OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

PROCESSING A SPONSOR REQUEST FOR WRITTEN FEEDBACK REGARDING DEVELOPMENT PLANS (INAD C SUBMISSION) FOR NEW ANIMAL DRUG PRODUCT APPROVALS

I. PURPOSE

This document defines when it is appropriate for sponsors to request written feedback for a development plan and describes the procedures for processing a sponsor request for written feedback on a proposed development plan [C submission to the investigational new animal drug (INAD) file].[1,2] This document applies to:

- all INADs and new animal drug applications (NADAs) that will culminate in original approvals, including Animal Drug Availability Act of 1996 (ADAA) combinations; and
- INADs and NADAs that will culminate in Category II supplemental approvals that may require a reevaluation of certain safety or effectiveness data in the parent application (i.e., B1 supplements).[3]

This document does not apply to Category I supplement approvals [labeling or Chemistry, Manufacturing, and Controls (CMC) supplements],[4] cellular therapy products, or generic products [including B1 (innovative) supplements to generics].

II. CONFIRMING DEVELOPMENT PLANS THROUGH A C SUBMISSION

Sponsors may use the C submission to request written feedback on development plans when seeking feedback on the following:

- proposed development plans for B1 supplements that may require the sponsor to submit safety and/or effectiveness data/information (e.g., new indication, dose regimen, addition of a new species/class). The development plan should clearly address all technical sections (TSs) applicable to the supplemental approval (including CMC and Environmental Impact).

[1] These submissions were previously classified and piloted under the H submission code (ONADE pilot project from March 15, 2021, through September 29, 2023). Any written feedback requests previously completed under the H submission code will not be recoded as a C submission. Sponsors do not need to request to have their acknowledgement letters reissued.
[2] The INAD C submission code was previously used for DIAL submissions, which are not used by ONADE under the electronic submission process. This submission also differs from a C submission for a supplement under an NADA.
[3] Category II supplements as described in 21 CFR 514.106(b)(2)
[4] Category I supplements as described in 21 CFR 514.106(b)(1)

- confirmation that a specific TS is considered complete; the sponsor proposes that no additional information is necessary for approval of a B1 supplement (e.g., CMC TS when the formulation is not changing; or Target Animal Safety (TAS) TS when the dosage regimen and species/class are not changing).

- confirmation of a previously agreed upon development plan, or feedback provided by CVM, for an original or B1 supplemental approval.

- confirmation of remaining TS requirements for an original or B1 supplemental approval under either the administrative NADA (phased review) or non-administrative NADA (180-day review timeframe) approach.

CVM encourages sponsors to contact their assigned ONADE Project Manager (PM) prior to submission of a C submission to determine if this C submission process is appropriate/applicable for the sponsor's situation. The C submission should not be used:

- in lieu of the first presubmission conference (PSC) to discuss the development plan for an original approval;

- in lieu of a PSC for an abbreviated NADA (ANADA) that will culminate in a B1 supplemental approval; or

- in lieu of a PSC for a 60-day ADAA combination product (eligibility to qualify for the ADAA combinations 60-day review process requires that a PSC is held with CVM under the INAD).[5]

III. INITIAL PROCESSING OF THE C SUBMISSION

Requests by sponsors seeking written feedback on their development plans are coded as a C submission to an INAD file in the Submission Tracking and Reporting System [STARS; INAD > Project Development (C) > Request for Written Feedback on Proposed Development Plan (WF)]. This submission is further defined by the Purpose of Submission field:

- Confirmation of technical section(s) status for a phased review project (administrative NADA)

- Confirmation of non-administrative (180-day) NADA requirements

- Other [e.g., written feedback on development plans for Minor Use and Minor Species (MUMS) approvals][6]

C submissions for written feedback on development plans are assigned to the PM responsible for the sponsor's projects. Upon receipt of the C submission, the PM reviews the request to determine if it is appropriate according to the definitions in Section II. If the request is incomplete (e.g., supporting information/justification is missing) or this pathway is not appropriate based on the definitions above (e.g., includes EI, etc.), the PM will determine whether it is necessary to void the submission and how the sponsor should resubmit the information to CVM. The PM will follow up with the sponsor as appropriate.

[5] See P&P 1243.5730 Review of 60-Day Original Animal Drug Availability Act of 1996 (ADAA) Feed Use Combination New Animal Drug Applications (NADAs), Section II.7.

[6] Internal information redacted.

This C submission has a **60-day calendar day** review timeframe. The PM will provide a timeline to the reviewers for reference.

If a sponsor includes Early Information (EI) or other substantive or complex information (e.g., extensive background information, references, data summaries) not appropriate for this C submission, the PM, in consultation with the PM's team leader, will determine the appropriate action (i.e., void and resubmit under the appropriate submission type).

IV. REVIEW OF THE C SUBMISSION

Review of the C submission involves at least one representative from each team involved in the review of TSs selected by the sponsor in the eSubmitter template and allows for confirmation of requirements across all applicable TSs.

- The PM has 2 days from the assignment of the C submission to review the submission for completeness/appropriateness and issue consult requests to all members of the review team.[7] The PM shares a timeline for review of the submission for reviewers' reference.
- Team leaders (TLs) assign consults within 3 days from the date they are sent.
- The assigned consulting reviewer (CR) confirms the status of their TS and identifies any concerns with the sponsor's proposed development plan. The CR notifies the PM within 5 days of receiving the consult if they have any concerns regarding the submission or have initial questions for other members of the review team. The PM, in consultation with the CRs, determines whether additional action is needed, such as:
    - advising the sponsor that a C submission is not the appropriate submission type;
    - requesting an amendment with additional information from the sponsor; or
    - scheduling an internal meeting of the review team to discuss the submission and CVM's response.
- The CR determines TS requirements based on the project scope as provided by the sponsor. The project scope includes information relevant to the application, such as: established name, dosage form, dose, duration, route of administration, species and class, and indication. For each applicable TS, the review team determines whether:[8]
    - no new submission is required (e.g., the TS is not affected by the proposed supplemental change; or the sponsor has appropriately referenced, including justification, a completed TS from another application in their proposed development plan);
    - new submission(s) is required to complete the TS, and whether the sponsor's proposal for completing the technical section is acceptable, including any recommendations/feedback from the CR; or

[7] See P&P 1243.3024 Scheduling and Holding Meetings With Outside Parties, section IV.A for details about creation and assignment of consults.
[8] See P&P 1243.3050 Determining Technical Section Requirements for New Animal Drug Product Approval

- CVM is unable to make a determination, because the sponsor needs to better define the scope of the project or provide additional information to justify their proposal for completing the TS.

- If after sufficient review of the materials in the C submission, a CR has significant concerns about one or multiple TS(s) in the sponsor's proposal or believes that a PSC is needed to discuss the requirements with the sponsor, then the CR should notify the PM of this determination as soon possible during the review period.

  - The PM, in consultation with the CR, will notify the sponsor that a meeting request will be needed to discuss the pertinent TS requirements of concern with CVM. Review of the C submission will be completed and, where appropriate, CVM will provide feedback in the acknowledgement letter on the remaining elements of the proposed development plan not for discussion during the PSC. The recommendation to hold a PSC to discuss pertinent TSs of concern, including clarification of the CVM's concerns, will be reflected in the C submission acknowledgement letter.

V. CONTENT OF THE ACKNOWLEDGEMENT LETTER AND INTERNAL DOCUMENTATION

A. Acknowledgement Letter

CVM provides written feedback, including confirmation of the status of each major TS (including TSs considered complete), in an acknowledgement letter to the sponsor using the Sponsor Development Plan Feedback (C Submission) Acknowledgement Letter Template. The PM prepares the acknowledgement letter, including any comments provided by the review team to be relayed to the sponsor.[9] Documentation of reviewer concurrence with the acknowledgment letter language is defined in Section B.

- The CR provides feedback in the acknowledgement letter commensurate with the level of detail provided by the sponsor to CVM.

- For any TS or component (in the case of the Human Food Safety TS) that the sponsor identifies in eSubmitter as complete, CVM provides feedback in the C submission acknowledgement letter that CVM agrees, disagrees, or cannot confirm the sponsor's assessment.

- For any TS confirmed to be complete, the acknowledgement letter language will inform the sponsor they should provide a copy of the acknowledgement letter in lieu of a TSC letter when they submit their NADA for approval.[10]

- Feedback provided in the acknowledgment letter is considered non-binding, as binding agreements can only be made during a PSC. CVM's feedback is predicated on the accuracy and completeness of the information included in the C submission. CVM's feedback may be modified in the future if substantiated scientific requirements essential to the determination of safety or effectiveness

[9] 1243.3025 Preparing Meeting Documentation (i.e., Memorandum of Conference, Acknowledgement Letter, Other Review Documentation)
[10] See P&P 1243.3050 Determining Technical Section Requirements for New Animal Drug Product Approval

arise after the review of the C submission, including new scientific issues/information.[11]

B. Submission Summary and Consulting Reviewer (CR) Reviews

The PM documents concurrence with the acknowledgment letter language from assigned CRs in a submission summary, which is prepared as a stand-alone document. CRs may submit their feedback to the PM through email or Appian comments, or they may write reviews if needed for completeness of the file. For example, if examination of background materials and any decisions relating to the C submission need to be documented, or if information related to the C submission that cannot or will not be transmitted to the sponsor in the acknowledgement letter needs to be captured, it should be included in a review.[12]

VI. TIMEFRAMES FOR PREPARING AND REVIEWING SUBMISSION DOCUMENTATION

Because the times allotted for preparing, circulating, and concurring or commenting on the documentation, and closing out the C submission, are relatively brief, it requires a collaborative effort. Individuals are expected to provide their text and concurrence or comment within the timeframes in the table below.

[11] Refer to 21 CFR 514.5(g) - Modification of presubmission conference agreements.
[12] See. P&P 1243.3009 Format and Style Conventions for Reviews and Submission Summaries

Table 1. Timeframes for the C Submission

Stage of the Review	Activity	Day of the 60-Day Review Clock
Consulting Reviewer (CR) Initial Comments and Review	CR notify the PM of any concerns with the submission (when applicable)	Day 10
	The CR provides draft text to the designated lead consultant, when applicable. If the CR provides text to the lead consultant (e.g., biostatistician providing text to a target animal division reviewer)	Day 29
	The CR(s) provides the PM comments for the sponsor to be included in the acknowledgment letter. The text provided to the PM must be cleared using the established procedures of the CR's division. The comments can be emailed or provided in a written consulting review.	Day 40
	The CR(s) closes out the consulting review request through Appian	Day 40
Review of and Concurrence on the Acknowledgement Letter	The PM prepares and provides access to the draft acknowledgement letter to the CR(s). The PM drafts the acknowledgement letter, as described above, incorporating the sections and comments written by the CR(s). The PM clears the draft letter through the PM's TL and then makes it available to the CR(s) for concurrence and comment. The documentation is posted in a shared location so that comments can be entered directly into the draft(s).	Day 47
	The CR(s) concurs or concurs providing suggested edits on the acknowledgement letter	Day 54
Closing Out the Submission	The PM finalizes the acknowledgment letter and submission summary, working through all submitted edits, compiling all concurrences from the CR(s) and following their team's established procedures for clearing the final action package.	Day 60

(Note the received date is Day 0 of the review clock.)

VII. REFERENCES

Code of Federal Regulations

Part 514 - New Animal Drug Applications

§514.5 - Presubmission conferences

§514.106 - Approval of supplemental applications

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

1243.3009 Format and Style Conventions for Reviews and Submission Summaries

1243.3024 Scheduling and Holding Meetings with Outside Parties

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

1243.3029 Closing Out Consulting Reviews for Submission Tracking and Reporting System (STARS) Submissions

1243.3050 Determining Technical Section Requirements for New Animal Drug Product Approval

1243.5730 Review of 60-Day Original Animal Drug Availability Act Of 1996 (ADAA) Feed Use Combination New Animal Drug Applications (NADAs)

ONADE Standard Operating Procedures (SOP)

Internal information redacted.

VIII. VERSION HISTORY

March 20, 2021 – Original version

July 13, 2022 – Quality systems review for minor formatting updates.

September 29, 2023 – The title of the P&P was changed to reflect the process change. Now these submissions will be made as C submissions under the INAD and will no longer be H submissions. Any H submission specific process references were removed. In addition, 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.