
OFFICE OF NEW ANIMAL DRUG EVALUATION
REVIEWERS' CHAPTER

ABBREVIATED NEW ANIMAL DRUG APPLICATION (ANADA) MEMORANDUM RECOMMENDING APPROVAL (MRA)

I. PURPOSE

This Guide describes the format for a memorandum recommending approval that is part of the approval package for an abbreviated new animal drug application (ANADA).

II. PROCEDURE TO FOLLOW

The approval package for an application typically contains (among other documents) the following documents as described in CVM Policy and Procedures Guide 1240.3120:

- MRA
- FOI Summary
- Approval Letter
- Draft Regulation
- Labeling (Pioneer and Generic)

Reviewers should provide these documents in **Draft** when forwarding the approval package through administrative review channels.

For original ANADA approvals, reviewers should address the MRA **to** the Center Director, **through** the Director, Office of New Animal Drug Evaluation (ONADE). For most supplemental approvals, reviewers should address the MRA

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to the Director, ONADE, **from** the appropriate Division Director. However, reviewers should address supplemental approvals that permit a new claim, new species, or change in RX/OTC status the same as for original approvals: **to** the Center Director, **through** the Director, ONADE.

NOTE: *Reviewers should include the following sixteen paragraphs (#1-16) in the MRA. Some sections, however, may not be applicable to all approvals (i.e., paragraphs 2-7, 9-11, and 14). If any of these paragraphs are not applicable, reviewers should indicate, "Not applicable to this submission" under the paragraph heading. For those sections that are applicable, the reviewer should include the language in non-italicized text verbatim, with specific information to address the italics.*

III. FORMAT FOR ANADA MRA

Date *<insert date>*

From Director, Division of *<name>* (HFV-xxx)

Subject ***<ANADA number and submission information; for example, "Original ANADA xxx-xxx, A-0000">*** **– MEMORANDUM RECOMMENDING APPROVAL**

To *<Director Name>*
Director, *<Center for Veterinary Medicine, (HFV-1) or Office of New Animal Drug Evaluation, CVM (HFV-100)>*

If to Center Director,
Through Director, ONADE (HFV-100)_____

Request Under Consideration: *<narrative paragraph describing the current approval request.>* The sponsor, *<company name,>* has submitted *<type of application>* requesting approval for *<xxxxx.>* The sponsor submitted a current signed Form FDA 356V dated *<insert date>* with this application.

1. General Information:

a. File Number:	*<insert file number e.g., ANADA xxx-xxx (JINAD xxxx)>*
b. Sponsor:	*<insert company name>* *<insert company address>* Drug Labeler Code: *<insert code number from 21 CFR 510.600>*
c. Established Name:	*<insert drug's established name>*
d. Proprietary Name:	*<insert product's proprietary name>*
e. Dosage Form:	*<insert dosage form>*
f. How Supplied:	*<insert how supplied>*
g. How Dispensed:	*<insert Rx, OTC, or VFD>*
h. Amount of Active Ingredients:	*<insert the amount of active ingredient>*
i. Route of Administration:	*<insert route of administration>*
j. Species/Class:	*<insert species/class>*
k. Recommended Dosage:	*<insert recommended dosage>*
l. Pharmacological Category:	*<insert pharmacological category>*
m. Indications:	*<insert indication(s)>*
n. Pioneer Product:	*Trade name (proprietary name); Established Name; ANADA xxx-xxx; Sponsor Name*

2. Target Animal Safety:
Refer to the Freedom of Information (FOI) Summary for more detail. *<Reference dates and submission numbers of review document(s), e.g., See Veterinary Medical Review dated <date,> (JINAD xxxx <submission code,> HFV-xxx, <name>).> <Insert additional animal safety information unique to the application, as appropriate.>*

3. Drug Effectiveness:
Refer to the FOI Summary for more detail. *<Reference dates and submission numbers of review document(s), e.g., See Veterinary Medical Review dated <date,> (JINAD xxx-xxx <submission code,> HFV-xxx, <name>).> <Insert additional drug effectiveness information unique to the application, as appropriate.>*

4. Human Safety:
If drug is intended for use in food species:
Refer to the FOI Summary for more detail. *<Reference dates and submission numbers of review document(s), e.g., See Human Food Safety Review dated <date,> (JINAD xxxx <submission code,> HFV-xxx, <name>).> <Insert any additional human food safety information (including tissue tolerances, ADI, withdrawal times, etc.) as appropriate.> <Address user safety as appropriate.>*

If drug is intended for use in non-food species:
Data on human food safety, pertaining to drug residues in food, were not required for approval of this ANADA. This new animal drug is to be labeled for use in *<insert non-food species,>* which are non-food animals.

The following is assigned to this product; *use as appropriate*:

- **Tolerance**
  The tolerance established for the pioneer product applies to the generic product. A tolerance *<xxx ppm>* is established for *<drug product or marker residue>* residues in the uncooked edible tissues *<or target tissue>* of *<target animal species>* under 21 CFR 556.xxx. *<Include the established Acceptable Daily Intake (ADI) if applicable.>*

- **Withdrawal Time**
  Under the CVM Bioequivalence Guidelines, when a generic product is granted a waiver of *in vivo* bioequivalence testing, the withdrawal period established for the pioneer product is also assigned to the generic product.

  For this reason, a withdrawal period of *<x days>* has been established for *<drug product, established name,> in <target animal species>* (21 CFR xxx.xxx).

- **Regulatory Method for Residues**
  The analytical method for the determination of *<drug product>* in tissues is *<name method.>*

5. Freedom of Information (FOI) Summary:

A summary of the basis of approval, in compliance with 21 CFR 514.11, will be available for public disclosure in the Dockets Management Branch (HFA-305) upon publication of the notice in the FEDERAL REGISTER.

6. Labeling:

a. The labeling for the generic product is identical to the current approved labeling for the pioneer product, NADA xxx-xxx, with the following exceptions: *<examples of exceptions: trade name, manufacturer's name, certain changes approved through a suitability petition, or deletion of claims subject to patent or exclusivity protection.>*

b. The generic product labeling *<state whether facsimile or final printed labeling>* was submitted on *<date of submission,>* and is attached to the FOI Summary.

7. Chemistry, Manufacturing Methods, and Controls:

The review of the manufacturing methods, facilities, and controls by the *<HFV-142 or HFV-143 Team name and mail code>* dated *<date of review>* recommended approval.

<For originals, cite date(s) of review(s); for supplemental applications, state whether there is a change from the original application. For example, "There

are no changes submitted for the Chemistry, Manufacturing Methods, and Controls.">
Expiry dating: *<not required for supplements if there are no CMC changes.>*

Commitments for ongoing stability studies: *<not required for supplements if there are no CMC changes.>*

GMP compliance: *<insert as appropriate:* According to the GMP status check dated <date,> HFV-140 has ascertained that the sponsor is in compliance with cGMP (current Good Manufacturing Practice) regulations. *Or, if there are no supplemental CMC changes,* GMP compliance verification is not required because there are no Chemistry, Manufacturing Methods, and Control changes.>

8. Environmental Assessment** (usual case)**:
The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

9. Special Concurrence** (usually none)**:
<Insert whether the agency requires special concurrence for this approval. Ordinarily there are none. If there are grounds for special concurrence, provide details here.>

10. Bioresearch Monitoring Status:
If a bioequivalence waiver is granted, no bioequivalence or tissue residue studies are conducted. The reviewer should cite date of "Waiver" letter, volume and JINAD No., and include the following statement:

No bioequivalence or tissue residue studies were conducted supporting approval of this application because a bioequivalence waiver was granted *<date and other document code information.>* Therefore, no bioresearch monitoring inspections were conducted.

The reviewer must check with HFV-234 to determine if establishment inspections have been conducted for the bioequivalence study(ies) or tissue residue study(ies).

If the records indicate no problems in the BIMO status check, the following statement is appropriate:

Bioresearch records in HFV-234 <*with reference to the GLP study*> were reviewed and do not provide an adequate basis for refusal to approve this application. Refer to memo dated <*date of HFV-234 status check*.>

11. Drug Experience Report (DER) Status:
The primary reviewer checks the annual report included in the Drug Experience Reporting History to determine if the pioneer product is currently marketed.

a. If the pioneer product is currently marketed, then use the following statement:

The annual report included in the Drug Experience Reporting History indicates that the pioneer product, NADA xxx-xxx, is currently marketed as of <*date of annual report submission.*>

b. If the pioneer product is not currently marketed, then a determination of why it is not currently marketed must be made before the ANADA approval can be granted. If the pioneer product has been withdrawn from sale, the primary reviewer should determine if information has been submitted by the generic sponsor that is adequate for the agency to concur in the generic sponsor's finding that the product was not withdrawn from sale for reasons of safety or effectiveness. The following statement should be used:

The annual report included in the Drug Experience Reporting History indicates that the pioneer product, NADA xxx-xxx, is not currently marketed. The generic sponsor has submitted information under cover letter dated <*date of submission.*> Following review of the information, the agency finds that it is adequate to support the generic sponsor's finding that the product was not withdrawn from sale for reasons of safety or effectiveness.

12. Patent Term:
The primary reviewer checks the FDA publication, Approved Animal Drug Products Green Book for the current year,

[see **http://www.fda.gov/cvm/greenbook/greenbook.html]** *and the monthly updates, to determine the patent and exclusivity status of the pioneer product, and adds the appropriate statement from the following:*

a. If no patent is listed for the pioneer, use:

Patent and Exclusivity Sections (and monthly supplements) in the Green Book were examined on *<date the sections were checked.>* No patent is listed for the pioneer product in the publication, FDA Approved Animal Drug Products in the Green Book, *<current year>*
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]**.

b. If a patent is listed in the Green Book, but the generic applicant has submitted a certification as described in sec. 512(n)(1)(H)(iv) that the patent is invalid or will not be infringed, use:

A patent is listed in the publication, FDA Approved Animal Drug Products in the Green Book, *<current year>*
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]** for the pioneer product, NADA xxx-xxx, but the generic applicant has submitted a certification on *<date of submission, document code, page number>* that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new animal drug for which the application is filed.

c. *If a patent is listed in the Green Book, but the generic applicant has submitted certification as described in 512(n)(1)(H)(ii) that the patent has expired, use the following language:*

A patent is listed in the publication, FDA Approved Animal Drug Products in the Green Book, *<current year>*
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]**, NADA xxx-xxx, but the generic applicant has submitted a certification on *<date of submission, document code, page number>* that such patent has expired.

d. *If the generic applicant has submitted certification as described in 512(n)(1)(H)(i) that the required patent information has not been filed, use the following language:*

The FDA Approved Animal Drug Products in the Green Book, *<current year>* **[**see **http://www.fda.gov/cvm/greenbook/greenbook.html]**, NADA xxx-xxx, has been reviewed, and the generic applicant has submitted a certification on *<date of submission, document code, page number>* that the required patent information has not been filed.

e. *If a patent is listed in the Green Book but the generic applicant has submitted certification, as described in 512(n)(1)(H)(iii) as to the patent expiration date, use the following language:*

A patent is listed in the publication, FDA Approved Animal Drug Products in the Green Book, *<current year>*
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]**, NADA xxx-xxx, but the generic applicant has submitted a certification on <d*ate of submission, document code, page number*> that such patent will expire on *<insert date provided.>*

13. Exclusivity:
The primary reviewer checks the FDA Approved Animal Drug Products in the Green Book, <current year>
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]**, *and the monthly updates to determine exclusivity status of the pioneer product, and adds the appropriate statement from the following:*

a. If no exclusivity is listed for the pioneer, use:

The Patent and Exclusivity Sections (and monthly supplements) of FDA Approved Animal Drug Products in the Green Book
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]** were examined on *<date the sections were checked.>* No exclusivity is listed for the pioneer product.

b. If a three-year exclusivity is listed in the Green Book for the pioneer, and the exclusivity period has not expired, use:

A three-year exclusivity for *<identify the specific subject of the exclusivity, such as a new claim or new species from the pioneer product FOI Summary>* is listed in the publication, FDA Approved Animal Drug Products in the Green Book, *<current year>*
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]** for the pioneer product, NADA xxx-xxx. The Patent and Exclusivity Sections (and monthly supplements) in the Green Book were examined on *<date the sections were checked,>* and confirmed that the exclusivity period expires on *<date.>* Therefore, the labeling for the generic product ANADA xxx-xxx is approved without the claim that is subject to exclusivity. *<Include explanation of claim and what part is protected by exclusivity.>*

c. If a three-year exclusivity is listed in the Green Book for the pioneer, and the exclusivity period has expired, use:

A three-year exclusivity for *<drug product>* is listed in the publication, FDA Approved Animal Drug Products Green Book, *<current year>*
[see **http://www.fda.gov/cvm/greenbook/greenbook.html]** for the pioneer product, NADA xxx-xxx, *<date.>* The Patent and Exclusivity Sections (and monthly supplements) in the Green Book were examined on *<date the sections were checked,>* and confirmed that the exclusivity period has expired. Therefore, generic product ANADA xxx-xxx may be approved.

14. Regulation:
The draft regulation (FRDTS #CVMxxxxx) is attached to amend the animal drug regulations *<insert CFR paragraph number(s) being amended>* to reflect the approval of a *<insert type of application>* abbreviated new animal drug application providing for safe and effective use of *<insert drug name>* in *<insert species, etc., as appropriate.>*

15. Communication Staff Notification:
Has the Division sent advance notification of this pending approval to HFV-12 following the appropriate criteria in P&P Guide 1240.2325?

☐ Yes ☐ No

16. Recommendation:
We recommend that the approval letter be signed and sent to the sponsor. *<Also include the following sentence, if applicable:>* We also recommend that the FEDERAL REGISTER document providing for approval of this Abbreviated New Animal Drug Application be signed and forwarded for publication in the FEDERAL REGISTER.

_____ _____
<insert Division Director's signature block> *<insert Team Leader's signature block>*

_____
<insert Reviewer's signature block>

V. DISTRIBUTION COPIES

cc: HFV-199, ANADA Orig.
HFV-102, Green Book

<Author's name, HFV-#, date>

The preparer should include name, date, and HFV code for each reviewing official in the draft review process. Example provided below:

Draft-Reviewing Officials: *<insert initials and date>*
HFV-###, Team Leader's name
HFV-###, Division Director's name
HFV-###, Quality Assurance Team Official's name

NOTES:
Send only one copy of the ***draft*** MRA initially with the Approval Package. After all necessary parties concur (and General Counsel concurs for certain approvals), the necessary corrections are made, and then the reviewer makes all the copies as outlined above.

No salmon copy is needed. Since the original MRA is retained in the jacket, there is no need for a salmon copy.