OFFICE OF NEW ANIMAL PRODUCT EVALUATION REVIEWER'S CHAPTER

FREEDOM OF INFORMATION (FOI) SUMMARY FOR AN ANIMAL DRUG AVAILABILITY ACT (ADAA) MEDICATED FEED COMBINATION NEW ANIMAL DRUG APPLICATION

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I. PURPOSE

This document provides instructions for preparing a Freedom of Information (FOI) Summary for a new animal drug application (NADA; original or supplement) for medicated feeds combined as permitted under the Animal Drug Availability Act of 1996 (ADAA).[1] It also describes the information we include in the FOI Summary for approved ADAA feed combination NADAs and their supplements other than minor labeling supplements (see P&Ps 1243.6020 and 1243.6030).

II. RESTRICTIONS AND LIMITATIONS

Abbreviated (generic) new animal drugs, indexed listed drugs, and conditionally approved drugs cannot be part of a combination approval as described in the ADAA. Section 512(d)(4) of the Federal Food, Drug, and Cosmetic (FD&C) Act does not apply to applications for combinations of new animal drugs that are based on the previous, separate Section 512(b)(2) approvals of the new animal drugs to be used in the combination, i.e., generic new animal drug approvals. Specifically, Section 512(d)(4) states that the ADAA combination approval process may only be used for combination new animal drugs when "the active ingredients or drugs intended for use in the combination have previously been separately approved pursuant to an application submitted under Section 512(b)(1)." (Emphasis added)

Supplementing an approved ADAA combination cannot be automatically allowed in all circumstances. Adding an indication to the combination drug product a parent (single drug) drug product was supplemented is likely permissible. However, there are rare situations where such a scenario may trigger the withdrawal of the combination drug

[1] The ADAA established a streamlined approval process for certain combination new animal drugs that contain active ingredients or animal drugs that have previously been separately approved, including combinations intended for use in animal feed. See 21 CFR 514.4(c).

product. Adding an indication that is specific to the combination drug product rather than one of the parent drug products may not be possible.[2]

III. WHY DO WE NEED AN FOI SUMMARY?

An FOI Summary provides the public with a summary of the safety and effectiveness data on which we based our decision to approve an original NADA or supplement to an approved NADA. After approval of an original or supplemental NADA is published in the FEDERAL REGISTER, we are required to make a summary of "the safety and effectiveness data and information submitted with or incorporated by reference in the NADA file" among other things "immediately available for public disclosure." We must make this disclosure "unless extraordinary circumstances are shown".[3]

IV. WHAT ADAA MEDICATED FEED COMBINATION NADAS NEED AN FOI SUMMARY?

ONAPE prepares an FOI Summary for each approved original and supplemental (other than a minor labeling supplement) ADAA feed combination application.

V. WHO PREPARES AN FOI SUMMARY?

CVM prepares the final version of the FOI Summary.[4] Generally, a reviewer in the division responsible for reviewing target animal safety and effectiveness information is responsible for preparing the FOI Summary, but the preparer may be any individual designated by office, division, or branch procedures. For questions about who prepares the FOI Summary, consult with your Branch Chief (BC) or division director.

VI. GENERAL PRINCIPLES FOR FOI SUMMARIES

The FOI Summary is a scientific publication authored by CVM and made available to the public. Use the ONAPE ADAA FOI Summary template to prepare the final FOI. The document should be of consistent format and fully compliant with this P&P. See standard operating procedure 1243.000.007 for information on grammar standards. Any deviation 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 use the ADAA Feed Combination boilerplate language for the effectiveness, target animal safety, and human food safety sections. It should summarize effectiveness and safety data and other information used to decide or support label statements in sufficient detail so people reading the FOI

[2] If the supplemental application is for an indication that has not been added to one of the individually approved new animal drugs in the combination, discuss it with the Policy Branch.

[3] Although the regulations do not use the specific term "FOI Summary," FDA uses this term to describe the summary we prepare under 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 FOI Act.

[4] 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 technical section (under the INAD) or with a non-administrative original or supplemental NADA. It is ONAPE policy that we prepare the FOI Summary.

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. This should not be misconstrued to mean studies with negative findings should not be discussed in 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 technical section (TS) complete letter(s), then the 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, then the 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. Ensure that information included in the text matches that in the tables and the tabular values are arithmetically valid.

   d. 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.

   e. Ensure only the claim(s)/indication(s) that are being approved can be found in the FOI Summary. Occasionally, some divisions/branches 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 ‘chickens’, if CVM is only approving the use in ‘broiler chickens’).

4. Define acronyms and abbreviations (e.g., FDA, FD&C Act) the first time they appear in the document

   Once an acronym is defined, it is permissible for preparers of final FOI Summaries to use the acronym or abbreviation 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 referenced (i.e., refer to the FOI Summary for NADA XXX-XXX, dated DATE).[5] If the FOI Summary being referenced does not have a date, reference the appropriate FEDERAL REGISTER notice. If neither the FOI Summary nor a FEDERAL REGISTER are available, it may be appropriate to reference the CFR citation.

   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.[6] Construct draft FOI Summaries in Word using Section 508 compliance.[7]

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.[8] In addition, Federal law prohibits the disclosure of trade secrets submitted to FDA.[9] If you have questions regarding what information to include in the FOI Summary, discuss them with your BC and the Center's FOI Officer.

VII. PREPARING THE FOI SUMMARY DOCUMENT

A. Under the INAD (FOI Q Submission)

Note that the following processes do not apply to the preparation of FOI Summaries for ADAA combinations intended to be submitted as ADAA combination NADAs with a

[5] We use the date of the FOI Summary because it is most closely associated with the information being referenced. 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 approval letter (or FOI Summary) date.

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

[7] Information on 508 compliance at https://fda.sharepoint.com/sites/CVM-ONAPE-ORRP/508%20Compliance/Forms/AllItems.aspx

[8] See 5 USC §552(b)(4). 21 CFR 20.61.

[9] See section 301(j) of the FD&C Act and 21 CFR §20.61.

60-day review time frame. See P&P 1243.5730 for instructions for preparing the draft FOI Summary under the INAD for this subset of submissions.

1. Creating a Q submission

   A Q submission is an agency-initiated submission. It is a submission type we use 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 All Other Information (AOI) (M) submissions (see P&P 1243.3250). The PM will assign the FOI Summary Q to the appropriate target animal division (TAD) branch. The FOI Q will have the same due date as the M submissions.

2. Assembling the FOI Summary

   The Human Food Safety (HFS) consulting review(s) includes the relevant FOI Summary language for that section (or sub-sections). The TAD reviewer obtains a copy of this language for incorporation in the FOI Summary. TAD reviewers and others may make changes to address consistency and style differences at the FOI Summary Q submission stage. If portions of the FOI Summary written by the primary reviewer (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 PR may communicate with the sponsor and/or consulting reviewers informally before issuance of the letter for the Q submission to allow them to review the FOI Summary document.

   Note: The last major TS may impact the completion of the AOI and Labeling submissions, as well as the FOI Summary submission, because they are typically assigned the same due date. For example, if the last TS needed for the FOI Summary is HFS, then the HFS reviewer works with the TAD reviewer to ensure the FOI Summary is completed appropriately and on time.

3. Preparing the Q submission final action package

   Final out the Q submission following current procedures (see P&P 1243.3030). If we issue a TS complete letter (TSC) 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. Load the FOI Summary as a Word document (draft FOI Summary) in Appian; Appian will create a PDF copy to send 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. Sponsor requests for changes

   The FOI Summary is a CVM document intended 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. Therefore, there is no guarantee that the sponsor's proposed changes will be incorporated into the final FOI Summary.

   If the sponsor disagrees with FOI Summary language and/or requests substantive content changes that you determine will make the FOI Summary more accurate or identifies factual errors after a TSC letter is issued and any time before approval of the new animal drug, we may have to reopen the relevant TS. If the sponsor proposes minor editorial changes that you determine will make the FOI Summary more accurate or identifies factual errors, then they may be incorporated into the FOI Summary without the need to reopen relevant TS(s). 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.

B. Under the Administrative NADA

For administrative NADAs, review the FOI Summary that was prepared under the INAD FOI Q submission. Minor errors or editorial changes, as well as apparent factual errors to the HFS section should be flagged for discussion with the appropriate reviewer(s) in the Division of Human Food Safety (DHFS).

A copy of the complete FOI Summary is sent to the DHFS to review the HFS language in the FOI Summary. The DHFS reviewer makes any necessary edits to their portion of the FOI Summary. The DHFS reviewer also 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 documents any discussion, if appropriate, and the resultant changes to the above items in the review or MRA.

Once any applicable minor changes have been incorporated, the final version of the FOI Summary should be checked for compliance with Section 508. The final document should be included in Folder A of the electronic approval package (see P&P 1243.3800).

C. Under the 60-day Original ADAA Feed-use Combination NADA

For 60-day ADAA feed-use combination NADAs, begin to prepare the final FOI Summary document when you receive the application. Use the draft FOI Summary text prepared and agreed upon previously under the INAD to fill into the most updated version of the ADAA combination FOI Summary template. See P&P 1243.5730 for further information regarding when the NADA A-0000 submission is received ahead of the draft FOI Summary text being closed out under the INAD.

TAD reviewers and others may make changes to address consistency and style differences. Minor errors or editorial changes, as well as apparent factual errors to the HFS section should be flagged for discussion with the appropriate reviewer(s) in the DHFS.

A copy of the complete FOI Summary is sent to the DHFS 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 also 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 documents any discussion, if appropriate, and the resultant changes to the above items in the review or MRA.

Time permitting, you may share a copy of the complete draft FOI Summary with the sponsor and tell the sponsor that they may request changes to correct errors. Once any applicable minor changes have been incorporated, the final version of the FOI Summary should be checked for compliance with Section 508. The final document should be included in Folder A of the electronic approval package (see P&P 1243.3800).

D. Under the Non-Administrative (Traditional) NADA

For non-administrative (traditional) NADAs, begin to prepare the final FOI Summary document, using the ONAPE template for ADAA FOI Summaries, when you receive an application. Continue building the FOI Summary document as you and the applicable consulting reviewers complete your reviews of each TS.

If applicable, incorporate any FOI Summary language that was agreed upon previously under the INAD. If the HFS TS is reviewed under the NADA, the consulting reviewer(s) includes the HFS section of the FOI Summary as a part of their review. Minor errors or editorial changes, as well as apparent factual errors to the HFS section that you identify should be flagged for discussion with the appropriate reviewer(s) in the DHFS.

A copy of the complete FOI Summary is sent to the DHFS 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 also 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 documents any discussion, if appropriate, and the resultant changes to the above items in the review or MRA.

Time permitting, you may share a copy of your FOI Summary with the sponsor and tell the sponsor that they may request changes to correct errors. Once any applicable minor changes have been incorporated, the final version of the FOI Summary should be checked for compliance with Section 508. The final document should be included in Folder A of the electronic approval package (see P&P 1243.3800).

VIII. CONTENTS OF THE FOI SUMMARY

Use the ONAPE template for the ADAA Feed Combination NADA FOI Summary located on the ONAPE Reviewer’s Reference Page.

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 ADAA FOI Summary Template

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

2. Words in italics within carrot marks 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 carrots or content control fields, you will provide information relating to your specific application.

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

5. Use the ONAPE style elements to format documents.

    a. Use heading styles (e.g., Heading 2, etc.), to create headers (do not just change the font or use bolded text, except for 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 or notes that follow tables.

    c. Footnotes are preferrable to endnotes. Both provide the reader with additional information or references. Endnotes come at the end of the document. Footnotes, which are inserted using the Reference tab, Insert Footnote option, will be in 9-point font.

    d. If you need to insert a citation, using the References tab, select Insert Citation and confirm the style is set to APA style.

    e. Use the bullets and numbers features in Word to create accessible lists.

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 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, both of which should 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. Wherever possible, avoid merging cells within tables. However, if cells are merged, make sure the table is Section 508 compliant.

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 I.1. 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 (mcg/mL)	15.01†	14.39†	1.04	0.99	1.08
Cmax (mcg/mL)	4.22†	4.17†	1.01	0.94	1.09
Tmax (h)	1.10‡	1.36‡	NE§	NE	NE

* Ratio = Test/Reference
† Geometric mean
‡ Arithmetic mean
§ 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 size 11 font.

    b. When writing formulas, there should be a space between function symbols and components of the formula.

    Ex. 2xy – ab = 42

    c. 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)

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

$$= \text{0.01 mg/kg/bw/day} = \text{10 µg/kg bw/day}$$

    d. 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.[10]

        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.

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

v. Right click on the image and copy and paste the image into the desired location of the FOI. Alternatively, you can right click on the image, save the image, and insert it separately.

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 inserting the copyright and registered trademark symbols using the Symbol option, you must manually superscript them (i.e., $^{©}$ and $^{®}$) to have them in the correct format. It is our policy that, regardless of the presentation of the symbol in the proprietary on the label, we will always include it in superscript format in the documents we prepare. Consult the GPO Style Manual for correct abbreviations of units of measurement. Do not use a space between numbers and symbols (e.g., >0.5 +0.5, >0.5, P<0.05), except when writing formulas, equations, or cited text. 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 names

   The proprietary name is the exclusive name the sponsor or distributor assigns to the drug product. It is more commonly known as the trade name and may include trademarked and non-trademarked words. The proprietary name of a medicated feed combination should be comprised of the individual proprietary names of each drug included in the combination, with each proprietary name separated by an "and". The proprietary name used for each drug product should match the

approved Type A medicated article labeling and should be formatted as described in P&P 1243.3015. If the proprietary name for any individual drug product includes a strength (typically following the trademarked information), it should not be included as part of the medicated feed combination proprietary name. For example, the combination of Deccox®, ChlorMax 50™, and MGA® 200 would appear as "Deccox® and ChlorMax™ and MGA®". Also, the combination of Pennitracin MD 50G® and Coban™ 90 would appear as Pennitracin MD® and Coban™. The proprietary names of the individually approved drugs and of the combination should be used consistently throughout the FOI Summary.

3. Drug established names[11]

   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. The drug product established name of a medicated feed combination should be the individual established names of each drug product included in the combination and written with each drug product established name enclosed in parentheses and separated by the word "and". The established name used for each drug product should be the drug product established name on the approved Type A medicated article labeling. For example, the drug product established name for the combination of Deccox® and ChlorMax™ and MGA® would be "(decoquinate Type A medicated article) and (chlortetracycline Type A medicated article) and (melengestrol acetate Type A medicated article)." Use all lower-case letters, except in "Type A". The drug product established names should be used consistently throughout the FOI Summary.

4. Dosage form

   The dosage form for an ADAA medicated feed combination refers to the physical description of the approved single drug products. For ADAA medicated feed combinations, the dosage form will be Type A medicated articles to be used in the manufacture of Type B and Type C medicated feeds. (Note: if the approved combination does not/will not include one or more Type B medicated feed labels, then "Type B and" should not be included as part of the dosage form.)

5. Species[12]

   This section should identify the target animal to which the approval applies exactly as stated on combination Type C medicated feed label(s) in the Indications section. Some approvals apply to a specific class within a species (e.g., lactating dairy cattle), and in this situation, the specific class should also match the labeling. 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).

[11] SOP 1243.130.003: Determining the Active Ingredient, Dosage Form, Route of Administration, and Product Established Name for New Animal Drugs

[12] Terminology used for food producing species should match the terminology presented in GFI #191.

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 the application.

   For an original ADAA medicated feed combination application, use the statement "Original approval of an Animal Drug Availability Act of 1996 (ADAA) feed combination for the indication(s) listed in Section I.L." The indication(s) will be identified in Section I.L. of the FOI Summary.

   For supplemental applications, the change(s) being approved should be listed. If a new indication is being included, the statement "Supplemental approval of an Animal Drug Availability Act of 1996 (ADAA) feed combination for the indication(s) listed in Section I.L.", and the new indications should be identified in section I.L. of the document. If the supplemental approval includes a new indication(s) and other changes, the statement may be modified to include this information as well. If the supplemental approval does not affect the indication, then the effects of the supplement should be described. The effect(s) of supplement should be descriptive enough to identify which indication(s) and/or species are affected by the supplemental approval. E.g., a supplemental NADA to reduce a withdrawal time in turkeys from 7 to 0 days would read "To reduce the withdrawal time from 7 to 0 days in turkeys." For the title page, you may paraphrase the effect(s) of supplement, if needed, to ensure that the effect(s) of supplement fits on one page.

7. Sponsor's name

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

E. 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 the content control field for Document Number.

F. Table of Contents

The template automatically generates the Table of Contents (TOC). Only the first two heading levels will 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 entire table.

G. 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.[13] If this is a sponsor's first approval, see your BC 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.[14] Delete the field if it is not applicable.

2. Proprietary Names and Drug Product Established Names

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

3. Pharmacological Categories

   This section describes the action of the drug product (e.g., anticoccidial, antimicrobial, or antiparasitic). The schedule should be included if it is a controlled drug substance.

4. Dosage Form

   This section should be the same as described above for the title page.

5. Amount of Active Ingredients in Currently Marketed Products

   This section describes the amount of drug per pound (g/lb) in the Type A medicated articles for each drug product in the combination. The amount should be expressed exactly as on the currently marketed product labeling, which may be based on the active moiety, the active ingredient, or both. If there are several approved levels of the active ingredient (i.e., multiple Type A medicated article labels with different drug strengths), those that are not marketed at the time of the approval should not be listed in the FOI Summary.

6. How Supplied

   This section describes the size(s) and description(s) of the currently marketed Type A medicated articles for each drug product in the combination (e.g., 50 lb bag).

7. Dispensing Status

   This section identifies whether the drug product is dispensed over the counter (OTC) or as a veterinary feed directive (VFD) drug.

8. Route of Administration

   This section describes the way to administer the drug product. For ADAA medicated feed combinations, this will be "Oral."

9. Species/Class(es)

   This section should be the same as described above for the title page.

[13] The electronic CFR (e-CFR) 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).

[14] 21 CFR §514.1(a).

10. Indication(s) and Dosage Regimen(s)

Copy the indication(s) for this section exactly from the combination Type C medicated feed labeling. In some cases, there may also be a Type C medicated feed label for an individual drug product that is included as part of the medicated feed combination approval (e.g., use of MGA as a top dress). As needed, this section should include information from both the individual and combination Type C labels, along with appropriate instructions for use.

Directly below each individual indication, the approved dose to be used in the combination and the indication associated with that dose should be provided for each of the individually approved drug products contributing to the combination indication.

Following the individual drug product dose and indication, the frequency and duration of use information for the combination product should be included (i.e., as printed on the Type C medicated feed labeling). For example, the indication and dosage information for the combination of Deccox® and ChlorMax™ and MGA® for beef heifers fed in confinement for slaughter would be written as:

"1. For the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*; for the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline; and for increased weight of rate gain, improved feed efficiency, and suppression of estrus (heat) in beef heifers over 700 pounds fed in confinement for slaughter.

a. 27.2 g/ton of Deccox® for the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*.

b. 0.5 mg/lb of BW/day of ChlorMax™ for the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline.

c. 0.25 to 0.5 mg/head/day of MGA® (administered at 0.5 to 2.0 lb/head/day of medicated feed containing 0.125 to 1.0 mg melengestrol acetate per pound) for increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).

Feed as the sole ration.

2. For the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii*; for the treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline; and for increased weight of rate gain, improved feed efficiency, and suppression of estrus (heat) in beef heifers fed in confinement for slaughter.

a. 27.2 g/ton of Deccox® for the prevention of coccidiosis in cattle caused by *Eimeria bovis* and *E. zuernii*.

b. 10 mg/lb of BW/day of ChlorMax™ for the treatment of bacterial enteritis caused by *Escherichia coli* and bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline.

c. 0.25 to 0.5 mg/head/day of MGA® (administered at 0.5 to 2.0 lb/head/day of medicated feed containing 0.125 to 1.0 mg melengestrol acetate per pound) for increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat).

Feed as sole ration for no more than 5 days."

For an original approval, list all indications (repeating the above list of information for each unique Type C medicated feed label). For supplemental NADAs, you may abbreviate the list to include only the indication(s) to which the supplement applies. If you include all of the previously approved indications with the new or modified indications, then highlight (by bolding) the new or modified indications so that the new or modified indications are readily distinguishable. In the rare instance that the supplement does not apply to a specific approved indication (e.g., a change in withdrawal period or feeding directions), include a statement that reads, "There was no change in the approved indications."

If there are overlapping indications and effectiveness studies were not conducted to show an increased effect as a result of combining the drug products in combination, then the boilerplate paragraph pertaining to overlapping indications should be included immediately following the frequency and duration of use information for the combination product. For example, if drug product 1 has an indication for improved weight gain and feed efficiency and drug product 2 has an indication for improved weight gain and suppression of estrus), the paragraph would state, "Approval of this combination indication did not require a demonstration of increased effectiveness for improved weight gain when Drug Product 1, Drug Product 2, and Drug Product 3 are used together vs. individually. Therefore, an increased benefit should not be assumed.

11. Effect(s) of Supplement

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

H. Effectiveness and Target Animal Safety[15,16]

After the introductory boilerplate paragraph, use the table provided in the template to describe for each drug product: the drug product proprietary name, the sponsor, the approved indication(s) brought to the combination from the drug product, the approved NADA number, the public notification of the approval (ideally the date of the FOI Summary should be included, but if not available the FR Notice information may be included; if neither the FOI or FR notice are available, cite the CFR citation), and

[15] An ADAA feed combination NADA approval generally does not require effectiveness or target animal safety studies. For a feed combination NADA that requires effectiveness or target animal safety data or information, discuss the format of the FOI Summary with your BC, as it may be necessary to use elements from both the NADA FOI Summary (see P&P 1243.5761) and this document.

[16] In rare cases, the preparation of an executive summary (ES) for an ADAA Medicated Feed Combination may be needed. The PR, in consultation with division and ONAPE management, determines whether an ES should be prepared. If there is agreement on the preparation of an ES, the PR drafts the ES with the other sections of the FOI Summary.

the NADAs to which the sponsor of the combination drug product has right of reference (if the application refers to NADAs held by other sponsors).

I. Human Food Safety (HFS)

1. Non-food-producing animals

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

2. Food-producing animals

   If the combination drug product is for use in food-producing animals, include the appropriate sections listed here after the introductory ADAA Feed Combination boilerplate paragraphs, or provide the reasoning for any sections that are not considered pertinent to the approval.

   a. Microbial Food Safety

      Use the appropriate language provided in the template.

   b. Toxicology

      Use the appropriate language and table provided in the template.

   c. Residue Chemistry

      The Summary of Residue Chemistry Studies section describes the residue chemistry studies that support FDA's decision to approve the new animal drug. Sequentially number and individually describe each study using the study summary outline in Appendix 1 of this guide. Identifying information for the 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.

   d. Analytical Method for Residues

      Describe the analytical method(s) in this section. Use the language provided in the template, as applicable.

J. User Safety

Copy the human warnings or user safety information from the labeling including steps to minimize potential harm to humans handling, administering, or exposed to the new animal drug. Do not include the contact information provided on the label. Note that human warning language may be found in a section called Human Warnings and/or 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.

If there is no user safety information on the label, include the statement "The labeling does not contain user safety information." in the User Safety section of the FOI. Do not delete the section.

K. Agency Conclusions

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

- Provide a detailed discussion of the basis for the approved marketing status (OTC or VFD) for the combination drug product.[17] For drugs with VFD status, list each substantial reason why adequate directions for laymen's use cannot be written. Appendix 2 contains sample language.
- Note whether we granted exclusivity or not. Exclusivity does not usually apply to ADAA combination approvals. In the rare case where we grant exclusivity, use the appropriate statement from P&P 1243.5780.
- If this is a supplemental application, identify whether the approval is a Category I or Category II change. If this is an original NADA, delete this section of the template.
- 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.

L. 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. § 301, Prohibited acts

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

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

Trade Secrets Act

18 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

[17] See P&P 1240.2220 for further information about classification of OTC and Rx drugs.

§ 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 Policies and Procedures Manual

1240.2220 - Classification of OTC and Rx Drugs

CVM Policies and Procedures Manual – ONAPE 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

1243.3250 – Q Submissions – Agency-Initiated Actions

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

1243.5730 – Review of 60-day Original Animal Drug Availability Act of 1996 (ADAA) Feed Use Combination NADA 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 in 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 Labeling Supplements (NL Subclass)

1243.6030 - Review of Labeling Changes in Manufacturing Supplements

ONAPE Standard Operating Procedures

1243.000.007 – Grammar Standards

X. VERSION HISTORY

November 16, 2001 – Original P&P version

December 10, 2007 – Revised to update and provide a standard outline format for an ADAA feed combination NADA FOI Summary using a template.

March 7, 2008 – Revised to include instructions for using the most recent 356V to determine the established 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. December 4, 2008 – Minor revisions made to document format.

August 29, 2018 - This document has been updated to incorporate changes introduced as a result of the ADUFA IV Goal of reviewing original ADAA feed-use combination NADA applications within 60 days. The new processes associated with these submission types should not be implemented prior to October 1, 2018.

April 8, 2019 – This document has been updated to incorporate changes to reflect changes made to the ADAA FOI Summary Template and provide example Marketing Status Language for OTC and VFD products (Appendix 2).

April 17, 2019 – Corrected the formatting information presented in the established name section to indicate how the drug product established names in the combination should be written.

August 06, 2019 – Updated FDA.gov URL links to new directed links due to migration of new FDA.gov Website. No other updates are needed.

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

June 24, 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.

September 23, 2020 – Updated to include specific information on formatting the trademark symbols.

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.

April 7, 2021 – Updated to fix some grammar and spelling errors. Updated language in multiple sections of the P&P for clarity.

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

March 30, 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.

April 5, 2024 – Updated to reference the SOP 1243.000.007 in section VI. The SOP provides information on grammar standards for final action packages that undergo a quality control review by the Quality Assurance Team. Revised section VIII. C. 3. to update information on hyperlinks to indicate active links should not be included in the FOI, but the full URL should be included. The document was put into the current template and format and other formatting and other minor edits made.

August 5, 2024 – Updated to revise format and grammar information. Revised reference to SOP 1243.000.007 to reflect its revised title. Updated the User Safety section to indicate the section should never be deleted and include instructions as to what to put in that section if there is no user safety information in the labeling.

August 7, 2026 – Revised Section VIII.D.2 to add additional examples of formatting for ADAA combo proprietary names that include the product strength. Revised to state that if cells are merged, make sure the table is Section 508 compliant. Revised to state that the symbol in proprietary names should be included in superscript format regardless of the presentation of the symbol on the label to be consistent with P&P 1243.3015. Revised to state that space should not be used between numbers and symbols except when writing formulas, equations, or cited text to be consistent with SOP 1243.000.007. Revised to indicate to choose to update the entire table when updating the Table of Contents so that the headings and page numbers can be updated. Revised to reflect the reorganization of the Office of New Animal Drug Evaluation (ONADE) into the Office of New Animal Product Evaluation (ONAPE). Changed all references from team leaders to branch chief and updated to reflect the other organizational and title changes. Changed references from shaded areas to content control fields templates.

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 the 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

A. 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.

B. VFD Products

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, consult your BC.

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 HFS 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.