APPROVAL LETTERS

I. PURPOSE

This document describes the procedures you use to prepare and route the approval letter for:[1]

- original new animal drug applications (NADAs) and abbreviated new animal drug applications (ANADAs)
- (A)NADA supplements classified as "B1" supplements,
- (A)NADA supplements classified as "NF" (non-fee supplements requiring prior approval),
- (A)NADA supplements classified as "NL" (non-fee labeling supplements), and
- manufacturing supplements.

II. SCOPE OF THE APPROVAL LETTER

The intent of our approval letter is to inform an applicant of the approval and the conditions of approval. It is not intended to provide the details of the basis for our decision to approve. Therefore, the approval letter does not specifically discuss findings relevant to particular sections (e.g., environmental impacts, human food safety, effectiveness) of an application.

III. ELEMENTS OF APPROVAL LETTERS

When preparing an approval letter, use the office or division template for the type of approval letter you are writing.[2] Follow P&P 1243.3010 Format and Style Conventions for Letters. Further specific instructions for how to fill in certain fields of the approval letter template follow.

[1] For purposes of this document, "you" refers to a reviewer, consumer safety officer (CSO), or other individual from the team or division in the Office of New Animal Drug Evaluation (ONADE) responsible for preparing the approval letter for an application.
[2] Use the Division of Manufacturing Technologies template for manufacturing supplement approval letters. Use the Office templates for all other letters covered by this P&P.

A. Inside address:

Direct the letter to the attention of the responsible official (sponsor or other party on the sponsor's behalf[3]) who signed the Form 356v of the paper submission or is named as the contact in the Responsible Official Information section of the eSubmitter form. Use the firm name and address provided for the responsible official in the Responsible Official Information section of the eSubmitter form or the Form 356v for scanned paper submissions. However, if you find obvious typographical (i.e., spelling) errors in either the firm name, firm address or responsible official information, you should use the correct information in the inside address instead of using the incorrect information from the form.

Additionally, if the firm name in the Responsible Official Information section of the eSubmitter form (or for paper submissions, in the cover letter) appears to be incorrect or is unclear regarding the identity of the drug application sponsor (for example, if the firm name is written in the eSubmitter form or cover letter as "Drug Company Animal Health" and the firm name listed in 21 CFR 510.600 is "Drug Company Animal Health, a Division of Drug Company Inc."), contact the responsible official to obtain the correct name. Note in your review documentation that you contacted the sponsor to clarify the information, and if applicable, make note of the corrected name in your review documentation and in the Request for QC Review form, and use the corrected name in the inside address.

You may also modify the stylistic presentation (capitalization, punctuation, and spacing) of the firm name and the official's name, titles, and degrees contained in the form to match the addressee's preference in the cover letter.

However, do not add information (e.g., degrees) if it is not in the information provided in the Form 356v or eSubmitter form.

B. Body of the letter:

1. Opening paragraph

   Format the proprietary name in the approval letter using the format exactly from the labeling. Typically, this means if there is a package insert, use the formatting for the proprietary name found at the beginning of the package insert. If there is no package insert, use the format for the proprietary name found on the front panel of the immediate container's carton labeling or the front panel of the immediate container label. Use that format throughout all approval documents in all locations where the proprietary name is used including any trademark symbol associated with the name.[4]

[3] Examples of when it is acceptable for a submission to be sent to us by another party on the sponsor's behalf: 1) the company is not a United States company, they will have U.S. Agent; 2) correspondence may come from consultants; 3) a parent company submits information on a subsidiary's behalf.

[4] For information on proprietary names, see P&P 1243.3015 Proprietary Names.

In situations where the application was submitted by another party on the sponsor's behalf, identify the sponsor by name in the opening paragraph of the letter.

For original (A)NADA approvals, include the full indication(s), and if appropriate, any additional conditions of use. An adequate description of what we are approving is critical to ensure that the applicant knows exactly what drug and uses we are approving and that we have a clear record on which to base an enforcement action if the applicant is marketing the drug for unapproved uses. Copy the indication(s) verbatim from the indication section of the package insert. If there isn't a package insert, copy it from the immediate container's carton labeling or the immediate container label. For supplemental approvals, include only the changes (indications, species, or other conditions of use) that are being approved in the supplement. If the proprietary name appears in the indication, format the name the same way the proprietary name is formatted elsewhere in the approval package.

In cases where the expiration dating changes as part of a supplemental (A)NADA approval, include the expiration dating sentence in the letter.

2. Standard language for certain antimicrobials

Include the standard language[5] as the second paragraph only in approval letters for original or supplemental applications for antimicrobials of human medical importance intended for use in food-producing animals in which no microbial food safety assessment (under Guidance for Industry [GFI] # 152) was conducted for the pending application. This applies to antimicrobials intended for production uses, prevention use, and all other therapeutic indications.

Standard language is provided in the applicable templates for the following types of approvals:

- supplemental (A)NADAs (NF subclass codes)
- supplemental (A)NADAs (NL subclass codes)
- supplemental (A)NADAs (manufacturing)
- original and supplemental NADAs (Animal Drug Availability Act [ADAA] combinations)
- original ANADA involving two, three or four Type A medicated articles to manufacture Type C medicated feeds.

For applications other than those listed above, contact the Policy Team as soon as possible for standard language for an approval of an antimicrobial of human

[5] See the ONADE policy for approval of antimicrobials for food animals at Internal information redacted.

importance intended for use in a food-producing animal. If you have any questions about whether your application requires the standard language, talk with your supervisor.

3. Labeling and veterinary feed directive (VFD) paragraph

   Choose the paragraph that pertains to the type of labeling submitted with the application.

   a. Dosage form products

      If the submission includes only facsimile labeling, or if it includes a mix of facsimile labeling and final printed labeling (FPL), use the paragraph that requests submission of FPL prior to marketing and references the date of the facsimile labeling submission and submission code. This paragraph explains that FPL must be identical to the facsimile labeling approved as part of the application.[6] This paragraph also instructs the applicant when to submit FPL to the Center for Veterinary Medicine (CVM).[7]

      If acceptable FPL for all components was provided with the application, use the paragraph acknowledging acceptability of the FPL.

   b. Medicated feeds

      In most cases, for single ingredient medicated feed products, we approve labeling for the Type A medicated article, representative labeling for Type B and Type C medicated feeds manufactured from the Type A medicated article, and if applicable, a representative VFD(s). If we are approving the application based upon facsimile labeling, the applicant needs to submit FPL for the Type A medicated article identical to the approved facsimile labeling for their product. Because Type B and Type C medicated feed labeling is representative labeling (i.e., it includes general information about the feed but varies depending on mixing), the applicant does not need to submit FPL for Type B and Type C medicated feeds or for the VFD(s).[8]

      For single ingredient medicated feed approvals, if a facsimile Type A medicated article was submitted, use the paragraph in the letter requesting

[6] In the rare occurrence that you find typographical errors in the labeling submitted with an (A)NADA, check with your supervisor to determine whether to 1) request revised labeling as an amendment or 2) describe the changes in the approval letter and allow the sponsor to make the changes when they submit FPL. For feeds, this would also include submission of updated Type B and Type C medicated feed labeling. Requesting corrections in the approval letter is strongly discouraged.

[7] 21 CFR 514(b)(3)(vi) requires sponsors to submit three copies of their final printed labeling. ONADE is currently accepting a single copy because submissions are received electronically.

[8] Type B and C medicated feed labeling generally includes the name of the drug, the indications, the active ingredients, a guaranteed nutrient analysis that must meet the Association of American Feed Control Officials (AAFCO) standards, a list of the ingredients mixed, mixing or feeding directions, warnings, and cautions.

the submission of FPL for the Type A medicated article label as described above. If acceptable FPL for the Type A medicated article was submitted, use the paragraph acknowledging acceptability of the FPL of the Type A medicated article.

For feed combinations (ADAA or non-ADAA) with no Type A medicated article labeling (i.e., because the combination approval is only for a Type B and/or Type C medicated feed), the boilerplate paragraph states that the Type B and Type C labels (and VFD(s), if applicable) are acceptable.

4. Manufacturing paragraph

For supplements or ADAA combination approvals that do not involve a change in the Chemistry, Manufacturing, and Controls (CMC) information, do not put a manufacturing paragraph in the approval letter.

For all other (A)NADA approval letters, use the manufacturing paragraph provided in the letter.

Type C free-choice feeds. In those instances in which we are approving an original or supplemental application for a Type C free-choice feed that does not require a feed mill license (i.e., manufactured from a Category I Type A medicated article using a formulation that will be published in the CFR), do not put a manufacturing paragraph in the approval letter. If we are approving an original or supplemental application for a Type C free-choice feed that does require a feed mill license (i.e., manufactured from a Category II Type A medicated article or using a proprietary feed formulation), use the following alternative manufacturing paragraph:

The manufacture of full-scale commercial batches using manufacturing instructions that have been determined to yield a properly mixed medicated feed product of the specified formulation is not a requirement for approval. However, medicated feed manufacturers must be able to assure that following the manufacturing instructions will result in a properly mixed feed under good manufacturing practices (GMPs) for medicated feeds (21 CFR 225.102(b)(1)(iv)).[9] Therefore, the feed mill should document the successful evaluation of multiple full-scale batches (usually a minimum of three (3)) of the specific free-choice formulation prior to shipment of the medicated feed product. In addition, adequate cleanout procedures for all equipment used in the manufacture and distribution of medicated feeds are essential to assure proper drug levels and avoid contamination (21 CFR 225.65).

[9] For medicated pet foods, contact the Division of Manufacturing Technologies for the appropriate GMP citation.

C. Complimentary closing and signature block:[10]

In the closing paragraph, provide the contact information for the division director and/or team leader according to your division procedures.

The center director signs the approval letter for original applications and supplements that would approve new animal species, significant new indications, and changes in Rx/OTC status[11]. The ONADE director signs the approval letter for other B1 supplemental applications (that approve changes other than those delegated to the center director). The division director signs the approval letter for NF supplements, NL supplements, and manufacturing supplements.

D. Enclosure notation:

Include a notation of any other documents that should be sent to the sponsor with the approval letter (e.g., FOI Summary or Finding of No Significant Impact [FONSI]).

IV. FINAL ROUTING FOR APPROVAL LETTERS

A. Approval letter for an original or supplemental (A)NADA

The approval letter for original or B1 supplemental (A)NADAs will be routed as part of the (A)NADA approval package. Routing for (A)NADA approval packages is described in P&P 1243.3800. When uploading files into Appian, select the radio button beside "Yes, send to firm" to send the sponsor a copy of the approval letter and a copy of the enclosures (e.g., FOI Summary or FONSI).

Routing of NF supplements is described in P&P 1243.6040.

Routing of NL supplements is described in P&P 1243.6030.

B. Approval letter for a manufacturing supplement

The director of the Division of Manufacturing Technologies, HFV-140, has signature authority for approval of manufacturing supplements described in 21 CFR 514.8. The approval letter for manufacturing supplemental (A)NADAs will be routed as part of the final action package.

V. REFERENCES

CVM Program Policy and Procedures Manual

1243.3010 - Format and Style Conventions for Letters

1243.3015 – Proprietary Names

[10] You can find the delegations of authority for approval of new animal drug applications, medicated feed mill license applications and their supplements in the Staff Manual Guide, Delegations of Authority (Volume II), Section 1410.502.

[11] For generic products, the ONADE Director signs the letter for new indications, species, etc. that are a result of the RLNAD exclusivity expiring in an NF supplement.

1243.3800 - Reviewing an (A)NADA and Preparing an Approval Package

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

1243.5780 - Exclusivity Wording for Use in the Following Documents: Memorandum Recommending Approval and Letter to Applicant

1243.6020 - Review of NADA and ANADA Labeling Supplements NL Subclass

1243.6030 - Review of Labeling Changes in Manufacturing Supplements

1243.6040 - Review of (A)NADA 60- and 180-day Non-Fee (NF) Prior Approval Labeling Supplements

VI. VERSION HISTORY

November 16, 2001 – original version

August 15, 2003 – Revised

December 10, 2007 - Revised to incorporate format and style conventions, changes and boilerplate language agreed upon by ONADE Management, incorporating active voice where possible, sample letters, and revised overall format.

March 12, 2008 – Revised to clarify what address to use for the inside address and to make grammatical changes.

July 1, 2008 – Revised to correct grammar in exclusivity paragraph of sample letter.

November 17, 2008 – Division of Manufacturing Technologies revised the document to add clarifying information regarding the manufacturing paragraph (paragraph 4) of the approval letter and free-choice feeds.

December 4, 2008 – Revised to properly format footnotes 8 and 9.

February 4, 2009 – Revised to correct citation in manufacturing paragraph in sample letters in Appendices 1 and 2. Paragraph now correctly cites Section 501(a). Added a citation to P&Ps 1243.3010 and 1243.5741 for information on how to format the proprietary name.

June 10, 2009 – Revised to reflect policy on facsimile labeling for a Type A medicated article that is reduced in scale and instructions in sample letters for NADA and ANADA and their supplements were added.

August 31, 2010 – Revised to replace sample letters with templates, and update boilerplate language to currently used wording.

October 31, 2017 - Revised to incorporate updated procedures. Internet version has been redacted to remove internal information.

March 9, 2018 – Revised to clarify procedures regarding the inside address of the letter.

August 6, 2018 – Revised to include specific information regarding formatting of the proprietary name and where to get the indications for the new animal drug product for the approval letter in section III. B. 1. and reference the P&P for proprietary names (i.e., 1243.3015).

December 14, 2018 – Revised to correct a typographical error.