OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

FREEDOM OF INFORMATION (FOI) SUMMARY FOR ORIGINAL AND SUPPLEMENTAL NEW ANIMAL DRUG APPLICATIONS (NADA)

I. PURPOSE

This document provides instructions on how to use the ONADE template to prepare a Freedom of Information (FOI) Summary for an original or supplemental new animal drug application (NADA). It also provides links to the Government Printing Office Style Manual, which should be used for formatting to ensure consistency across the Office. This document also describes the information we include in the FOI Summary for original and supplemental NADAs other than minor labeling supplements (for information on labeling supplements, see P&Ps 1243.6020 and 1243.6030).[1]

II. WHY DO WE NEED AN FOI SUMMARY?

An FOI Summary provides the public a summary of the safety and effectiveness data on which we based our decision to approve the new animal drug. After we publish an approval of an original or supplemental NADA in the FEDERAL REGISTER, we are required to make "immediately available for public disclosure", among other things, a summary of "the safety and effectiveness data and information submitted with or incorporated by reference in the NADA file." We must make this disclosure "unless extraordinary circumstances are shown."[2]

III. WHAT NADAS NEED AN FOI SUMMARY?

ONADE prepares an FOI Summary for each approved original application [see 21 CFR 514.11(e)]. In addition, it is our current practice to prepare an FOI Summary for a supplemental NADA that includes safety and/or effectiveness data. For questions about which applications need FOI Summaries, consult your team leader (TL).

[1] This P&P does not apply to conditional approvals.

[2] Although the regulations do not use the specific term "FOI Summary," FDA uses this term to describe the summary we prepare pursuant to 21 CFR 514.11(e). We refer to this document as an FOI Summary because it contains the information that we would disclose in response to an information request under the Freedom of information act.

IV. WHO PREPARES THE FOI SUMMARY?

CVM will prepare the final version of the FOI Summary.[3] Generally, a reviewer in the target animal division (TAD) will be responsible for preparing the final FOI Summary, with the exception of the executive summary (ES) section, for publication with the approval, but the preparer may be any other individual designated by office, division, or team procedures. The ES is prepared by a Communications Writer in CVM's Office of the Director, with direct input from the primary reviewers (PRs) of the technical sections (TSs) for the approval (see P&P 1243.5760). For questions about who prepares the FOI Summary, FOI Summary language, or the ES, consult your TL or division director.

V. GENERAL PRINCIPLES FOR FOI SUMMARIES

The FOI Summary is a scientific publication authored by CVM and made available to the public. Use the ONADE FOI template to prepare the final FOI. The document should be of consistent format and fully compliant with this P&P. Any deviations from the template and/or P&P should be explained when the FOI Summary is submitted for administrative review.

A. The FOI Summary Should:

1. Be detailed

   The FOI Summary should summarize effectiveness and safety data and other information in sufficient detail so people reading the FOI can put into context how the studies led us to the decision to approve the new animal drug. When doing this the following questions may help the preparer,

   Is it clear how we decided the drug is safe and effective?

   Have we explained certain complexities or things that may be unclear to the outside reader to avoid misconception or misunderstanding? For example, a study done using a different route of administration or dose that is not the one approved.

   Do we need to explain why negative findings from a study do not preclude approval?

   Be clear and accurate. Only include studies and information used to make a decision or that support label statements. Not all studies conducted or submitted may need to be included.

   For supplemental NADAs, only include data relevant to the approval of the current supplemental NADA in the FOI Summary. When applicable, include references to data reviewed and summarized in previous FOI Summaries.

[3] FDA regulations allow either CVM or the sponsor (with CVM review and revision) to prepare the FOI Summary [21 CFR 514.11(e)(2)(ii)]. Sponsors often submit a draft FOI Summary with each applicable TS under the INAD or with a non-administrative original or supplemental NADA. It is ONADE policy that we prepare the FOI Summary.

2. Be consistent with all reviews conducted for the approval

   If there are differences between the final FOI Summary and the FOI Summary language provided in the TS complete letter(s), reviewers should explain these differences in the FOI Q submission (phased review) or as part of the AA review (non-administrative NADAs). In the rare instance they are discovered during the preparation of the approval package, reviewers should document the differences in the Memorandum Recommending Approval (MRA).

3. Be internally consistent

   a. When summarizing a study, use the study summary outline format in Appendix 1 to maintain consistency.

   b. Reference the new animal drug identifier (i.e., proprietary name, active drug ingredient, drug product established name) in the same manner throughout the entire document. It may be more appropriate for some studies (e.g., toxicology) to use the active drug ingredient, rather than the proprietary name and vice versa.

   c. Only use 'sponsor' and not 'firm' when referring to the drug company. Firm is the general term for ANY company. Sponsor is the firm that owns the application, so it is appropriate to use 'sponsor' in our FOI Summaries.

   d. Ensure only the claim(s)/indication(s) that are being approved can be found in the FOI Summary. Occasionally, some divisions/teams evaluate broader claims in their assessments, and these should not be included in the FOI Summary if they are not part of the current approval (e.g., do not provide language for 'all finfish', if CVM is only approving the use in 'salt-water reared finfish').

4. Define all acronyms the first time they appear in the document.

   Once defined, it is permissible for preparers of final FOI Summaries to use the acronym in subsequent sections.

5. Reference previous approvals when needed

   If the FOI Summary includes references to previous approvals, each reference should include the NADA number and the date of the FOI Summary that contains the information you reference (i.e., refer to the FOI Summary for NADA XXX-XXX dated DATE).[4] If no FOI Summary can be found, use the date from another reference (i.e., approval letter, or, if you cannot find a dated approval letter, a FEDERAL REGISTER notice). Clearly identify the document to which you refer and its date (i.e., NADA XXX-XXX, approved DATE or approval of NADA XXX-XXX, as published in the FEDERAL REGISTER (volume number FR page number) on DATE).

[4] ONADE uses the date of the FOI Summary because it is most closely associated with the referenced information. Some older FOI Summaries contain approval dates or FR notice dates. In general, the date on the front page of the FOI Summary is the same as the date on the approval letter. In most cases, the FR notice date will not match the date of the approval letter (or FOI Summary).

The purpose of the FOI Summary (made available to the public) is to explain the basis for the approval in a clear, concise, and logical way, tailored for a scientific audience (e.g., veterinarians, animal scientists, toxicologists, chemists, or other applicable scientific disciplines).

6. Section 508 compliance.

   The final FOI Summary must be Section 508 compliant.[5] Reviewers should construct draft FOI Summaries in MS Word using Section 508 compliance.[6]

B. Do Not Include Trade Secrets or Confidential Commercial Information in the FOI Summary

The Freedom of Information Act (FOIA) exempts trade secrets and confidential commercial information from disclosure.[7] In addition, Federal law prohibits the disclosure of trade secrets submitted to FDA.[8] If you have questions regarding what information to include in the FOI Summary, discuss them with your team leader and the Center's FOIA Officer.

VI. PREPARING THE FOI SUMMARY LANGUAGE FOR EACH TECHNICAL SECTION UNDER PHASED REVIEW

Each TS complete (TSC) letter under the investigational new animal drug (INAD) file should include the relevant FOI Summary language for that section. The division issuing the TSC letter will determine who (within their division) will prepare the FOI Summary language. If you send a consult during review of the Target Animal Safety, Effectiveness, or Human Food Safety (HFS) TS, the consulting reviewer provides input on the draft FOI Summary sections related to those studies. If portions of the FOI summary written by the PR incorporate or reference the consulting review or if changes are made to the language provided by the consulting reviewers, the PR works with the consulting reviewer to make sure that the language is acceptable.

If time permits, the reviewer of the TS may informally provide the sponsor the language that they have incorporated into the FOI Summary for that TS before issuance of a TSC letter. If the sponsor disagrees with FOI Summary language that is included in a TSC letter and wants changes (after the letter is issued and any time before approval of the new animal drug), we may have to reopen the relevant TS. Remember that the FOI Summary is a CVM document because its purpose is to describe our basis for recommending approval of a new animal drug. CVM makes the final decision regarding which information to include in the FOI Summary.

Reviewers should be aware that the last major TS may impact the completion of the All Other Information and Labeling (M) submissions, as well as the FOI Summary (Q) submission because typically they are assigned the same due date. For example, if the

[5] HHS Section 508 Accessibility checklists at https://www.hhs.gov/web/section-508/accessibility-checklists/index.html

[6] For information on 508 compliance, see the ONADE Review Aids SharePoint Library.

[7] 5 USC §552(b)(4). 21 CFR 20.61.

[8] See Section 301(j) of the FD&C Act (21 USC §331(j)), 18 USC §1905, and 21 CFR §20.61.

last TS needed for the FOI Summary is HFS, the HFS reviewer works with the TAD reviewer to ensure the FOI Summary is completed appropriately and on time.

VII. PREPARING THE FOI SUMMARY DOCUMENT

A. Assembling the Draft FOI Summary under the INAD (FOI Q Submission)

1. Creating a Q submission

   A Q submission is an agency-initiated submission and is used for the creation of the draft FOI summary. A project manager (PM) creates a Q submission under the INAD when the sponsor submits their labeling and/or AOI (M) submissions.[9] The PM assigns the FOI Summary Q to the appropriate TAD team. The FOI Q will have the same due date as the M submissions.

2. Assembling the FOI Summary

   If the FOI Summary is for an application for use in a food-producing species, request a consulting review from the Division of Human Food Safety (DFHS) to review the HFS language in the FOI Summary. The DHFS reviews and makes any necessary edits to their portion of the FOI Summary. The DHFS reviewer informs the PR whether the tolerance and withdrawal time information in the regulation will need to be changed when the application is received to assist in the preparation of the FEDERAL REGISTER Notice. The PR discusses any changes to the FOI Summary language provided by any consulting reviewer with that reviewer and documents the discussion, if appropriate, and the resultant changes in the review.

   Assemble the FOI Summary from the FOI Summary language contained in each TSC letter and prepared for any pending submissions. The ES process is initiated at the same time by notifying the Communications Writer (see P&P 1243.5760). TAD reviewers and others may make changes to address consistency and style differences at the FOI Summary Q submission stage. Issues related to minor errors and editorial changes should have been resolved within each TS. Apparent factual errors should be addressed through open communication between divisions.

   If time permits, the PR may communicate with the sponsor and/or consulting reviewers informally before issuance of a Q letter to allow them to review the FOI Summary document. If the sponsor requests changes that result in the reopening of a TS while the Q submission is still open, then the appropriate final action for the Q submission is FNR/memo.

3. Preparing the Q submission final action package

   The PR finals out the Q submission following current procedures (see P&P 1243.3030). If we issue a TSC letter for the last TS (i.e., the last P or M submission), the appropriate final action for the Q submission is to issue an acknowledgement letter to the sponsor enclosing a copy of the FOI Summary document. If the Communications Writer has finished the ES, then the ES is

[9] The Q submission is created in Appian.

included in the FOI Summary that is sent to the sponsor. If the ES is not completed when the Q submission is ready to be finaled, it is acceptable to final out the FOI Summary without the ES and, in its place, include the placeholder language found in the FOI template. Load the FOI Summary as an Word document (draft FOI Summary) in Appian; Appian will create a PDF copy to be sent to the sponsor. The letter should inform the sponsor that they may request changes to correct errors.

If we cannot issue a TSC letter for the last TS, your review should state that we could not complete the Q submission because we could not issue a TSC letter for the last TS. In this case, the appropriate final action is FNR/memo. The Q submission final action package should include a copy of the draft FOI Summary document as a stand-alone document and your review. Your review should summarize the extent and substance of the preparation of the FOI Summary document up to the point that you stopped review of the last TS. In the "Date of Approval" field of the FOI Summary title page, type "Draft Incomplete – See Review" and the date.

4. Requests for changes

   If the sponsor requests substantive content changes, review the request and reopen the relevant TS(s), if needed. If the sponsor proposes minor editorial changes that you determine will make the FOI Summary more accurate or identifies factual errors, then we might not reopen relevant TSs. Incorporate those minor changes into the FOI Summary that you include in the NADA approval package. Because the FOI Summary is a CVM document, there is no guarantee that the sponsor's proposed changes will be incorporated into the final FOI Summary.

B. Administrative NADAs

Include the FOI Summary that was prepared under the INAD FOI Q submission in Folder A of the electronic approval package. Incorporate any applicable minor changes, and the completed ES if not in the Q, into the final version before submitting the approval package for administrative review. Ensure the final document is Section 508 compliant. See P&P 1243.3800 for additional instructions for preparing and routing the approval package.

C. Non-administrative NADAs

For non-administrative NADAs, begin to prepare the final FOI Summary document when you receive an application. Continue building the FOI Summary document as you and the applicable consulting reviewers complete your reviews of each TS. The ES process should be initiated at the same time by notifying the Writer (see P&P 1243.5760).

If you send a consult during review of the Target Animal Safety, Effectiveness, or HFS TS, the consulting reviewer provides input on the draft FOI Summary sections related to those studies. If portions of the FOI summary written by the PR incorporate or reference the consulting review or if changes are made to the language provided by the consulting reviewers, the PR works with the consulting reviewer to make sure

that the language is acceptable. This interaction should take place during the drafting stage, prior to the final action package going to the TAD TL and division director.

If applicable, incorporate any FOI Summary language that was agreed upon previously under the INAD. Time permitting, you may share a copy of your FOI Summary document with the sponsor and tell the sponsor that they may request changes to correct errors.

Include the complete FOI Summary in Folder A of the electronic approval package (see P&P 1243.3800).

VIII. CONTENTS OF THE FOI SUMMARY

Use the ONADE template for the NADA FOI Summary and refer to the ONADE Review Aids SharePoint for guidance on Section 508-Compliance issues. The Government Printing Office (GPO) Style Manual should be used for style and formatting to ensure consistency across the Office, and this style and formatting must be consistent throughout the document.[10] See the ONADE Template Information Page for more information on using the office templates. This section describes the contents of each section of the FOI Summary in more detail than the template. Refer to this section as you use the FOI Summary template.

A. General Instructions for Using the FOI Summary Template

1. Words not in italics or brackets, (i.e., < >), in the FOI Summary are boilerplate and should be included in your FOI Summary verbatim.

2. Words in bracketed italics may provide instruction, describe the information you will provide, or may give examples of the type of information that you will include in a particular portion of the FOI Summary.

3. Where you see brackets or shaded areas, provide information relating to your specific application.

4. Consider using active voice instead of passive voice whenever prudent.

5. Use style elements to format documents.

    a. Use Heading 1, Heading 2, etc., to create headers (do not just change the font or use bolded text, with the exception of the study summary outline as shown in Appendix 1).

    b. Use Normal style font set to Arial 11 point for regular text including Table text and footnotes.

    c. Use the bullets and numbered lists feature in MS Word to create accessible lists.

[10] https://www.govinfo.gov/collection/gpo-style-manual?path=/GPO/U.S.%20Government%20Publishing%20Office%20Style%20Manual

6. Data tables and figures

   a. Number all tables and figures according to the section of the FOI Summary (e.g., Table II.2. for the second table appearing in the Effectiveness section; Figure IV.1. for the first figure appearing in the HFS section).

   b. To be Section 508 compliant, table column headers must be formatted as a header row (Select Row -> right click and choose Table Properties -> choose Row tab -> select Repeat as Header Row at the top of each page)

   c. DO NOT check the box to allow table rows to break across pages.

   d. Tables must have a title and a header row, which should both be bolded. The title does not need to be repeated on the next page if the table carries over, but the header row should repeat

   e. Some header rows may be left blank if appropriate. Use "NA" in cells if appropriate.

   f. Never merge cells

   g. Abbreviations and footnotes should be included immediately after the Table as separate text. The same abbreviations and sequence of footnote symbols should be used throughout the FOI Summary (see GPO Style Manual). See the table below for an example.

   h. Alternative Text is not required for tables. Figures need Alternative Text in the form of a long description (e.g., not just the title pasted)

   i. For CVM-generated/verified data, numerical values should be reported consistently by rounding to significant figures as scientifically appropriate (i.e., whole numbers vs. numbers to the first or second decimal place) within each data group (i.e., column or row). Historical, published, or proprietary data should be reported as presented for scientific interpretation, e.g., results transcribed exactly from the sponsor's submission or an article, without rounding.

B. Example of Recommended Table Formatting for FOI Summaries:

Table IV.2. Concentrations in Muscle, Skin and Combined Muscle and Skin

Withdrawal Time (Days)	Muscle (86% of reported value)	Skin (14% of reported value)	Muscle and Skin Combined (86%:14%)
1	< LOQ*	12.0	12.0
1	78.0	60.0	138
1	NA†	26.1	3.65
1	< LOQ	ND‡	< LOQ
1	< LOQ	ND	< LOQ
1	< LOQ	20.6	2.88
2	NA	< LOQ	< LOQ
2	NA	< LOQ	< LOQ
3	NA	< LOQ	< LOQ

* LOQ (limit of quantitation) – 2.56 ppb
† NA, not analyzed
‡ ND, not detected
§ next footnote, if needed

C. Example of CVM Generated/Verified Data:

Table II.1. Bioequivalence Evaluation in Dogs

Parameter	Test	Reference	Ratio*	Ratio Lower Bound	Ratio Upper Bound
AUC (µg/mL)*h	15.01†	14.39†	1.04	0.99	1.08
Cmax (µg/mL)	4.22†	4.17†	1.01	0.94	1.09
Tmax (h)	1.10‡	1.36‡	NE	NE	NE

† Geometric mean
‡ Arithmetic mean
* Ratio=Test/Reference
NE =not estimated

1. Add Alternative Text to figures, images, and other graphic elements

    a. Alternative Text is required for all images (including equations and formulas) in our FOI summaries. Alternative Text is not required for tables.

    b. To enter Alternative Text, right-click on the image, go to format picture, and then Alt-text. Provide a detailed description (not just the pasted title) in the Alternative Text box. Subject matter experts must provide these written explanations because they are best qualified to interpret the content.

2. Formulas

    a. Insert formulas with a division line or with special characters as an image file. Use Arial 11-point font.

b. For the formula example below, as Alternative Text, enter the Equation number for the Title and then the description information. This description does not need to reside in the FOI Summary document text.

(Equation 1: Acceptable Daily Intake (ADI) equals the lowest NOEL divided by the Safety Factor, which equals 2.1 mg/kg BW/day divided by 200, which equals 10 µg/kg BW/day)

$$ADI = \frac{NOEL}{Safety\ Factor} = \frac{2.1\ mg/kg\ bw/day}{200}$$

$$= 0.01\ mg/kg/bw/day = 10\ \mu g/kg\ bw/day$$

c. Use the following procedure to convert an equation into an image and insert it back into the FOI document:

i. Open the program Snipping Tool from your Start button on the bottom left corner of your monitor.[11]

ii. A box will pop up telling you to draw a box around the equation.

iii. Draw a box around the equation.

iv. When you release the mouse button, it will automatically open a Snipping Tool window with your new image.

3. Hyperlinks

a. Do not include active hyperlinks. Web addresses and emails must be inactive.

b. Include the entire URL for web addresses (http://www.fda.gov, and NOT www.fda.gov)

c. To remove the hyperlink, right click on the email or web address and choose remove hyperlink

4. Scientific units of measurement and symbols

Present scientific units of measurement and their abbreviations using their respective symbols/abbreviations throughout the document (e.g., µg/mL, °). For example, do not use micrograms/mL or a superscript letter 'o' for the degree symbol. To insert a symbol in your review documentation, select the Insert ribbon in Microsoft Word and select the Symbol dropdown at the far right. Make sure the font is Arial 11 point. In our documentation, the standard format for the trademark (™), copyright ©, and registered trademark symbols (®) is superscript. When using the copyright and registered trademark symbols using the Symbol option, you must manually superscript them (i.e., © and ®) to have them in the

[11] Alternatively, statistical equations and similar situations can be saved as an image file with appropriate alternative text.

correct format. In the event that the labeling in an approval package formats the trademark symbol in a manner that is acceptable but different from our standard (e.g., you may see the trademark symbol subscripted in the labeling we receive), throughout the approval package present the trademark symbol as it is formatted on the labeling. Consult the GPO Style Manual for correct abbreviations of units of measurement.

Use a space before and after <, ≤, >, ≥, =, and other similar mathematical symbols. Do not use a space before a % symbol.

5. Subscript and superscript fonts

Subscript and superscript text should be entered as such, (do not just create them by reducing the font size). These font types can be achieved using the subscript and superscript Font options on the Home Ribbon in Word.

D. Title Page

1. Date of Approval

Leave this blank in the final version. The date will be added before the final document is posted.

2. Proprietary Name

The proprietary name is the exclusive name the sponsor or distributor assigns to the drug product. It is commonly known as the trade name and may include trademarked and non-trademarked words. The proprietary name should match the product labeling. Use the proprietary name consistently throughout the FOI Summary.[12] Format the proprietary name as described in P&P 1243.3015.

3. Drug Product Established Name[13]

The drug product established name is the non-proprietary name of the drug product and may or may not include the route of administration and dosage form. Carprofen tablets and mebendazole oral suspension are some examples of product drug established names. To identify the drug product established name, refer to the product labeling.[14] Use the drug product established name consistently throughout the FOI Summary.

4. Dosage Form

The dosage form refers to the physical description of the approved manufactured product. For example, aerosol, enteric-coated capsule, cream, emulsion, granule, implant (pellets), infusion, inhalant, paste, soluble powder, solution for injection, suspension, chewable tablet, or Type A medicated article.

[12] For a product with an excessively long proprietary name, you may use a shortened proprietary name throughout the FOI Summary provided the full proprietary name (followed by the shortened name in parentheses) is used the first time the proprietary name appears.

[13] ONADE Policy: Drug Product Established Name for New Animal Drugs

[14] In some cases, the product established name as written on the labeling may be inconsistent. In these cases, refer to the ONADE Policy: Drug Product Established Name for New Animal Drugs or discuss with your TL.

For additional dosage form examples consult Appendix I of Guidance for Industry (GFI) #191.[15] If the dosage form is part of the proprietary name or drug product established name, do not include the dosage form line on the title page.

5. Species

   This section should identify the target animal to which the approval applies exactly as stated on product labeling, in the "Indications" section. Some approvals apply to a specific class within a species (e.g., Lactating Dairy Cows), and in this situation the specific class should also match the labeling. If there is no class limitation, enter the species in plain language (e.g., Cattle rather than Bovine, Dogs rather than Canine).

6. Indication(s) or Effect(s) of Supplement

   The indication(s) or effect(s) of supplement in the FOI Summary refers to the indications (for an original application) or changes (for a supplemental application) being approved in this application. For an original application, the indication(s) you include in the FOI Summary should be identical with those on the labeling. For supplemental applications, list the change(s) being approved (i.e., describe the new indication, new species, new route(s) of administration, new dosage(s), or label changes). The effect(s) of the supplement should be descriptive enough to identify which indication(s) and/or species are affected by the supplemental approval. For example, a supplemental NADA to reduce a withdrawal period from 7 to 0 days would read, "To reduce the withdrawal period from 7 to 0 days in turkeys." Another example may be "To replace the previously approved determinative and confirmatory procedures for cattle liver with new LC-MS/MS methods, addition of determinative and confirmatory procedures for cattle muscle, and inclusion of a tolerance of 10 ppb for drug X in cattle muscle. For the title page, you may paraphrase the indication(s) or effect(s) of supplement, if needed, to ensure that the indication(s) or the effect(s) of the supplement fit(s) on one page.

7. Sponsor's Name

   Copy the sponsor's name exactly as it appears in 21 CFR 510.600(c).

E. Executive Summary

This page will contain the final ES once completed. Boilerplate text is provided in the template if the ES is not complete at the time the Q submission is closed.

F. Header

The header will appear on all pages (except the cover page) of the FOI Summary. Double click in the header to insert the NADA number in place of <XXX-XXX>.

[15] GFI #191, Changes to Approved NADAs – New NADAs vs. Category II Supplemental NADAs

G. Table of Contents

The template automatically generates the Table of Contents (TOC). Only the first two heading levels should appear in the TOC.

After you complete the body of the FOI Summary, update the TOC headings and page numbers. To update the TOC, move the mouse cursor over one of the lines in the TOC and click the right mouse button. Select “Update Field” and choose “Update page numbers only.”

H. General Information

The FOI Summary’s General Information table should be identical to that in the Memorandum Recommending Approval (MRA), except the INAD number will not appear in the FOI Summary.

1. Sponsor, their address, Drug Labeler Code, and U.S. Agent

   If this is not the first approval for a sponsor, copy the sponsor name, address, and drug labeler code exactly as it appears in 21 CFR 510.600(c). Use the listing in the electronic CFR to obtain the most recent information.16 If this is a sponsor’s first approval, see your team leader for assistance.

   If the sponsor does not reside or have a place of business within the U.S., insert the name and address of the authorized U.S. agent.17 Delete the U.S. agent field if not applicable.

2. Proprietary Name(s) and Drug Product Established Name(s)

   These sections should be the same as described above for the title page.

3. Pharmacological Category

   This section describes the action of the drug product (e.g., anticoccidial, antimicrobial, or antiparasitic). Include the schedule if this is a controlled substance.

4. Dosage Form(s)

   Include the dosage form even if it is part of the proprietary name or drug product established name.

5. Amount of Active Ingredient(s)

   This section describes the amount of drug(s) per tablet, mL, percentage, or other measure of concentration. The amount should be expressed exactly as on product labeling, which may be on the basis of the active moiety, the active ingredient, or both.

[16] The electronic CFR (eCFR) provides the most up to date information. It is a different site than the online CFR, which is an electronic copy of the most recent printed CFR (issued in April of each year).

[17] 21 CFR §514.1(a).

6. How Supplied

   This section describes the size and description of the containers (e.g., 50- and 100-mL vials, 50 lb. bag).

7. How Dispensed

   This section identifies whether the marketing status is by prescription (Rx), over the counter (OTC), or veterinary feed directive (VFD).

8. Dosage

   This section describes the approved dose, frequency, and duration of treatment as printed on the approved labeling. Detailed dosage and administration information from the product insert (e.g., dosing tables provided for the convenience of calculating dosage) should not reside here. However, tables that provide information on different doses by weight bands, clarifying the amount of new animal drug to give or apply when there are multiple concentrations or tablet sizes/strengths approved for the new animal drug can be included here.

9. Route(s) of Administration

   This section describes the way to administer the product;[18] e.g., transdermal, immersion, implantation, inhalation, intramuscular injection, insertion, instillation, intramammary, intranasal, ocular, oral, otic, or topical. For additional examples of routes of administration, see GFI #191, Appendix II.

10. Species/Class(es)

    Some approvals apply to a specific class within a species (e.g., lactating dairy cows). If there is a specific class for the approval, include that information here. If there is no class limitation, enter the species in plain language (e.g., cattle rather than bovine, dogs rather than canine).

11. Indication(s)

    Copy the information for this section exactly from the labeling. For supplemental applications, if the supplement does not apply to a specific approved indication (e.g., a change in Acceptable Daily Intake [ADI]), include a statement that reads, “There was no change in the approved indications.”

12. Effect(s) of Supplement

    If this is a supplemental approval, this section should briefly describe the changes we are approving. For original approvals, delete this row from the General Information section.

[18] For an original approval, list all information. For supplemental NADAs, abbreviate the information to include only that to which the supplement applies, unless the currently approved information is needed to provide context. If you include all of the previously approved information with the new or modified information, then highlight (by bolding) the new or modified information so that the new or modified information is readily distinguishable.

I. Effectiveness

1. Introductory Paragraph

   You may insert an introductory paragraph before the dosage characterization section if it provides additional relevant information.

2. Dosage Characterization

   Dosage includes the dose or dose range, the dosing frequency, and the dosing duration. Sponsors do not have to demonstrate dosage characterization by substantial evidence. This section should provide a narrative summary of the individual studies, literature, or other information that explains how the dosage or dosage range was selected for further evaluation. When applicable, this section should also include a summary of the information provided to characterize the critical aspects of the dose relationship relevant to the dose or dose range selected, such as pharmacokinetic data. See Appendix 1 for recommended contents and formatting of study summaries. Identifying information for persons or companies who conducted the study(ies) should not be provided. For studies conducted outside the US, include the city, state/province (if provided by the sponsor), and country only. If you refer to published literature, list the reference citations at the end of this section.

3. Substantial Evidence

   This section describes the adequate and well-controlled effectiveness study(ies) and/or other information that support FDA's decision to approve the new animal drug. Use the study summary outline in Appendix 1. Check with your TL if you have questions about which studies to include in the FOI Summary.

   Identifying information for persons or companies who conducted the study(ies) should not be provided. List the city and state only. For studies conducted outside the US, include the city, state/province, and country only. If you include information in the FOI Summary from more than one study, use the same format to summarize each study. Summarize a multi-location field study for which study results are pooled to assess statistical significance as a single study.

   It is not necessary to describe all aspects of the study. The level of detail you provide should allow a general understanding of how each study was performed and the summarized results of each study. For example, if a study uses a 6- point scoring system to evaluate an endpoint, provide enough description so that readers who are not familiar with that scoring system can interpret numerical summaries in the results section.

4. Supplemental NADA Approval Information

   Some supplemental NADAs may not include dosage characterization information or new studies to demonstrate effectiveness, because they reference information from previous approvals. In these cases, use the language in the template, and include the NADA number and date of the FOI Summary that contains the information you reference.

J. Target Animal Safety

The Target Animal Safety section describes the safety study(ies) and/or other information that support FDA's decision to approve the new animal drug. Use the study summary outline in Appendix 1 of this guide. Check with your team leader if you have questions about which studies to include in the FOI Summary.

Identifying information for persons or companies who conducted the study(ies) should not be provided. List the city and state only. For studies conducted outside the US, include the city, state/province, and country only.

As with the effectiveness data, the level of detail you provide for each study should allow the reader to understand how each study was performed and to understand the results of each study. It is not necessary to describe all aspects of the study.

For supplemental NADAs that do not include new target animal safety studies, use the language in the template, and include the NADA number and date of the FOI Summary that contains the information you reference.

K. Human Food Safety (HFS)

1. Non-food Producing Animals

   If the product is for use in non-food producing animals, include the standard language in the template explaining that we did not require HFS data.

2. Food-Producing Animals

   If the product is for use in food-producing animals, include information for seven sections [Microbial Food Safety, Toxicology, Establishment of the Final ADI, Safe Concentrations for Total Residues (edible tissues and injection sites, if applicable), Residue Chemistry, and Analytical Methods for Residues], or provide the reason(s) a particular section(s) was (were) not pertinent to the approval. Use the study summary outline in Appendix 1. Check with your TL if you have questions about which studies to include in the FOI Summary. For supplemental approvals, include a reference to previous FOI Summaries, as appropriate.

   For supplemental applications that do not include HFS studies, use the language in the template, and include the NADA number and date of the FOI Summary that contains the information you reference.

   a. Microbial Food Safety (Antimicrobial Resistance)

      This section will describe the microbiology studies and/or information that support FDA's decision to approve the new animal drug. Use the study summary outline in Appendix 1. Identifying information for persons or companies who conducted the study(ies) should not be provided. List the city and state only. For studies conducted outside the US, include the city, state/province, and country only.

b. Toxicology

This section will describe the toxicology studies that support FDA's decision to approve the new animal drug. Use the study summary outline in Appendix 1. Identifying information for persons or companies who conducted the study(ies) should not be provided. List the city and state only. For studies conducted outside the US, include the city, state/province, and country only.

Other subheadings in this section identify the No-Observed Effect Level (NOEL)/No-Observed Adverse Effect Level (NOAEL) for Chronic Exposure and provide the calculation of the toxicological ADI and microbiological ADI, and Acceptable Single-Dose Intake (ASDI)/Acute Reference Dose (ARfD), if applicable, based on the toxicology studies.

c. Establishment of the Final ADI (and ARfD, if applicable)

The Toxicology Team will provide the text for this section.

d. Safe Concentrations for Total Residues in Edible Tissues and Injection Sites (if applicable)

The Toxicology Team will provide the text for this section. See earlier section on Formulas for instructions.

e. Residue Chemistry

This section will describe the residue chemistry studies that support FDA's decision to approve the new animal drug. Use the study summary outline in Appendix 1 of this guide. Identifying information for persons or companies who conducted the study(ies) should not be provided. List the city and state only. For studies conducted outside the US, include the city, state/province, and country only.

Other subheadings in this section identify the target tissue and marker residue, provide the tolerance assignments, and withdrawal period and/or milk discard time based on the residue chemistry studies.

f. Analytical Method for Residues

Describe the analytical method(s) in this section.

L. User Safety

Copy the human warnings exactly from the product labeling for this section, including steps to minimize the potential harm to humans handling, administering, or exposed to the new animal drug, and any contact information provided on the label. Human warning language may be found in multiple sections of the labeling, and it is at the discretion of the TAD reviewer which statements are appropriate for inclusion in the FOI summary.

M. Agency Conclusions

This section contains a summary of considerations involved in the approval of the subject drug. In this section:

1. Provide a detailed discussion of the basis for the approved marketing status (Rx, OTC, or VFD) for the product. For drugs with Rx and VFD status, list each substantial reason why adequate directions for laymen's use cannot be written. Appendix 2 contains sample language.

2. Note whether we granted exclusivity or not. Copy the appropriate boilerplate language from the exclusivity P&P into the FOI Summary (see P&P 1243.5780 to support the decision on granting exclusivity). The boilerplate language explains why we have or have not granted exclusivity. In some cases, the boilerplate language may not be appropriate; in such a case, you should contact the ONADE Policy Team.

3. If this is a supplemental application, identify whether the approval is a Category I or Category II change.[19] If this is an original NADA, delete this section of the template.

4. Patent information is not included in the FOI summary. This section should include boilerplate language that directs readers to the Animal Drugs @ FDA database, or the Green Book online.

N. Attachments

Do not attach labeling to the FOI summary. If applicable, attach the Determinative and Confirmatory Method.

IX. REFERENCES

Statutes

Federal Food, Drug, and Cosmetic Act

21 U.S.C. § 512, New animal drugs Freedom of Information Act

Freedom of Information Act

5 U.S.C. § 552, Public information, agency rules, opinions, records, and proceedings

Trade Secrets Act

18 USC U.S.C. § 1905, Disclosure of confidential information generally Code of Federal Regulations (Title 21)

Code of Federal Regulations (Title 21)

Part 20 – Public Information

[19] 21 CFR 514.106(b) defines the category change types.

§ 20.61, Trade secrets and commercial or financial information which is privileged or confidential

Part 299 – Drugs; Official Names and Established Names

§ 299.4, Established names for drugs

Part 510 – Sponsors of Approved Applications

§ 510.600, Names, addresses, and drug labeler codes of sponsors of approved applications

Part 514 – New Animal Drug Applications

§ 514.1, Applications

§ 514.8, Supplemental new animal drug applications

§ 514.11, Confidentiality of data and information in a new animal drug application file

§ 514.106, Approval of supplemental applications

CVM Program Policies and Procedure Manual – ONADE Reviewer's Chapter

1243.3010 - Format and Style Conventions for Letters

1243.3015 – Proprietary Names

1243.3030 - Completing Final Action Packages for Submission Tracking and Reporting System (STARS) Submissions

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

1243.5760 – Process for Preparing an Executive Summary for a Freedom of Information Summary

1243.5780 - Exclusivity and Exclusive Marketing Rights Boilerplate Language for Use the Following Documents: Memorandum Recommending Approval, Letter to Applicant, and Freedom of Information Summary

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

X. VERSION HISTORY

November 16, 2001 - ONADE Reviewers Manual revised and incorporated into CVM's Program Policy and Procedures Manual; this is the original P&P version.

September 7, 2006 - Revised to update and provide a standard outline format for an NADA FOI Summary using a template, and to reorganize the General Information Section of the NADA FOI Summary.

December 19, 2006 – Revised to correct typographical errors and modify format for Center-wide email announcement of approvals.

December 10, 2007 – Revised to make compatible with ADAA FOI and MRA and to remove information now contained in P&P 1243.3800 (i.e., preparing the Center-wide notification of approval).

March 6, 2008 – Revised to include instructions for using the most recent 356v to determine the established and proprietary name of a product and to clarify that if there is an animal class associated with the approval, that information is included on the Species line of the title page and in the general information table.

May 14, 2008 – Minor adjustments made in formatting of the document.

February 29, 2012 – Updated to conform to new processes resulting from electronic submission and review.

January 26, 2016 – Major updates made to provide Office-wide style recommendations to ensure consistency.

March 17, 2016 – Minor adjustments made in formatting of the document and minor edits to text.

June 27, 2016 – Minor formatting changes and redacting of internal information in the internet version.

September 14, 2016 - Minor edits to text and formatting change to the Appendix 1 outline.

July 3, 2017 – Updated bioequivalence table and redacted internal information for version that will be on the internet. Redactions appear as greyed out boxes.

August 29, 2018 – Updated Appendix 2 Marketing Status Information language to provide examples for Rx and VFD products.

April 5, 2019 – Updated to change the format for the study summary. Removing the underlining from the study summary outline in the appendix.

July 22, 2019 - Updated FDA.gov URL links to new directed links due to migration of new FDA.gov Website. No other updates needed.

February 13, 2020 – Updated to mention and reference the new process for preparing an executive summary for a Freedom of Information Summary.

June 25, 2020 - Updated all internal links for SharePoint sites because FDA has migrated this information to a new version of SharePoint.

August 5, 2020 – Revised language within Appendix 2. Marketing status to use the word ‘mitigate’ instead of the words ‘to slow or prevent’ or ‘reduce’ in the suggested wording for marketing status descriptions.

August 25, 2020 – Updated to direct to a new link in footnote number 8 for the HHS site 508 Checklist.

October 6, 2020 – Updated to include specific information on formatting the trademark symbols. Updated broken links and revised the Study Summary outline.

December 1, 2020 – Updated the Human Food Safety Section to match the language in the current FOI template.

January 26, 2021 – Updated information in section VIII C. 4. Scientific units of measurement and symbols to clarify information about inserting and formatting symbols within our documents.

July 12, 2022 – Quality systems review for minor formatting updates.

July 29, 2022 – Remove reference to retired CVM P&P 1240.2220.

January 18, 2023 – Section VIII. I. was updated to state for studies conducted outside the United States provide the information as to the state/province when that information is provided by the sponsor.

March 14, 2023 – Updated footnote 14 on page 11 to remove the mention the established name P&P, which is still in draft, and direct them to the ONADE policy on the established name.

March 29, 2023 – Updated the information on standards to reflect the office switch to Arial 11-point font as our standard font. 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.

August 15, 2023 – Updated to explain that we should not include active hyperlinks for web addresses and email addresses within our FOI. Reviewers are instructed to deactivate or remove hyperlinks but include the url or email address. All hyperlinks have been removed from letter templates and other templates because of potential maintenance issues.

APPENDIX 1. STUDY SUMMARY OUTLINE

Note: When summarizing a study, use the study summary outline formatting and headings below. Depending on the type of study, it may be more appropriate to combine outlined items under a single heading, or further expand a particular heading; in those cases, it is acceptable to modify the headings. It may also be appropriate to provide the study information in paragraph format rather than in outline format. Please note, this outline is intended to be left justified directly under the appropriate heading (Dosage Characterization, Toxicology, etc.).

Title: <Title. Written in title case.> <(Study No. XXXXXX)>

Study Date(s): Month YYYY <to Month YYYY, if needed> Note: Insert the study initiation date (i.e., the date the protocol was signed) and completion date (i.e., the date the study report was finalized) here. If day/DD is known, include it.

Study Location(s): <city, state/province, country>

Study Design: (examples provided, modify or delete as needed)

Objective: <description of study objective>

Study Animals: <number, breed/class, gender, age, weight, or other pertinent animal information>

Experimental Design: <general description of randomization, blocking, masking, treatment group assignments, and other pertinent information like which study standards were followed (GCP, GLP or OECD GLP)>

Drug Administration: <description of test and control articles, treatment group assignments, and dosage regimens>

Measurements and Observations: <decision variables and other (secondary) variables/observations; include brief description of study schedule; for food safety studies, include a brief description of the method used to analyze drug residues>

Statistical Method(s): <description of the statistical methods, if appropriate, otherwise delete>

Result(s): <tabular format and/or descriptive>

Adverse Reaction(s): <description of adverse reactions, or statement such as, “No adverse reactions were reported in this study.” This section does not apply to some studies, such as safety studies, in which case it can be deleted.>

Conclusion(s): <study conclusion(s), if appropriate, otherwise delete>

APPENDIX 2. MARKETING STATUS INFORMATION

Note: The options included below are boilerplate intended to address the majority of situations. If you believe you have a unique situation and need to create new language for an approval, speak with your team leader.

A. Prescription (Rx) products

This product may be dispensed only by or on the order of a licensed veterinarian (Rx marketing status). Adequate directions for lay use cannot be written because <Provide all reasons, for example, "professional expertise is required to properly administer the injection, provide adequate instructions for post treatment care, or to monitor the safe use of the product, including treatment of any adverse reactions.">

<For antimicrobial drugs intended for use in food-producing animals, also, discuss why professional supervision of a licensed veterinarian is needed. For example:

Option 1: This option is for a product that will be prescription because we are unable to write adequate directions for laypersons and there are antimicrobial resistance aspects that were part of the decision-making process. "This product may be dispensed only by or on the order of a licensed veterinarian (Rx marketing status). This decision was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this drug product, and because restricting this drug product to use by or on the order of a licensed veterinarian is critical for assuring the safe and appropriate use of this drug product in animals in order to mitigate the potential for development of bacterial resistance to antimicrobial drugs."

Option 2: This option is for a product that will be prescription because we are unable to write adequate directions for laypersons because there are specific reasons related to the drug product itself and there are antimicrobial resistance aspects that were part of the decision-making process.

"The decision to restrict this drug to use by or upon a lawful prescription (Rx) issued by a licensed veterinarian was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnosis and subsequently use this drug product, because <<[insert any non AMR reasons], and because>> use by or on the order of a licensed veterinarian assures safe and appropriate use of this drug to help mitigate the potential risk of bacteria developing resistance to this and other antimicrobial drugs.">

B. Over the Counter (OTC) products

This product can be marketed over the counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the label are reasonably certain to be followed in practice.

C. Veterinary Feed Directive (VFD) products

A valid veterinary feed directive (VFD) is required to dispense this drug. Any animal feed bearing or containing this drug will be fed to animals only by or on a lawful veterinary feed directive issued by a licensed veterinarian in the course of their professional practice. <State whether the VFDs for this drug are refillable. For example, "In addition, the veterinary feed directives issued for this drug are not refillable.">

Also, discuss why professional supervision of a licensed veterinarian is needed. For example, for antimicrobial drugs intended for use in food-producing animals:>

Option 1: This option is for a product that will be VFD because we are unable to write adequate directions for laypersons and there are antimicrobial resistance aspects that were part of the decision-making process.

The decision to restrict this drug to use by or upon a lawful veterinary feed directive issued by a licensed veterinarian was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnose and subsequently use this drug product, and because restricting this drug product to use by or on the order of a licensed veterinarian is critical for assuring the safe and appropriate use of this drug product and to mitigate the potential for development of bacterial resistance to antimicrobial drugs.

Option 2: This option is for a product that will be VFD because we are unable to write adequate directions for laypersons and there are antimicrobial resistance and human food safety aspects involved in the making of the decision.

The decision to restrict this drug to use by or upon a lawful veterinary feed directive issued by a licensed veterinarian was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnosis and subsequently use this drug product, because restricting this drug product to use by or on the order of a licensed veterinarian is critical for assuring the safe and appropriate use of this drug product in animals in order to mitigate the potential for development of bacterial resistance to antimicrobial drugs, and to ensure that edible tissue derived from animals treated with this drug product is safe with regards to human consumption.

Option 3: This option is for a product that will be VFD because we are unable to write adequate directions for laypersons because there are specific reasons related to the drug product itself and there are antimicrobial resistance and other aspects involved in the making of the decision.

The decision to restrict this drug to use by or upon a lawful veterinary feed directive issued by a licensed veterinarian was based on the following factors: adequate directions cannot be written to enable lay persons to appropriately diagnosis and subsequently use this drug product, because <insert any non AMR reasons>, and because restricting this drug product to use by or on the order of a licensed veterinarian assures safe and appropriate use of this drug to help mitigate the potential risk of bacteria developing resistance to this and other antimicrobial drugs.