follow the format described in P&Ps 1243.3010 and 1243.5820.

[13] Check with your TL or division director on the appropriate DER status check procedure to use.

J. Prepare or Update the Volume 0

Use the instructions in P&P 1243.3810 for the preparation or update of Volume 0.

K. Prepare the Green Book and Animal Drugs (GBAAD) Form

Use P&Ps 1243.3801 and 1243.3900 and the GBAAD form to provide information on the approval that will be included in the Green Book and Animal Drugs@FDA (ADAFDA).

If the application contains labeling with OSC-initiated labeling changes, use the OSC-Initiated Labeling Changes email template to email OSC and request they provide the language that should be included in the GBAAD form for the Green Book Monthly Update. Include the email response from OSC in the approval package. See P&P 1243.3801 for additional information.

L. Prepare the OSC Notification Email for Approvals with a Tolerance Change

If there is a tolerance change as a result of an approval, prepare an email to OSC using P&P 1243.3760 and the ONADE Drug Tolerance Notification email template.

M. Ensure Section 508 Compliance

All documents are prepared in compliance with Rehabilitation Act (29 U.S.C. 794d), Section 508 as amended by the Workforce Investment Act of 1998 (P.L. 105-220). However, only the FOI Summary created by CVM for public display must be checked for Section 508 compliance prior to moving the draft package forward.[14] Information is provided on the ONADE Reviewer Reference SharePoint to assist in the creation of Section-508-compliant Word documents.

N. Complete the Review Summary Field in STARS

Complete the Review Summary field in STARS with a short description of the approval during preparation of the draft approval package.

For example:

Original approval for <Proprietary Name®> (<drug product established name>) for <indications and conditions of use> in <species/class.>

For ANADAs, also include reference product information:

This reference listed new animal drug is <Proprietary Name®> (<drug product established name>) sponsored by <applicant's name> under (A)NADA <XXX-XXX>.

O. Ensure the Accuracy of the Document Overview Section in STARS

Confirm the information in the Document Overview section of STARS is complete for the application. This includes ensuring the accuracy of the document overview, chemical name, and species information. In addition, any generic investigational new animal drug file (JINAD), INAD, (A)NADA, or veterinary medical file (VMF) that the

[14] If an EA and FONSI are part of an approval package, they are also made publicly available. The BI Team checks the FONSI for Section 508 compliance prior to uploading it for public display. CVM does not check the EA for Section 508 compliance because it is a sponsor-created (not CVM-created) document.

application relies upon or otherwise references should be listed in either the Referenced Documents and Pioneer Documents sections, as appropriate (e.g., a generic new animal drug will identify a reference listed new animal drug (RLNAD); an ADAA feed combination NADA combination will identify one or more previously approved NADAs). If information is missing or inaccurate and the primary reviewer does not have STARS editing privileges, then an email requesting a STARS Correction should be sent to the EDSR Mailbox.[15]

V. ASSEMBLING AND ROUTING THE APPROVAL PACKAGE FOR FIRST-PASS REVIEW

Create an electronic folder in your team's/division's designated location and name it with the (A)NADA code and number (e.g., N123456). Create a subfolder in this folder named with the submission code and number (e.g., C1234). In that subfolder, create two folders named "Folder A" and "Folder B"; add the document listed below in each folder. Note: not all documents are required for all approvals.

Folder A contains a copy of:

- draft MRA;
- draft FOI Summary;
- draft approval letter for applicant;
- draft FR documents;
- GBAAD form; and
- EA and FONSI or EIS and ROD, if applicable

Folder B contains a copy of:

- final primary reviews for the current submission (generally non-administrative (A)NADAs only)[16]
- other pertinent information (e.g., MTF, copies of sponsor emails);
- BIMO status check PDF;
- DER status check email or DER history report (as a PDF);
- email from DHFS documenting their email review of the draft FR document (if applicable) or applicable non-administrative (A)NADA documents;
- email from the EST documenting review of the environmental documents (if applicable);

[15] Internal information redacted.

[16] Do not include copies of any referenced documents that were not created as part of the current (A)NADA application review and approval. For example., do not include copies of TS complete letters, reviews associated with previously completed TSs, FOI Summaries, or FR notices for previous approvals. This also applies to reactivations. Reviews from completed submissions are archived in CDMS where the QA Team can access them.

- email sent to OSC (if a new tolerance will be approved);
- email response from OSC (if there are OSC-initiated labeling changes);
- email from HFV-6 confirming that there are no pending citizen petitions (for packages signed by the CD).

In addition to Folders A and B, the main application folder contains a copy of:

- draft Volume 0 Excel sheet; and
- Appian consult return notification email(s) (if applicable) to allow the QA Team access to the consulting reviews for the current submission.

Follow your appropriate team or division procedures for the supervisory review of the draft approval package. Note: This is done outside of Appian and Appian sign-off is NOT initiated during the review of the draft approval package. We use informal methods (e.g., email) to notify the next person in the chain that the draft approval package is ready. The review chain for the draft approval package may look like this.

1. The PR or consumer safety officer reviews the package for accuracy and completeness of the information and consistency with current laws and policies and notifies the TL.
2. The TL reviews the package for accuracy and completeness and notifies the DD.
3. The DD confirms the accuracy and completeness of the package and notifies the preparer.
4. If errors are found during review at the reviewer, team, or division level, the appropriate person is notified for correction.

For non-administrative (A)NADAs for approvals in food-producing animals, the DHFS reviews the pertinent parts of the draft package before it moves to the QA Team. If the ANADA is granted a bioequivalence waiver, this step is not required. The target animal division (TAD) makes any needed changes before forwarding the package to QA for review. Convert the email documenting DHFS review/concurrence into a PDF and include it in Folder B.

When the draft package is ready for a quality control review by the QA Team, add the documents to the S: drive WORKAREA QA Team Approval Packages Draft Folder and send a consult request to the QA Team notify them that the draft package is ready for review (per P&P 1243.3210).

VI. ASSEMBLING AND ROUTING THE APPROVAL PACKAGE FOR FINAL CLEARANCE

The final approval package is electronic and consists of the documents described above (Folder A and Folder B).

1. When the QA Team has verified that the final package is acceptable, they return the consult in Appian. The TAD notifies the division personnel responsible for checking Section 508 compliance that the FOI summary is ready for review per division procedures.

2. Once a Section-508-compliant PDF of the FOI Summary is created, the TAD reviewer forwards the electronic approval package through the appropriate team or division supervisory chain (i.e., PR, TL, and DD) following division procedures, and then initiates sign-off in Appian.

3. Choose the relevant final action code in Appian from Table 1.

Table 1: Final action codes for approval packages covered in this P&P

Application type	**Doc and sub code**	**Final action code in Appian**
NADA - original approval	NADA A and E	(ORG APP LD) ORIGINAL APPLICATION APPROVED DATE OF LETTER; LETTER SENT
NADA - B1 supplemental approval	NADA C and R (subclass B1)	(SUP SIG LD) SIGNIFICANT SUPPLEMENT APPROVED DATE OF LETTER; LETTER SENT
NADA – conditional approval	NADA A	(ORG APP LD) ORIGINAL APPLICATION APPROVED DATE OF LETTER; LETTER SENT
ANADA - original approval	ANADA A and E	(ORG APP LD) ORIGINAL APPLICATION APPROVED DATE OF LETTER; LETTER SENT
ANADA – B1 supplemental approval	ANADA C and R (subclass B1)	(SUP SIG LD) SIGNIFICANT SUPPLEMENT APPROVED DATE OF LETTER; LETTER SENT
ANADA – NF supplemental approval	ANADA C and R (subclass NF)	(SUP MIN LD) MINOR SUPPLEMENT APPROVED DATE OF LETTER; LETTER SENT

4. Build the Appian sign-off according to the longest chain needed for your package. Use Table 2 as a guide for the signatures needed for each document in the approval package. As described above, the actual documents and signatures required for each package may vary.

Table 2: Signature reference for the approval package components

Document	PR	TL	DD	DHFS	QA	OD	CD
MRA	Y	Y	Y	N	Y	*	N
FOI Summary	Y	Y	Y	Y for non admin (A)NADA for food animal	Y	Y	*
Approval letter	Y	Y	Y	N	Y	Y	*
Draft FR documents	Y	Y	Y	N	Y	Y	*
GBAAD form	Y	Y	N	N	N	N	N
Primary reviews	Y	**	**	N	N	N	N

Y means yes and N means no
* means yes if CD is the signature authority for the letter
** means yes if required by division procedures

When including documents in Appian, select “Yes” to the question “Should file be sent to the firm?” for the approval letter and the FOI Summary. The remaining documents do not require signature, but if they are part of the approval package, upload them into Appian with the above documents to get them correctly archived into FDA’s record. These documents include:

- a copy of the EA/FONSI or EIS/ROD; and
- other pertinent information (e.g., MTGs, sponsor emails).

Save the following documents as PDFs and designate them as “other review related files” when they are uploaded into Appian:

- email from DHFS documenting review of FR notice or other applicable documents in non-administrative (A)NADAs;
- email confirmations from the EST, if applicable;
- email sent to OSC, if a new tolerance will be approved;
- email from OSC, if there are OSC-initiated labeling changes; and
- email from HFV-6 confirming that there are no pending citizen petitions

The following PDFs should be designated as “Status Check (BIMO, DER)” when they are uploaded into Appian:

- BIMO status check document; and
- DER status check email or DER history report

The following documents, although they were prepared as part of the approval package process, are NOT uploaded in Appian:

- draft Volume 0 Excel sheet; and
- Appian consult returns notification email(s) (if applicable).

VII. FINALIZING APPROVAL PACKAGES

A. Appian Sign-Off

It is the PR's responsibility to ensure that the correct personnel are available and entered into the Appian concurrence chain and that the package moves through Appian for concurrences in a timely manner. The PR initiates communication with the appropriate individuals if the package is stalled.

B. Who Signs Approval Packages if the OD or CD is Out?

1. Who Signs When the ONADE OD is Out?

   - If the ONADE OD is out, either the Deputy OD or the Senior Science Advisor may sign the approval package.

   - If the ONADE OD, Deputy OD, and Senior Science Advisor are out, the acting OD (as designated by the OD's email) will sign.

2. Who Signs When the CD is Out?

   - When the PR selects HFV-001 in the Appian clearance chain, Appian automatically sends the approval package to the Appian queues of the CD, Deputy CD and Deputy CD for Science Policy. Any of these individuals will pick up the task and sign-off on the approval based upon their availability.

C. Document Control Unit (DCU)/Business Informatics (BI) Team

When the DCU receives the completed and signed approval package, they mail the letter and enclosures to the applicant for packages received in paper, if applicable.[17] The BI Team updates STARS as appropriate when the approval is finalized, as part of the Green Book/Animal Drugs@FDA monthly update process.

VIII. PREPARING THE NOTIFICATION OF THE APPROVAL AND POSTING THE APPROVAL DOCUMENTS

A. Send the CVM Product Approval Announcement

After the division receives notification that the approval letter is signed, issue the CVM Product Approval Notification email using the ONADE email template. This is sent center-wide for any approval that has a FOI Summary. All information in the email comes from the FOI Summary title page (except the submission code and the approval date). The approval date is the date listed in STARS. This notification serves to alert the reader that the electronic files for the approval will soon be available in CDMS. It also alerts Strategic Communications Staff that they should release any communications prepared for external distribution (e.g., CVM Updates, social media), if applicable, as described in SOP 1243.100.004.

[17] If the application was submitted in paper, the project manager associated with the project emails a copy of the approval letter to the sponsor.

B. Notify OSC if Final Printed Labeling (FPL) was Submitted

If the submission contained FPL, during close out of the submission in Appian, on the "Additional Actions" screen, check the box next to the option "Does the submission contain FPL that is acceptable to CVM". Appian sends an email to the CVM OSC FPL Notification mailbox. This email is used to notify OSC that ONADE has received FPL to aid in OSC's maintenance of the DER database.

C. Volume

After the division receives notification that the approval letter is signed, update the Volume 0 with the approval date.

D. Post the Approval Documents to Animal Drugs @ FDA

The month following the approval of the (A)NADA, the BI Team will prepare and post a Green Book Monthly Update document under the Green Book Reports on the ADAFDA website. The BI Team also performs a final Section 508 compliance/accessibility check on the FOI Summary, and if applicable, the FONSI, and uploads them and the EA (if applicable) to the ADAFDA website.

IX. PRESENT SUMMARY PRODUCT INFORMATION AT THE QUARTERLY MONITORED ADVERSE REACTION COMMITTEE (MARC) MEETING, IF APPROPRIATE

Contact your division representative during the approval process to determine if a presentation at the MARC meeting will be appropriate. If a MARC meeting presentation is appropriate, prepare a summary of significant findings from the studies conducted, mechanism of action, any adverse reactions noted, and any pharmacokinetic data at a MARC meeting after the (A)NADA approval. This data may be helpful to the OSC as they evaluate promotional and advertising materials and adverse drug event reports for the product.

X. REFERENCES

Federal Food, Drug, and Cosmetic Act, Section 512

FDA Staff Manual Guides (SMGs)

1410, Regulatory Delegations of Authority

CVM Policies and Procedures Manual – ONADE Reviewer's Chapter

1243.2050 – Refuse to File and Refuse to Review

1243.3002 - Handling and Rejecting Paper Applications and Submissions

1243.3005 - Creating Clean Electronic Files

1243.3009 - Format and Style Conventions for Reviews and Submission Summaries

1243.3010 - Format and Style Conventions for Letters

1243.3011 – Voiding Submissions and Discontinuing the Review of Pending Submissions and Applications

1243.3026 – Assessing Submission Quality and Amending and Resetting the Clock on Submissions

1243.3100 –Refuse to Review (RTR) and Refuse to File Assessments (RTF) Assessments of Submissions and Applications That Contain Data

1243.3200 – Routing a Request to Obtain a Consulting Review of a Submission Tracking and Reporting System (STARS) Submission

1243.3210 - Requesting a Quality Control Review from the Quality Assurance Team for Final Action Packages Signed by the Office or Center Director

1243.3760 – Drug Tolerance Notification Process

1243.3801 – Completing the Green Book and Animal Drugs @ FDA (GBAAD) Form

1243.3810 – Creating and Maintaining a Reference Copy of the Currently Approved Labeling for an Application (Volume 0)

1243.3900 – Updating the Animal Drugs @ FDA Website and Green Book

1243.5741 - Memorandum Recommending Approval (MRA) for Original and Supplemental (Abbreviated) New Animal Drug Applications (A)NADA)

1243.5761 - Freedom of Information Summary (FOI) for Original and Supplemental New Animal Drug Applications (NADA)

1243.5762 - Freedom of Information (FOI) Summary for an Animal Drug Availability Act (ADAA) Feed Combination New Animal Drug Application

1243.5820 - Approval Letters

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

1243.6030 - Review of Labeling Changes in Manufacturing Supplements

1243.6040 - Review of Abbreviated and New Animal Drug Application 60- and 180-Day Non-Fee Prior Approval Labeling Supplements

1243.8220 - Requesting a Bioresearch Monitoring (BIMO) Status Check

1243.8500 - Making a Request for a Current Good Manufacturing Practice (cGMP) Status for an Approval Package

ONADE Standard Operating Procedures

1243.100.004 Process for Preparing Communications about New Animal Drug Approvals

1243.130.001 ONADE Process for Accessing the Drug Experience Reporting (DER) Database to Perform Status Checks

ONADE Office Policy Page

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

Appian User Guide

Internal information redacted.

XI. VERSION HISTORY

November 16, 2001 – original version

August 15, 2003 – revised

December 11, 2007 - revised to incorporate format and style conventions, changes and boilerplate language agreed upon by ONADE Management, incorporating active voice where possible, and revised overall format.

March 12, 2008 – revised to incorporate information on the Division of Human Food Safety's review of the draft regulation for administrative NADAs and how to document this in the approval package. Also includes instructions to refer to the most recent 356V to determine the proprietary and established name when filling out the Reviewer's Summary field in STARS

August 31, 2010 – Revised to incorporate the ERA process, GBAAD forms, and Volume 0 information, and to incorporate current Office practices.

August 17, 2011 – Revised to incorporate new electronic review and sign-off procedures.

September 7, 2012 - Revised to improve flow of the document, incorporate the Fact Sheet process, incorporate 508 compliance process, and incorporate additional Appian information.

April 12, 2013 - Clarified the Fact Sheet/Communications email procedures.

June 28, 2017 - Revised to incorporate new and updated procedures.

August 29, 2017 - Revised to clarify procedures to state if a FONSI is prepared for the approval a copy is included with the approval letter sent to the sponsor and update the information on posting approval information to Animal Drugs @ FDA.

August 2, 2018 – Revised to add clarification of final action codes and information about the new process for preparing draft CVM updates for new chemical entities. Removed reference to outdated P&P 1240.2325 from section IV. I and added instruction that for supplemental approvals signed by the ONADE OD the notification email is not necessary. Added information on who signs the approval if the ONADE OD and CVM CD are out creating a new part B in section VII. Added reference to the new P&P on how to fill out the GBAAD form P&P 1243.3801. Revised the title.

April 04, 2019 – Revised to add instructions on when and how to ask for addition of "Approved by FDA…" statements to labeling. Revised to reflect the Finding of No Significant Impact (a.k.a. FONSI) is no longer sent to the sponsor. Updated information

regarding the Fact Sheet to reflect that all approvals going to the Center Director for signature are required to have a Fact Sheet.

August 27, 2019 – Revised to remove the instruction about using the DVPS ADE and PD Consult Request Form when requesting a Drug Experience Report status check. The form should not be used. Updated also to add information on how to name an approval Fact Sheet and mention that if an approval is going to be signed by the Center Director and a Fact Sheet has not been sent, the ONADE QA Team will make sure one is sent as soon as possible. Added a new item in section VIII to remind reviewers to update the Volume 0 with the approval date.

October 7, 2019 – Revised to update information on the location of the Fact Sheet. On Page 6 the P&P stated that, "any original or supplemental (A)NADA approval with a letter intended for the CD's signature will have a Fact Sheet (located on the ONADE Forms page)." However, the Fact Sheet is not located on the ONADE Forms page, but rather on the ONADE Templates page.

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

July 8, 2020 – Updated the final action code for ANADA NF supplements to SUP SIG LD and not minor. This change is for NF supplements that are signed by the ONADE OD.

August 18, 2020 – Edited to include information about the use of the GMP Status Check Form when requesting a GMP status check.

September 17, 2020 - Updated to include instructions related to applications that include OSC-initiated labeling changes.

January 15, 2021 – Updated the final action code for ANADA NF supplements to SUP MIN LD (reversed July 8, 2020 revision). Also, updated the title for 1243.3026 to reflect the change in the title for this P&P and corrected errors in a couple of other P&P titles in the Reference section.

March 4, 2021 – Updated section VIII to include information about release any comms prepared for external distribution, if applicable, per CVM SOP 1243.100.004.

June 1, 2021 – Updated section IV to include that an email notification is not needed for supplemental NADA approvals but is needed for supplemental ANADA NF approvals signed by the OD.

October 19, 2021 – Updated section III and added Appendix 1 to incorporate the previous ONADE Policy “Handling Deficiencies in Administrative (A)NADAs”. Also. in section VIII changed Strategic Initiative Staff to the Strategic Communications Staff.

August 16, 2022 – Updated OSC team names and HFV codes to reflect office reorganization. Updated to reflect change in GMP status check process from a form to an Appian consult. Removed erroneous footnote that stated this P&P did not apply to conditionally approved products and added conditional approval to Table 1. Quality systems review for minor formatting updates.

October 4, 2022 - Updated section IV. C. to reflect the timeline of requesting cGMP status checks.

November 16, 2022 – Updated to clarify that the Strategic Communications Staff will notify whether or not external communication is required.

March 8, 2023 – Updated Part IV, Part F to notify that the notification email is sent to HFV-6 and the Strategic Communication Staff. Also, added a statement that the email the Strategic Communication Staff sends the primary reviewer is not included in the approval package.

April 3, 2023 – Minor typo corrected (i.e., citizen's petition to citizen). 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.

June 12, 2023 – Updated section III. C. to include information about when to send the antimicrobial alert email. This information came from the ONADE policy "Approval of Antimicrobials for Food Animals" The information in this policy is being incorporated into our existing process documentation and the policy itself will be retired from the policy page in SharePoint.

September 30, 2023 – Sections III.C.4 and IV.H. updated for changes associated with the law requiring the "Approved by FDA" labeling statement taking effect.

December 7, 2023 – Updated section III. A. to remove the STARS Change Request Form information. That form has been retired. The instructions are to now send an email request to the EDSR Mailbox when the subclass code on a paper submission is not correct.

March 29, 2024 – Inclusion of section VI. O. as a reminder to ensure the accuracy of information in the STARS database. Updated section III. C. 2. to allow for consults to be sent for admin and non admin applications. This is to reflect the process for requesting a GMP status check for an admin application has changed and now it is to send a consult in Appian. Updated to remove all reference to the retired Fact Sheet template.

April 10, 2024 - Updated section IV. D to fix grammar error. Removed the extra "Use the" in the beginning of the second sentence in the first paragraph.

August 13, 2024 – Revised section IV. A. to clarify what should be sent to PRS when requesting a draft regulation and to clearly identify what PRS will provide in response to the request.

APPENDIX 1. OPTIONS FOR PROCESSING DEFICIENT ADMINISTRATIVE (A)NADAS

See P&P 1243.3026 for information on assessing submission quality and requesting amendments

A. Allow an Amendment and Keep the Administrative Review Clock:

CVM may request an amendment for missing or incorrect information (examples listed below). Per P&P 1243.3026, the review divisions should set a reasonable date that will permit the sponsor to submit the information and for CVM to complete the review of the amended submission within the established review time.

- Missing or incorrect 356v (paper submissions only)
- Missing a TS complete letter that CVM issued
- Missing all or parts of the required labeling CVM reviewed as part of the labeling TS and referenced in the TS complete letter
- Submitted the wrong version of labeling
- Need to update/correct patent information

If a sponsor cannot meet the deadline for submission of a minor amendment, then the review division should convert the application to a non-administrative (A)NADA.

B. Refuse to File because the Information Concerning Required Matter is so Inadequate that the Application is Clearly not Approvable (21 CFR 514.110):

- Failure to address a required TS (i.e., CVM did not issue a required TS complete letter).
- Multiple, significant deficiencies that suggest a poor quality, incomplete or inadequate submission

C. Convert to a Non-Administrative (A)NADA because the Submission does not Meet Definition of an Administrative (A)NADA:

- Sponsor made labeling changes that CVM was not aware of or did not agree to previously, such that (A)NADA labeling does not match the M submission. It is acceptable for the sponsor to have corrected typographical errors, added the (A)NADA number, or made other minor changes to which CVM agrees.
- New information that CVM has not previously reviewed is included in the submission
- Submission of the administrative NADA more than 90-days after the date of the All-Other Information (AOI) TS complete letter (see P&P 1243.4085)
- Sponsor cannot meet the deadline for submission of a minor amendment

Note: you cannot reset the clock for an administrative (A)NADA.