
OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

APPROVAL LETTERS

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I. PURPOSE

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

- original and supplemental New Animal Drug Applications (NADAs), including supplements classified as "NF" (non-fee supplements requiring prior approval) and manufacturing supplements
- original and supplemental Abbreviated New Animal Drug Applications (ANADAs).

This document does not apply to labeling supplements classified as "NL" (non-fee labeling supplements).²

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, food safety, effectiveness) of an application.

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 See P&P 1243.6020 for information on NL labeling supplements.

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.³ 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.

A. Inside address:

Direct the letter to the attention of the responsible official (sponsor or U.S. agent) who signed the cover letter of the submission or is named as the contact in the eSubmitter form. Use the address provided for the responsible official on the e-Submitter form (or the cover letter for scanned paper submissions).

In situations where the sponsor is not the company identified in eSubmitter or the cover letter letterhead, identify the sponsor by name in the opening paragraph of the letter.⁴ The address on the cover letter may not be the same as the corporate address listed in 21 CFR 510.600.

B. Body of the letter:

1. Opening paragraph

For original (A)NADA approvals, include the full description of the indications and 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. For supplemental approvals, include only the changes (indications, species, or other conditions of use) that are being approved in the supplement.

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

³ 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.

⁴ Examples of when a letter or submission may not be sent to us directly by the sponsor and may be sent 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.

Modify the first sentence as needed if the letter is being sent to a U.S. agent on behalf of a sponsor. For example, the sentence may read:

We approve the original new animal drug application (NADA) for *<insert proprietary name>* you submitted on behalf of *<insert sponsor name>* on *<insert date as Month Day, Year>*, and amended on *<insert date as Month Day, Year>* (*<insert submission code>*) under section 512(c)(1) of the Federal Food, Drug, and Cosmetic Act (the act).

2. Standard Language for Certain Antimicrobials Paragraph

Include the standard language 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 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 (manufacturing)
- supplemental NADAs (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 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 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 STARS code. This paragraph explains that FPL must be identical to the facsimile labeling approved as part of the application.⁵ This paragraph instructs the applicant to submit a single copy of each component of the FPL to CVM before distributing and marketing the drug product.⁶

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 and representative labeling for Type B and Type C medicated feeds manufactured from the Type A medicated article. 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.⁷

For single ingredient medicated feed approvals, use the paragraph in the letter requesting the submission of FPL for the Type A medicated article label as described above. 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), use the paragraph stating that the Type B and Type C labels are acceptable.

⁵ 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.

⁶ 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 being reviewed electronically.

⁷ 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.

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

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. In those instances in which 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 GMPs for medicated feeds (21 CFR 225.102(b)(1)(iv)).⁸ 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).

⁸ For medicated pet foods, contact the Division of Manufacturing Technologies for the appropriate GMP citation.

C. Complementary closing and signature block:⁹

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

The center director signs original applications and supplements that would approve a new species, significant new indications, and changes in Rx/OTC status. The ONADE director signs other supplemental applications, including prior approval labeling supplements (NF), except manufacturing supplements.

D. Enclosure notation:

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 FOI Summary.

E. cc: block notation:

For original applications, include in the cc: block a notation of a distribution copy of the letter (without an FOI Summary) to the FDA District Office (DO) for any FDA DOs as identified in the GMP status check email. A DO copy is not needed for products manufactured outside the U.S. or if no new drug will be manufactured, e.g., ADAA feed combinations and concurrent use approvals of previously approved drugs.

IV. FINAL ROUTING FOR APPROVAL LETTERS**A. Approval Letter for an Original or Supplemental (A)NADA**

The approval letter for original or 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.

B. Approval Letter for a Manufacturing Supplemental (A)NADA

The director of the Division of Manufacturing Technologies, HFV-140, has signature authority for approval of manufacturing supplements described in 21

⁹ 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.

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

1243.3800 - Preparing and processing 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

1243.6030 - Review of labeling changes in manufacturing 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.