
OFFICE OF NEW ANIMAL PRODUCT EVALUATION REVIEWER'S CHAPTER

**REVIEW OF 60-DAY ANIMAL DRUG AVAILABILITY ACT OF 1996 (ADAA) FEED USE
COMBINATION NEW ANIMAL DRUG APPLICATIONS (NADAs)**

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I. PURPOSE

This document describes how the Office of New Animal Product Evaluation (ONAPE) evaluates and processes Animal Drug Availability Act (ADAA) feed use combination new animal drug applications (NADAs) that may qualify for a reduced 60-day review timeline, including how to:

- determine the eligibility of an ADAA feed use combination NADA for the 60-day review process;
- determine the required documents that we need to receive from the sponsor and those we will prepare under the investigational new animal drug (INAD) file before the ADAA feed use combination NADA can be submitted;
- review an ADAA feed use combination NADA within the 60-day timeline; and
- review an ADAA feed use combination NADA that initially qualifies for a 60-day review timeline but requires additional changes such that the timeline is increased to 100 or 180 days.

II. BACKGROUND AND SCOPE

As part of the Animal Drugs User Fee Act (ADUFA) IV reauthorization,¹ effective October 1, 2018, the Center for Veterinary Medicine (CVM) agreed to reduce the review timeline from 180 to 60 days for eligible ADAA combination drugs used in or on animal feeds submitted as original NADAs filed under section 512(b)(1) of the Federal Food, Drug, and

¹ As captured in 82 FR 49380, dated October 25, 2017. Language from the ADUFA IV reauthorization and draft recommendations that applies to the review of 60-Day ADAA combination NADA applications are captured in Appendix 1 of this document.

Cosmetic Act (FD&C Act). In 2025, CVM agreed to permit eligible supplemental NADAs to qualify for the 60-day process.

If a proposed ADAA NADA qualifies for the 60-day process, as described in Section III below, then ONAPE will complete the review of the Environmental Impact (EI) and Labeling technical sections under the NADA within a 60-day timeframe rather than the traditional 180-day timeframe. During this time, ONAPE will also prepare the final Freedom of Information (FOI) Summary.

This process differs from the administrative NADA process, which also has a 60-day timeframe. In the administrative NADA process, all technical sections must be complete under the INAD file prior to submission of the NADA.

III. ELIGIBILITY OF AN ADAA FEED USE COMBINATION FOR A 60-DAY REVIEW TIMELINE

An NADA for an ADAA feed use combination is eligible for a 60-day review timeline when the following conditions are met and the application, as submitted, is both complete and accurate. These criteria are tightly aligned with the agreed upon language provided in the ADUFA IV reauthorization and are formally assessed when the NADA is submitted. When the sponsor establishes the INAD for the ADAA feed use combination, CVM considers the applicability of these criteria to the future NADA and may discuss any potential issues with the sponsor.

1. The ADAA feed use combination NADA is a non-administrative original NADA (submission code A); a non-administrative B1 supplemental NADA (submission code C); or reactivations of these submission types.
2. The combination is administered in or on animal feed. Combinations administered via drinking water or any other dosage form are not eligible for the 60-day review timeline.
3. Each new animal drug included in the proposed feed use combination has been **previously and separately approved** under section 512(b)(1) of the FD&C Act for the particular uses and conditions of use² for which they are intended in the combination. The requirement that the animal drugs be approved under section 512(b)(1) **excludes** generic animal drugs from consideration, as they are approved under section 512(b)(2) of the FD&C Act. It also **excludes** conditionally approved animal drugs, as they are approved subject to section 571 of the FD&C Act.
4. Each new animal drug is different from all other animal drugs in the proposed feed use combination and provides appropriate concurrent use for the intended target animal population.
5. The feed use combination contains no more than one antibacterial.³

² Conditions of use may include, but are not limited to, the indication(s), dose, duration, frequency, and species or classes of species.

³ 21 CFR 514.4(c)(1)(iii) excludes the classification of ionophores and arsenicals as antibacterials for the purposes of their inclusion in an ADAA combination in animal feed or drinking water.

6. Each active ingredient or new animal drug is intended for at least one use that is different from all other active ingredients or new animal drugs in the feed use combination (i.e., each individual drug brings a unique indication to the combination).
7. A presubmission conference (PSC) to discuss the approval requirements for the combination was held under the INAD opened specifically for the ADAA feed use combination and resulted in a PSC memorandum of conference (MOC) and/or an early response letter (ERL) issued to the sponsor. A copy of this MOC and/or ERL needs to be included in the future ADAA feed use combination NADA submission. The MOC and/or ERL should confirm which technical sections are satisfied (review of information or data to support a technical section is not required). If the review of information or data, other than as noted below, is required to support a technical section, then that information should have been reviewed under the INAD for the combination (as a P submission) and a technical section complete letter issued.
8. Specifically, for Human Food Safety (HFS) either:
 - a. no data are needed (no tissue residue non-interference⁴ study is required) and this agreement is documented in the MOC and/or ERL for the PSC; or
 - b. a justification for not conducting a tissue residue non-interference⁴ study was submitted, reviewed, and found acceptable under an INAD, before the submission of the ADAA feed use combination application; or
 - c. a tissue residue non-interference⁴ study was submitted, reviewed, and found acceptable under an INAD, before the submission of the ADAA feed use combination application.
9. Specifically, for Chemistry, Manufacturing, and Controls (CMC):
 - a. Feed Assay Methods, either:
 - i. A justification for not conducting a feed assay method non-interference study was submitted, reviewed, and found acceptable under an INAD before submission of the ADAA feed use combination application (e.g., feed assay method non-interference data were submitted under the individually approved Type A medicated articles); or
 - ii. A feed assay method non-interference study was submitted, reviewed, and found acceptable under an INAD before submission of the ADAA feed use combination application.
 - b. Feed Mixing Studies:
 - i. For combinations in dry medicated feeds, a justification for not conducting homogeneity, non-segregation, and stability studies for the combination medicated feed was submitted, reviewed, and found acceptable under an INAD before submission of the ADAA feed use combination application [e.g., no new data required because the combination medicated feed contains each

⁴ Non-interference refers to whether any active ingredient or drug intended for use in the combination exceeds its established tolerance at the longest withdrawal time of any of the active ingredients or drugs in the combination, and whether any of the active ingredients or drugs of the combination interferes with the methods of analysis of another active ingredient or drug in the combination [section 512(d)(4)(A) of the FD&C Act].

drug at the already approved concentrations and the presence of a small amount of another drug(s) in a ton of feed should not impact the stability of each drug, tendency to segregate, or ability to mix uniformly into the feed].

ii. For combinations in liquid medicated feeds:

- Homogeneity and chemical stability data for all drugs in the liquid medicated feed were submitted, reviewed, and found acceptable under an INAD before submission of the ADAA feed use combination application;
- Positional stability data were submitted for all drugs in the liquid medicated feed, reviewed, and found acceptable under an INAD before submission of the ADAA feed use combination application, or the agitation and recirculation statements in 21 CFR 558.5(d)(3) will be included on the Blue Bird label; and
- Freeze/thaw study data were submitted for all drugs in the liquid medicated feed, reviewed, and found acceptable under an INAD before the submission of the ADAA feed use combination application, or a “do not freeze” statement will be included on the Blue Bird label.

10. As part of All Other Information (AOI) submitted to the ADAA feed use combination NADA, the sponsor references the drug experience reports (DERs) submitted annually for each of the individually approved drugs included in the combination.

11. The ADAA feed use combination NADA submission includes the following labeling components, as applicable to the combination:

- a. Type B medicated feed representative labeling;
- b. Type C medicated feed representative labeling; and
- c. veterinary feed directive.

12. The ADAA feed use combination NADA submission includes a claim of categorical exclusion citing 21 CFR 25.33(a)(2) and certification that to the sponsor’s knowledge there are no extraordinary circumstances. Extraordinary circumstances per 21 CFR 25.21 have not been previously identified by CVM; therefore, preparation of an environmental assessment (EA) is not required.

13. A Right of Reference (RoR) letter(s) to the NADA(s) not owned by the filing sponsor of the ADAA feed use combination application was received by the agency in the INAD or NADA submission, if applicable.

IV. SUBMISSIONS TO THE INAD PRIOR TO THE SUBMISSION OF AN ADAA FEED USE COMBINATION APPLICATION

CVM may not discuss specific approval requirements for the ADAA medicated feed use combination or provide feedback that could be construed as agreements unless the specific combination is identified; an INAD has been opened for the combination; and a PSC has been requested to discuss the feed use combination. For example, during a PSC for an individual Type A medicated article, if a sponsor has not identified a specific

combination or opened an INAD for the combination, CVM may only provide general comments regarding eligibility for the 60-day process and approval requirements for ADAA medicated feed use combinations.

A. Opening an Investigational File for the ADAA Feed Use Combination

Once the sponsor has identified a specific combination of drugs, the project manager (PM) reminds the sponsor to open an INAD file⁵ to house the documents that will be used to support the approval of the proposed ADAA feed use combination. The INAD will contain the PSC MOC and/or ERL in which agreements are made and copies of the draft FOI Summary sections. This INAD file also may be used to submit any information to complete a technical section (if required) or labeling (if the sponsor chooses to submit labeling ahead of the NADA). While preferable that each proposed combination have its own INAD file, it is acceptable for multiple, related proposed combinations to share a single INAD file (e.g., a proposed four-way drug combination, which the drug sponsor might also intend to pursue approval of the related two- and three-way combinations).

B. PSC for the ADAA Feed Use Combination

When the sponsor is ready to discuss the ADAA approval requirements for the specific feed use combination, they submit a PSC meeting request⁶ to the INAD for the combination to confirm the technical section requirements⁷. The discussion of the combination(s) may occur in one of the following ways:

- in combination with a PSC for one of the individual Type A medicated articles that is under development;⁸ or
- in a separate PSC that only discusses the combination and is unrelated to the discussion of an individual Type A medicated article.

The PM consults each impacted review unit [i.e., target animal division (TAD), Division of HFS, Environmental Branch, and Division of Manufacturing Technologies (DMT)]. The consult request will prompt each division to begin additional review work in preparation for the eventual receipt of a 60-day ADAA feed use combination NADA.

The review team should be prepared to address the approval requirements for the specific feed use combination per the ADAA, as outlined in detail below and summarized in checklist format in Appendix 2:

1. The TAD reviewer:

- a. confirms whether the proposed combination meets requirements outlined in section 512(d)(4)(D) of the FD&C Act, thus confirming that an assessment of the Effectiveness technical section is not needed;

⁵ See P&P 1243.4000 for information on opening an INAD file.

⁶ See P&P 1243.3024 for information on PSC meetings.

⁷ See P&P 1243.3050 for information on confirming technical section requirements.

⁸ It is possible to discuss multiple projects (Type A medicated articles and/or combinations) in a single PSC. However, the sponsor must submit a copy of the meeting request to each relevant INAD file. The resulting documentation (MOC and/or ERL) may address multiple projects but should clearly delineate each project.

- b. confirms that the proposed combination meets requirements outlined in section 512(d)(4)(B) of the FD&C Act, thus confirming that no new data is required to complete the Target Animal Safety technical section. Alternatively, if the reviewer is aware of existing, well documented safety concerns to the target animal when the proposed drug combination is administered, then the reviewer should determine what target animal safety information or data are needed to support the combination approval;
 - c. addresses any questions or considerations for the labeling components to be included in the future ADAA feed use combination NADA submission;
 - d. reminds the sponsor to check for AOI. If any information is available, it should be submitted to the INAD a minimum of 80 days prior to the submission of the ADAA feed use combination NADA. If information is submitted for review as part of the NADA, the submission will not qualify for a 60-day review timeline;
 - e. reminds the sponsor to obtain right of reference, if required; and
 - f. begins preparation of the draft FOI Summary, as described in section IV.E.
2. The HFS Residue Chemistry reviewer determines whether residue chemistry information or data are needed to support the combination approval and begins preparation of the draft FOI Summary, as described in section IV.E.
3. The HFS Toxicology and Microbial Food Safety reviewers confirm that the proposed combination meets requirements outlined in section 512(d)(4)(A) of the FD&C Act, thus confirming that an assessment of the Toxicology and Microbial Food Safety sections of the HFS technical section are not needed.
4. The DMT reviewer instructs the sponsor to submit feed assay methods and non-interference information under the CMC technical section and determines whether feed mixing studies are needed to support the combination approval.
5. The Environmental reviewer determines if the proposed combination(s) will be eligible for a categorical exclusion under 21 CFR 25.33(a)(2), citing no increase in use, for a combination of previously approved animal drugs.
6. If the feed use combination will be a NADA A-0000, the PM:
 - a. instructs the sponsor to request to reserve an NADA number before submitting the application⁹ and to include the reserved NADA number on all applicable portions of the labeling;
 - b. reminds the sponsor to fill out the eSubmitter template to correctly identify the product as an ADAA combination qualifying for 60-day review; and
 - c. advises the sponsor to reach out to the PM about any questions with the administrative processes noted above.

Eligibility for the 60-day process and approval requirements for the specific ADAA medicated feed use combination should be confirmed. Each technical section for the combination use will be addressed. The documentation will specify which technical

⁹ See P&P 1243.3750 for information on the process for reserving an application number.

sections do not require further assessment and the additional information or data needed to complete the other technical sections.

C. P Submissions

If, as part of the PSC, it is determined that additional information or data are needed to support the completion of a technical section, the sponsor is instructed to submit information or data to the INAD for the combination as a P submission. The EI technical section should be submitted under the NADA; there is no required submission under the INAD.

To be eligible for the 60-day review process for an ADAA feed use combination NADA, the review of all P submissions that required additional information or data must have concluded and resulted in a Technical Section Complete letter(s) prior to the sponsor's submission of the ADAA feed use combination NADA.

D. M Submissions

If AOI beyond a reference to the DERs submitted annually for each of the individually approved drugs included in the combination is identified (i.e., types of information listed in section IV. of P&P 1243.4085), the sponsor must submit this information to the INAD for the combination as an M submission. The sponsor does not need to reference the DERs until the ADAA feed use combination NADA is submitted. To be eligible for the 60-day review process for an ADAA feed use combination NADA, the review of this M must have concluded and resulted in a Technical Section Complete letter prior to and within 90 days of the sponsor's submission of the ADAA feed use combination NADA.

The sponsor may, but is not required to, choose to submit labeling for the combination to the INAD as an M submission. It is acceptable that the labeling is not submitted until the ADAA feed use combination NADA is submitted.

E. Preparation of the Draft FOI Summary Sections

The procedure for preparing the FOI Summary for the 60-day ADAA feed use combination is different from the process used for INAD phased review because there may not be any M submissions that normally trigger a Q submission to draft a complete FOI Summary.¹⁰ Therefore, portions of the FOI Summary will need to be drafted under separate Q submissions early in the INAD phased review process to ensure that the complete FOI summary can be drafted quickly and efficiently once the 60-day ADAA feed use combination NADA is received.^{11,12}

1. By the date of the ONAPE premeeting for the PSC for the ADAA feed use combination, the TAD reviewer and HFS Residue Chemistry reviewer will perform the following tasks, respectively.

¹⁰ As described in the Background section, for qualifying 60-day ADAA NADAs, ONAPE reviews the Labeling technical section and prepares the final FOI Summary under the NADA within a 60-day timeframe rather than the traditional 180-day timeframe. This differs from an administrative NADA in which all technical sections, including the M submissions, must be complete under the INAD prior to submission of the NADA.

¹¹ See P&P 1243.5762 for additional information on preparing an FOI Summary for ADAA combinations.

¹² See P&P 1243.3250 for information on opening a Q submission.

- a. The **TAD reviewer** opens a Q submission to draft the following sections of the FOI Summary for an ADAA combination based on the available information:
 - i. Title page, except for the NADA number,
 - ii. Section I. General Information,
 - iii. Section II. Effectiveness,
 - iv. Section III. Target Animal Safety, and
 - v. Section VI. Agency Conclusions.

The TAD Q submission also includes the following, if available, for each of the individual Type A medicated articles proposed for use in the feed use combination:

- the date of the approval,
- the submission number under which the approval was completed,
- the date of the FOI Summary,
- the date the approval was posted in the FEDERAL REGISTER (formatted as <volume no.> FR <pg no.>, dated <mm/dd/yyyy>), and
- appropriate CFR citation used to establish effectiveness and target animal safety.

This information will aid the TAD reviewer in preparing the approval package documents under the future ADAA feed use combination NADA.

- b. If the **Residue Chemistry reviewer** determines that no new information is needed to support the Residue Chemistry section, then the Residue Chemistry reviewer opens a separate Q submission to draft the HFS section of the FOI Summary. The Division of HFS (DHFS) follows their normal process of requesting consulting reviews from Toxicology and Microbial Food Safety reviewers to complete relevant portions of this section.

If the Residue Chemistry reviewer determines that additional information to support the Residue Chemistry section will need to be submitted for review under a P submission to the INAD, then a Q submission is not opened at this time. Instead, the DHFS will follow their normal process of drafting the HFS section of the FOI summary during the review of the P submission.

Whether completed under a Q or P submission, the HFS draft FOI Summary also includes, as available, the following for each of the individual Type A medicated articles proposed for use in the feed use combination:

- the date(s) of the approval,
- the submission number(s) under which the approval was completed, the date(s) of the FOI Summary(ies),

- the FEDERAL REGISTER citation(s) (formatted as <volume no.> FR <pg no.>, dated <mm/dd/yyyy>), and
- the appropriate CFR citation(s) used to establish human food safety (i.e., toxicology, residue chemistry, microbial food safety, and analytical method for residues).

This information will aid the TAD reviewer in preparing the approval package documents under the future ADAA feed use combination NADA.

2. The Q submission due date is set to 60 days after the date of the scheduled PSC. This intended timeline is to have the Q submission complete no later than Day 15 of the timeline for the NADA.¹³ If the sponsor receives an ERL and chooses to cancel the PSC, the FOI Q submission timeline may need to be adjusted. Each Q submission is closed out as a “FNR with Memo” and option for “Draft FOI Summary text” to upload the prepared draft FOI Summary text is selected. Copies of these draft sections of the FOI Summary should not be provided to the sponsor for comment prior to closing out the Q submissions.
3. If the NADA is received while the Q submissions are still open, the HFS reviewer closes out the Q submission by the due date to ensure that the TAD reviewer has the draft FOI language early during the 60-day review time. The HFS reviewer notifies the TAD reviewer when the Q submission is closed out and attaches a courtesy copy of the draft FOI Summary language to the notification email.

The review team may also use key times during the review of the new Type A medicated article (e.g., the end game meeting under the INAD; receipt of the NADA for the single ingredient) to reassess the original reviews completed under the Z or Q submissions for the ADAA feed use combination to determine whether the decisions still support the approval of the combination application. If changes have occurred that warrant documentation, then a new review will be prepared. If the changes will impact CVM’s ability to approve the ADAA feed use combination (e.g., changes to the conditions of use for one or more of the drugs proposed for use in the combination), then the PM will be notified and will work with the review team to determine the appropriate next steps.

V. REVIEW OF THE ADAA FEED USE COMBINATION NADA

A. Initial Processing

1. Initial Check for Eligibility of the ADAA Feed Use Combination NADA for a 60-day Review Clock

Once assigned to the TAD, an initial assessment of the submission is performed to determine whether it is eligible for the 60-day review clock. This assessment is described in detail below and summarized in checklist format in Appendix 3.

¹³ If the sponsor submits the application immediately upon receipt of the MOC, Day 15 of the NADA coincides with Day 60 after the MOC (presuming the MOC does not go out earlier than the CVM due date, 45 days after the PSC) is issued and Day 60 of the FOI Summary Q submissions.

If the application does not meet the eligibility criteria, the application is transitioned to a 180-day review clock (see section VI. below) and follows the normal procedures for reviewing a 180-day NADA.

This eligibility check is a separate process from the refuse to file (RTF) assessment (as described in P&P 1243.2050) because it is possible that the eligibility requirements for the 60-day review may not be met, but the application can be filed. However, the eligibility check and RTF assessment should be conducted at the same time because of the reduced review timeframe.

- a. Verify the application is assigned to the correct TAD. If the application is incorrectly assigned, identify the correct TAD, and send an email to the EDSR Mailbox requesting it be reassigned.¹⁴ The subject line should be STARS Correction Request. The ONAPE Business Informatics (BI) Branch manages the mailbox. When the change in STARS has been made, the requestor will get a notification email from the EDSR Mailbox.
- b. Verify that each of the individual drugs proposed for use in the combination are individually and separately approved under section 512(b)(1) of the FD&C Act for the particular uses and conditions of use for which they are intended in the combination.
- c. Verify that the following are included in the eSubmitter report:
 - i. A copy of the PSC MOC held under the INAD and/or ERL for the ADAA combination and any Technical Section Complete letters (if applicable) to address the completion of all major technical sections, except for EI.
 - ii. For AOI, a statement referencing the DERs submitted annually for each of the individually approved drugs included in the combination. AOI also includes either a statement that a search for additional information was performed and no information exists, or that AOI information was submitted and reviewed under the INAD and a copy of the Technical Section complete letter is included in the approval package.
 - iii. All proposed labeling components.
 - iv. Claim of categorical exclusion under 21 CFR 25.33(a)(2), no increase in use for a combination of previously approved animal drugs, and a certification that to the sponsor's knowledge no extraordinary circumstances exist that may significantly affect the quality of the human environment (21 CFR 25.21).
 - v. If applicable, a copy(ies) of the ROR letter(s) or the principal submission identification number under which the ROR letter(s) was submitted to CVM. The reviewer reviews the wording of the ROR letter(s) to ensure that the information it references will support the drug combination being considered for approval (e.g., is for the drug product included in the combination; reference extends to the dosage and indication intended for use in the combination).

¹⁴ Internal information redacted.

If the submission does qualify for a 60-day review clock, ensure the correct timeframe was assigned in STARS. If a 180-day review clock was erroneously assigned, the review clock may need to be reset. If this occurs, the review time change may be completed by the reviewer in Appian or with consultation with the ONAPE BI Branch.

2. Request Consulting Reviews

The TAD reviewer requests consulting reviews from the following groups within five days of receipt using the current office policy (P&P 1243.3200):

- a. A scientific reviewer within the TAD to review the labeling components, if the primary reviewer for the submission is not a scientific reviewer (for example, if a consumer safety officer is the primary reviewer.)
- b. The Feed and Topical Branch (for combinations intended for use in terrestrial species) or the Biotherapeutics Branch (for combinations intended for use in aquaculture species) to review the labeling components.
- c. A Residue Chemistry reviewer in the DHFS to:
 - i. Reconfirm any agreements made under the PSC (and/or ERL) or conclusions made under the phased review process.
 - ii. Review the labeling components for information relevant to residue chemistry.
 - iii. Confirm that the residue chemistry draft FOI Summary language prepared under the Q or P submission of the associated INAD is still acceptable and reference the appropriate Q or P submission in their consulting review back to the TAD reviewer.
 - iv. Confirm, via email with Toxicology and Microbial Food Safety reviewers, that the toxicology and microbial food safety draft FOI Summary language prepared under the Q or P submission of the associated INAD is still acceptable.
- d. The Environmental Branch to review the request for a categorical exclusion from the requirement to prepare an EA.
- e. The Medicated Feed Specialist in the Office of Surveillance and Compliance's (OSC), Division of Pharmacovigilance and Surveillance to review the labeling components.

B. Reviewing the A-0000 Submission

If the submission meets the eligibility criteria, is sufficient for review upon receipt, and does not require amending, then the review time is 60 days and the review team should follow the 60-day review timeline (see section V.B.1. below).

However, if an amendment(s) is needed, the timeline will be extended by 40 days (see section V.B.2. below) or by 120 days (see section V.B.3. below).

1. 60-Day Review Timeline

- a. The TAD reviewer prepares the approval package per P&P 1243.3800.
 - i. By **Day 8**, the TAD reviewer requests a DER status check from OSC's Marketed Product Information Branch or completes the DER status check.
 - ii. By **Day 15** of the review timeline for the 60-day NADA, the TAD and HFS reviewers close any open FOI Q submissions under the INAD (see section IV.E. above). The HFS reviewer notifies the TAD reviewer once they have closed their Q submission.
 - iii. By **Day 20**, the TAD reviewer prepares the complete draft Federal Register (FR) notice and FOI Summary.
 - iv. By **Day 24**, the TAD reviewer's division management completes review of the draft FR notice and FOI Summary.
 - v. By **Day 24**, the TAD reviewer emails a copy of the complete draft FOI Summary and FR notice to DHFS for final concurrence. Their concurrence and/or edits for both documents are emailed to the TAD reviewer by Day 30.
 - vi. Optional: By **Day 24**, the TAD reviewer can provide a courtesy copy of the draft FOI Summary to the sponsor for review. If a courtesy copy is provided to the sponsor for review, the sponsor should return the draft FOI Summary with any comments by Day 27.
- b. By **Day 30**, the consulting reviewers complete their reviews and return the consults in Appian according to the procedures in P&P 1243.3029.
- c. By **Day 32**, the TAD reviewer confirms that all consulting reviews conclude that the labeling and categorical exclusion are acceptable as submitted. If any of the consulting reviews conclude that the submission is unacceptable as submitted and an amendment is being considered, the TAD reviewer will follow the process outlined in Sections V.B.2. or V.B.3, as applicable.

If acceptable, the TAD reviewer completes review, finalizes the draft approval package, and begins routing it through the final approval package process.

The approval package will be assembled and routed in accordance with P&P 1243.3800 and using the 60-day ADAA combination timeline.

2. Changing the Review Timeline from 60 Days to 100 Days (i.e., a 100-Day Timeline)

The timeline is extended to 100 days if the need for minor changes is identified during the labeling review. This is an extension of the review clock, not a resetting of the clock to 100 days upon receipt of the amendment. For information on changing the timeline to 180 days in Appian, see section VI. below.

- a. The TAD reviewer follows the steps in Sections V.B.1.a. and V.B.1.b.

- b. If one or more of the reviews concludes that the labeling is unacceptable, but could be fixed with minor changes, the TAD reviewer prepares an amendment request.¹⁵ Minor changes to the labeling components are considered those that the TAD reviewer can easily review without requesting an additional consulting review. For example, a minor change may include misspelled words, rearrangement of sections, or the addition of missing statements on the Blue Bird label(s) that originate from one or more of the individual Type A medicated article labels.
- c. The TAD reviewer emails the amendment request to the sponsor by **Day 40**. In addition to the changes needed to the labeling, the amendment request notifies the sponsor that the review clock will be changed from 60 to 100 days.

The CVM due date in STARS will automatically update to align with the 100-day timeline when the amendment is received. To maintain the 100-day review timeline, the sponsor must return the amendment by no later than 10 days from the date the amendment request is made; the TAD reviewer and Branch Chief (BC) may elect to provide the sponsor less than a 10-day turn around depending on the number of labels being amended.

By **Day 60**, the TAD reviewer reviews the amendment. If the labeling is confirmed to be acceptable as amended, the TAD reviewer completes review and updates and finalizes the draft approval package by **Day 66**. The approval package is assembled and routed through the final review process per P&P 1243.3800 and using the 100-day ADAA combination timeline.

3. Changing the Review Timeline from 60 or 100 Days to 180 Days (i.e., a 180-Day Timeline)

The timeline is extended to 180 days if situations outlined below are encountered. This is an extension of the review clock, not a resetting of the clock to 180 days upon receipt of the amendment. For information on changing the timeline to 180 days in Appian, see section VI. below.

- Major changes to the labeling, including those that would require additional consulting reviews (e.g., missing entire sections; incorrect calculations to the mixing directions);
- Additional amendments to labeling beyond the first amendment;
- The original amendment to labeling is received more than 10 days after requested;
- An amendment is required for any technical section besides labeling; or
- AOI submission includes information beyond a reference to the DERs submitted annually for each of the individually approved drugs included in the combination.

In these scenarios, the review process is as follows:

¹⁵ See P&P 1243.3026 for information on amending STARS submissions.

- a. The TAD reviewer follows the Steps outlined in Sections V.B.1. and V.B.2.
- b. If the review team encounters one of the above-listed scenarios, then the review period is changed to 180 days:
 - i. For major changes to the labeling: The TAD reviewer updates the review time in Appian from 60 to 180 days by **Day 40**. The TAD reviewer emails the amendment request to the sponsor by **Day 40**.
 - ii. For additional amendments beyond the first, those amendments received late, or for AOI that needs to be reviewed: The TAD reviewer updates the review time from 100 to 180 days in Appian by **Day 70** if additional minor amendments are determined to be needed. The TAD reviewer emails the amendment request to the sponsor by **Day 70**.
- c. If a consulting reviewer needs to review the amendment, the TAD reviewer requests a second consulting review from the appropriate consulting reviewers within 5 days of receiving the amendment request, and by no later than **Day 75**. The second round of consulting reviews are returned by **Day 130**.
- d. By **Day 140**, the TAD reviewer reviews the amendment. If the labeling is confirmed to be acceptable as amended, the TAD reviewer completes their review and finalizes the draft approval package by **Day 146**. The approval package is assembled and routed through the final review process per P&P 1243.3800 and using the 180-day ADAA combination timeline.

VI. APPIAN PROCESS FOR CHANGING THE REVIEW TIMELINE

If it is determined that the submission is not eligible for a 60-day review (i.e., does not meet the eligibility requirements as listed in Section III; is missing components upon submission; or requires amendments), the TAD reviewer prepares the Review Time Change letter template to inform the sponsor that the review timeline was changed. The TAD reviewer includes the BC and Division Director in the sign-off chain in the Appian Review Time Change workflow. The option to issue correspondence is selected in Appian and the letter is uploaded. Completing the Appian workflow updates the review period in STARS. Refer to the Appian User Guide for instructions on completing the Review Time Change.¹⁶

VII. REFERENCES

CVM Program Policies and Procedure (P&P) Manual – ONAPE Reviewer’s Chapter

- 1243.2050 – Refuse to File and Refuse to Review
- 1243.3024 – Scheduling and Holding Meetings with Outside Parties

¹⁶ Internal information redacted.

1243.3025 – Preparing Meeting Documentation (i.e., Early Response Letter, Memorandum of Conference, Acknowledgement Letter, Other Review Documentation)

1243.3026 – Amending and Resetting the Clock on Submission Tracking and Reporting System (STARS) Submissions

1243.3029 – Closing Out a Consulting Review for Submission Tracking and Reporting System (STARS) Submissions

1243.3050 – Determining Technical Section Requirements for a New Animal Drug Product Approval

1243.3200 – Routing a Request to Obtain a Consulting Review of a Submission Tracking and Reporting System (STARS) Submission

1243.3250 – Q submissions Agency-Initiated Actions

1243.3750 – Sponsor Requests to Reserve an Application Number for a New Animal Drug or an Abbreviated New Animal Drug Application

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

1243.4000 – Processing a Request to Open an Investigational (INAD) or Generic Investigational New Animal Drug (JINAD) File

1243.4085 – All Other Information

1243.5762 – Freedom of Information (FOI) Summary for Animal Drug Availability Act (ADAA) Feed Combination New Animal Drug Applications

Other References

Review Time Change Letter template

PM Timeline for 60-day ADAA Combination Applications

VIII. VERSION HISTORY

October 1, 2018 – Original version

June 26, 2020 – Updated all internal links for SharePoint sites because FDA has migrated this information to a new version of SharePoint.

August 25, 2020 – Updated to fix broken link in footnote number 12 for the Appian User Guide.

December 18, 2023 – Updated to include a new section regarding preparation of application submissions for PMs to use to guide sponsors on the process and edits to improve clarity about the process. The document was also put into the current office template and format. 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. Also, updated section V.A. to remove mention of the STARS Correction Request Form. The STARS Correction Request Form has been retired. The instructions are now to send the request for a correction or change in proprietary name to the EDSR mailbox.

July 14, 2026 – Updated to reflect the agreements made under the ADUFA V ADAA working group, expand the 60-day ADAA process to allow for supplemental (B1) applications and reactivations, add Appendix 2. 60-day ADAA feed use combination INAD checklist, add Appendix 3. 60-day ADAA feed use combination NADA checklist, updated to reflect new ONAPE reorganization terminology, and added clarification on PSC with ERL.

APPENDIX 1. LANGUAGE FROM THE ADUFA IV REAUTHORIZATION AND DRAFT RECOMMENDATIONS THAT PERTAINS TO THE REDUCTION OF THE REVIEW TIMEFRAME FROM 82 FR 49380, DATED OCTOBER 25, 2017

The Agency will review and act on 90 percent of qualifying ADAA combination medicated feed applications within 60 days after the submission date when all of the following conditions are met:

- i. Basic regulatory requirements for an ADAA combination medicated feed application have been met as outlined in 21 CFR 514.4(c)(2)(ii)
- ii. A presubmission conference has been conducted and either:
 - a. No data (no tissue residue non-interference study is required) are needed and this agreement is documented in the memorandum of conference for the presubmission conference; or
 - b. a justification for not conducting a tissue residue non-interference study has been submitted, reviewed, and found acceptable under an INAD, prior to the submission of the ADAA combination medicated feed application; or
 - c. a tissue residue non-interference study has been submitted, reviewed and found acceptable under an INAD, prior to the submission of the ADAA combination medicated feed application.
- iii. No effectiveness or target animal safety data are required.
- iv. No manufacturing data requirements - sponsor can address in meeting assay non-interference, but data submission is not required.
- v. All other information is referenced to previous drug experience reports.
- vi. Sponsor makes submission and it includes: Representative (Blue Bird) labeling, Veterinary Feed Directive (if applicable).
 - a. Includes a request for categorical exclusion from the need to prepare an environmental assessment (EA); i.e., no EA required.
 - b. Reference to presubmission conference.
 - c. Right of reference (if applicable) to NADA(s) not owned by the filing sponsor of the ADAA combination medicated feed application has been received by the Agency.

Review and act on 90 percent of ADAA medicated feed combination applications within 100 days if the application was accepted for the 60-day timeframe and there is a need for minor amendments.

If any of the above conditions cannot be met, the ADAA combination application performance metric will be placed in the original NADA application cohort with a 180-day review timeframe.

APPENDIX 2. 60-DAY ADAA FEED USE COMBINATION INAD ADAA PSC MOC/ERL CHECKLIST

The following criteria should be reviewed/assessed as part of the presubmission conference documenting approval requirements for the combination **under the INAD for the ADAA feed use combination** (INAD ADAA PSC). The MOC and/or ERL should confirm the following items for the proposed combination to determine if the NADA will qualify for the 60-Day ADAA. For any sections/components that do not require new data, the sponsor should be informed that the MOC and/or ERL can be submitted in lieu of a technical section complete letter.

Basic ADAA requirements per 21 CFR 514.4(c)(2)(ii) and 60-d ADAA process	
NADA Type	NADA submission will be a non-administrative original NADA (submission code A); a non-administrative B1 supplemental NADA (submission code C); or reactivations of these submission types (Section III.1)
ADAA	Combination is administered in or on animal feed. (Section III.2)
ADAA	Each new animal drug included in the proposed feed use combination has been previously and separately approved under section 512(b)(1) of the FD&C Act for the particular uses and conditions of use. ¹⁷ (Section III.3)
ADAA	Each new animal drug is different from all other animal drugs in the proposed feed use combination and provides appropriate concurrent use for the intended target animal population. (Section III.4)
ADAA	The feed use combination contains no more than one antibacterial. ¹⁸ (Section III.5)
ADAA	Each active ingredient or new animal drug is intended for at least one use that is different from all other active ingredients or new animal drugs in the feed use combination (i.e., each individual drug brings a unique indication to the combination). (Section III.6)
RoR	If Right of Reference is required, that copy(ies) of the Right of Reference letter(s) should be submitted to the INAD or with the NADA. (Section III.13)
TAS	- No new data is required to complete the technical section (meets requirements outlined in section 512(d)(4)(B) of the FD&C Act); or - TAS information/data needed (P submission¹⁹). (Section IV.B.1.b)

¹⁷ Conditions of use may include, but are not limited to, the indication(s), dose, duration, frequency, and species or classes of species.

¹⁸ 21 CFR 514.4(c)(1)(iii) excludes the classification of ionophores and arsenicals as antibacterials for the purposes of their inclusion in an ADAA combination in animal feed or drinking water.

¹⁹ The P data submission to support the combination approval should be submitted under the INAD for the ADAA feed use combination.

Basic ADAA requirements per 21 CFR 514.4(c)(2)(ii) and 60-d ADAA process	
EFF	No new data is required to complete the technical section (meets requirements outlined in section 512(d)(4)(D) of the FD&C Act). (Section IV.B.1.a)
HFS	• Toxicology and Microbial Food Safety components, that an assessment of the components are not needed (meets requirements outlined in section 512(d)(4)(A) of the FD&C Act) (Section IV.B.3); and • Residue Chemistry component (Section III.8), either ○ No HFS (tissue residue non-interference²⁰ study) data are needed; or ○ HFS information/data are needed (P submission¹⁹), and the sponsor should submit: ○ Justification for not conducting a tissue residue non-interference study; or • Tissue residue non-interference study
CMC	• CMC information needed (P submission¹⁹) (Section III.9); ○ Feed assay methods and non-interference information; and ○ Justification for not performing feed mixing study or feed mixing data
ENV	The proposed combination is eligible for a claim of categorical exclusion under 21 CFR 25.33(a)(2) and a certification that to the sponsor's knowledge no extraordinary circumstances exist that may significantly affect the quality of the human environment (21 CFR 25.21). (Section III.12.)
LB	Questions or considerations for the representative Type B and/or Type C labeling, Veterinary Feed Directive (if applicable) (Sections III.11 and IV.D)
AOI	• No new information is required to complete the technical section (sponsor refers to the annual drug experience reports (DERs) for each of the individually approved drugs included in the combination and a statement that a search for additional information was performed and no information exists); or • AOI information/data needed (M submission²¹). (Sections III.10, IV.B.1.c, and IV.D)

²⁰ Non-interference refers to whether any active ingredient or drug intended for use in the combination exceeds its established tolerance at the longest withdrawal time of any of the active ingredients or drugs in the combination, and whether any of the active ingredients or drugs of the combination interferes with the methods of analysis of another active ingredient or drug in the combination (section 512(d)(4)(A) of the FD&C Act).

²¹ The M submission to support the combination approval should be submitted under the INAD for the ADAA feed use combination; refer to the types of information listed in section IV. of P&P 1243.4085.

APPENDIX 3. 60-DAY ADAA FEED USE COMBINATION NADA CHECKLIST

The submitted application must meet the following criteria **at the time of NADA submission to qualify for the 60-Day ADAA.**

Basic ADAA requirements per 21 CFR 514.4(c)(2)(ii) and 60-d ADAA process	
ADAA	Combination is administered in or on animal feed. (Section III.2)
ADAA	Each new animal drug included in the proposed feed use combination has been previously and separately approved under section 512(b)(1) of the FD&C Act for the particular uses and conditions of use. ¹⁷ (Section III.3)
ADAA	Each new animal drug is different from all other animal drugs in the proposed feed use combination and provides appropriate concurrent use for the intended target animal population. (Section III.4)
ADAA	The feed use combination contains no more than one antibacterial. ¹⁸ (Section III.5)
ADAA	Each active ingredient or new animal drug is intended for at least one use that is different from all other active ingredients or new animal drugs in the feed use combination (i.e., each individual drug brings a unique indication to the combination). (Section III.6)
NADA submission contents (certified in or included as attachments in application)	
NADA Type	NADA submission is a non-administrative original NADA (submission code A); a non-administrative B1 supplemental NADA (submission code C); or reactivations of these submission types. (Section III.1)
INAD ADAA PSC MOC	The MOC and/or ERL from the presubmission conference documenting approval requirements for the combination <u>under the INAD for the ADAA feed use combination</u> . (Section III.7)
RoR	If applicable, copy(ies) of the Right of Reference letter(s) or the principal submission identification number under which the Right of Reference letter(s) was submitted. (Section III.13)
Documents included in NADA for each Technical section	
TAS	ADAA INAD PSC MOC or ERL or INAD P-TAS technical section complete letter (Section IV.B.1.b)
EFF	ADAA INAD PSC MOC or ERL (Section IV.B.1.a)
HFS	ADAA INAD PSC MOC or ERL and/or INAD P-HFS technical section complete letter (Sections III.8 and IV.B.3)
CMC	INAD P-CMC technical section complete letter (Section III.9)
ENV	Claim of categorical exclusion under 21 CFR 25.33(a)(2) and a certification that to the sponsor's knowledge no extraordinary circumstances exist that may significantly affect the quality of the human environment (21 CFR 25.21). (Section III.12)
LB	All representative Type B and/or Type C labeling, Veterinary Feed Directive (if applicable), with the NADA number assigned to the combination and (if applicable) INAD M-LB technical section complete letter (Sections III.11 and IV.D)
AOI	Reference to the drug experience reports (DERs) for each of the individually approved drugs included in the combination and a statement that a search for additional information was performed and no information exists and/or INAD M-AOI technical section complete letter (Sections III.10, IV.B.1.c, and IV.D)