
OFFICE OF NEW ANIMAL DRUG 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 (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.²

II. RESTRICTIONS AND LIMITATIONS

Use of this document presumes that the decision to approve a new animal drug combination application under the authority of the ADAA was appropriate. For the reader looking for help in making this decision, please consult with your managers and the Office of New Animal Drug Evaluation's Policy Team. The few brief points below may help direct your query.

Abbreviated new animal drugs (generic), 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 Act (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

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).

² See P&P 1243.6020 and 1243.6030 for information on minor labeling supplements.

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 automatically be allowed in all circumstances. Adding an indication to the combination drug product because one of the parent (single drug) drug products was supplemented is likely permissible.

However, there are rare situations where such a scenario may trigger the withdrawal of the combination drug product. Adding an indication that is specific to the combination drug product rather than one of the parent drug products may not be possible.³

III. 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 or a supplement to an approved new animal drug. After we publish an approval of an original or supplemental NADA 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".⁴

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

ONADE 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 will prepare the final version of the FOI Summary.⁵ Generally, a reviewer in the division responsible for reviewing target animal safety and effectiveness information will be responsible for preparing the FOI Summary, but the preparer may be any other individual designated by office, division, or team procedures. If the reviewer has questions about who prepares the FOI Summary, they should consult with their team leader 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 ONADE ADAA FOI Summary template to prepare the final FOI. The

³ 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 Team.

⁴ 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 Freedom of Information Act.

⁵ 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 ONADE policy that we prepare the FOI Summary.

document should be of consistent format and fully compliant with this P&P. 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 to show the basis on which the agency approved the NADA. Be clear and accurate.

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 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. Make sure 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/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 'chickens', if CVM is only approving the use in 'broiler chickens').

4. Define acronyms 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 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).⁶ If the FOI Summary being referenced does not have a date, reference the appropriate FEDERAL REGISTER notice. If neither the FOI Summary or a FEDERAL REGISTER are available, it may be appropriate to reference the CFR citation.

6. Use plain language

The purpose of the FOI Summary is to explain the basis for the approval to the public. Write it using plain language [www.plainlanguage.gov].

7. Section 508 compliance

The final FOI Summary must be Section 508 compliant.⁷ You should construct draft FOI Summaries in MS Word using Section 508 compliance.⁸

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.⁹ In addition, Federal law prohibits the disclosure of trade secrets submitted to FDA.¹⁰ If you have questions regarding what information to include in the FOI Summary, discuss them with your team leader and the Center's FOI Officer.

⁶ 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.

⁷ HHS Section 508 Accessibility checklists at <https://www.hhs.gov/web/section-508/making-files-accessible/checklist/html/index.html>

⁸ For information on 508 compliance see the ONADE Review Aids Library in SharePoint
Internal information redacted

⁹ See 5 USC §552(b)(4). 21 CFR 20.61.

¹⁰ See section 301(j) of the Federal Food, Drug, and Cosmetic and 21 CFR §20.61.

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 original ADAA combination NADAs with a 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 project manager (PM) will create a "Q" submission under the INAD when the sponsor submits their labeling and/or AOI ("M") submissions.¹¹ The PM will assign the FOI Summary "Q" to the appropriate target animal division team. The FOI "Q" will have the same due date as the "M" submissions.

2. Assembling the FOI Summary

The Human Food Safety consulting review(s) should include the relevant FOI Summary language for that section (or sub-sections). The TAD reviewer should obtain 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 incorporate or reference the consulting review, or if changes are made to the language provided by the consulting reviewers, the primary reviewer should work with the consulting reviewer to make sure that the language is acceptable.

If time permits, the primary reviewer 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.

Reviewers should be aware that the last major technical section 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 last technical section needed for the FOI Summary is Human Food Safety, the Human Food Safety reviewer should work with the target animal division reviewer to ensure the FOI Summary is completed appropriately and on time.

¹¹ See the STARS Forms page for the Agency Initiated Submission Request Form.

3. Preparing the "Q" submission final action package

Reviewers should final out the "Q" submission following current procedures.¹² If we issue a TSC letter for the last technical section (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 an MS 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 technical section, your review should state that we could not complete the "Q" submission because we could not issue a TSC letter for the last technical section. 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 technical section. 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 technical section.

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 technical sections.

¹² See P&P 1243.3030

If the sponsor requests changes that result in the reopening of a technical section 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, you should 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 Human Food Safety section should be flagged for discussion with the appropriate reviewer(s) in the Division of Human Food Safety.

A copy of the complete FOI Summary should be sent to the Division of Human Food Safety to review the Human Food Safety language in the FOI Summary. The Division of Human Food Safety will review and make any necessary edits to their portion of the FOI Summary. The Division of Human Food Safety reviewer also should inform the primary reviewer 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 primary reviewer should document 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 for additional instructions for preparing and routing the approval package.

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

For 60-day original ADAA feed use combination NADAs, you should begin to prepare the final FOI Summary document when you receive the application. You should use the draft FOI Summary text prepared and agreed upon previously under the INAD to fill in 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 Human Food Safety section should be flagged for discussion with the appropriate reviewer(s) in the Division of Human Food Safety.

A copy of the complete FOI Summary should be sent to the Division of Human Food Safety to review the Human Food Safety language in the FOI Summary. The Division of Human Food Safety will review and make any necessary edits to their portion of the FOI Summary. The Division of Human Food Safety reviewer also should inform the primary reviewer 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 primary reviewer should document 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 for additional instructions for preparing and routing the approval package.

(Note: the process for review of original ADAA feed use combination NADAs within 60 days is currently underway. Anything related to or tied to that process may be revised during the beta test and upon completion of the beta test phase.)

D. Under the Non-administrative (traditional) NADA

For non-administrative (traditional) NADAs, you should begin to prepare the final FOI Summary document, using the ONADE 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 technical section.

If applicable, incorporate any FOI Summary language that was agreed upon previously under the INAD. If the Human Food Safety technical section is reviewed under the NADA, the consulting reviewer(s) will the Human Food Safety section of the FOI Summary as a part of their review.

Minor errors or editorial changes, as well as apparent factual errors to the Human Food Safety section that you identify should be flagged for discussion with the appropriate reviewer(s) in the Division of Human Food Safety.

A copy of the complete FOI Summary should be sent to the Division of Human Food Safety to review the Human Food Safety language in the FOI Summary. The Division of Human Food Safety will review and make any necessary edits to their portion of the FOI Summary. The Division of Human Food Safety reviewer also should inform the primary reviewer 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 primary reviewer should document 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 for additional instructions for preparing and routing the approval package.

VIII. CONTENTS OF THE FOI SUMMARY

Use the office template for the ADAA Feed Combination NADA FOI Summary. Instructions for finding and using templates are located on the ONADE Reviewer's Reference Page under Review Aids/Approved Products on the ONADE Templates 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 brackets (i.e., < >) in the FOI Summary are boilerplate and should be included in the 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, you will provide information relating to your specific application.
4. Consider using active voice instead of passive voice whenever prudent.
5. Use the ONADE 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, except for the study summary outline as shown in Appendix 1).
 - b. Use Normal style font set to Verdana size 10 for regular text including Table text and footnotes.
 - c. Use the bullets and numbered lists feature in MS 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 Human Food Safety 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, 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 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	12
1	78	60	138
1	NA†	26.05	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	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.
 - 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)

$$\begin{aligned}
 \text{ADI} &= \frac{\text{NOEL}}{\text{Safety Factor}} = \frac{2.1 \text{ mg/kg bw/day}}{200} \\
 &= 0.01 \text{ mg/kg/bw/day} = 10 \text{ } \mu\text{g/kg bw/day}
 \end{aligned}$$

- 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.
 - 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.
 - 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. Web addresses must be active hyperlinks (use Insert Hyperlink function on the "Insert" ribbon in MS Word).
- b. Use the entire URL (<http://www.fda.gov>, and NOT www.fda.gov).

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., $\mu\text{g/mL}$, $^{\circ}$). For example, do not use micrograms/mL or a superscript letter 'o' for the degree symbol. All symbols should be inserted using the Symbol option on the "Insert" ribbon in MS Word and should be in Verdana font. The copyright and trademark mark symbols should be superscripted © and TM. Consult the GPO Style Manual for correct abbreviations of units of measurement.

Use a space before and after $<$, \leq , $>$, \geq , $=$, 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 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[®]".

The proprietary names of the individually approved drugs and of the combination should be used consistently throughout the FOI Summary.

3. Drug product established names¹³

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 "(decoquinatate 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

¹³ ONADE Policy: Drug Product Established Name for New Animal Drugs at Internal information redacted

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. Species¹⁴

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).

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 or changes 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 supplement is approving includes a new indication(s) and plus other changes (i.e. different or additional us of a new species, new route(s) of administration, new dosage(s), or label changes), the statement may be modified to include this information as well. If the supplemental approval is 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. For example, 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

¹⁴ Terminology used for food producing species should match the terminology presented in GFI #191, Changes to Approved NADAs – New NADAs vs. Category II Supplemental NADAs
<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-191-changes-approved-nadas-new-nadas-vs-category-ii-supplemental-nadas>

paraphrase the effect(s) of supplement if needed, to ensure that the effect(s) of 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. 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>.

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 page numbers only."

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.¹⁵ 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.¹⁶ 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.

¹⁵ 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).

¹⁶ 21 CFR §514.1(a).

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.

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

Copy the indication(s) for this section exactly from the combination Type C medicated feed labeling (or Type B medicated feed labeling, if the approval is to only approve the combination for use in Type B medicated feed). 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 weight of rate 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 weight of rate 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 you should 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), you should 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 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 should briefly describe the changes we are approving. For original approvals, you should delete this row from the General Information table.

H. Effectiveness and Target Animal Safety¹⁷

After the introductory boilerplate paragraph, include an Executive Summary (if needed per current ONADE Policy) and 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 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

1. Non-food producing animals

If the combination drug product is for use in non-food producing animals, then include the standard language, Executive Summary (if needed per current ONADE Policy), and table in the template explaining that we did not require human food safety 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 and Executive Summary (if needed per current ONADE Policy), 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 should describe the residue chemistry studies that support FDA's decision to approve the new animal drug. You should sequentially number and individually describe each study using the study summary outline in Appendix 1 of this guide.

¹⁷ 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 team leader, as it may be necessary to use elements from both the NADA FOI Summary (P&P 1243.5761) and this document.

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.

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 exactly from the Type B and/or Type C medicated feed 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 labeling. Human warning language may be found in multiple sections of the labeling, and it is the discretion of the target animal division reviewer which statements are appropriate for inclusion in the FOI Summary.

K. Agency Conclusions

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

In this section, you should:

- Provide a detailed discussion of the basis for the approved marketing status (OTC or VFD) for the combination drug product.¹⁸ 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.

¹⁸ See P&P 1240.2220 for further information about classification of OTC and Rx drugs.

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- 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 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

§ 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 Policy and Procedures Manual

1240.2220 - Classification of OTC and Rx Drugs

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

1243.5730 – Review of 60-day Original Animal Drug Availability Act of 1996 (ADAA) Feed Use Combination NADA Applications

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

1243.6020 - Review of New Animal Drug Application (NADA) and Abbreviated New Animal Drug Application (ANADA) Labeling Supplements (NL Subclass)

1243.6030 - Review of Labeling Changes in Manufacturing Supplements

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 needed.

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.

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

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

Objective: <description of study objective, include which study standards were followed (GCP, GLP or OECD GLP).>

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

Experimental Design: <general description of randomization, blocking, masking, treatment group assignments, and other pertinent information>

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, speak with your team leader.

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 slow or prevent any potential for the 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 slow or prevent any potential for the 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 reduce the risk of bacteria developing resistance to this and other antimicrobial drugs.