OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

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

I. PURPOSE

The purpose of this document is to:

- Define when it is appropriate for sponsors to request written feedback for a development plan.
- Describe the procedures for processing a sponsor request for written feedback on a proposed development plan (H submission to the investigational new animal drug (INAD) file).

This document applies to:

- All INAD or new animal drug application (NADA) projects that will culminate in original approvals, including Animal Drug Availability Act of 1996 (ADAA) combinations, and
- INAD or NADA projects that will culminate in Category II supplemental approvals that may require safety and/or effectiveness data/information.[1]

This document does not apply to Category I supplement approvals (labeling supplements or Chemistry, Manufacturing, and Controls (CMC) supplements),[2] cellular therapy products, or generic products (including B1 (innovative) supplements to generics).

II. CONFIRMING DEVELOPMENT PLANS THROUGH AN H SUBMISSION

Sponsors may use the H submission for written feedback on development plans (herein referred to as H submission) when seeking feedback on:

- Proposed development plans for Category II supplemental approvals that may require the sponsor to submit safety and/or effectiveness data/information

[1] Category II supplements as described in 21 CFR 514.106(b)(2)

[2] Category I supplements as described in 21 CFR 514.106(b)(1)

(e.g., new indication, dose regimen, addition of a new species/class). The development plan should clearly address all technical sections applicable to the supplemental approval (including CMC and Environmental Impact).

- Confirmation that a particular technical section is considered complete; the sponsor proposes that no additional information is necessary for the approval of a Category II supplement (e.g., CMC technical section when the formulation is not changing; or Target Animal Safety (TAS) technical section when the dosage regimen and species/class is not changing).

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

- Confirmation of remaining technical section requirements for an original or Category II supplemental approval.

- Confirmation of remaining requirements for a non-administrative NADA (180-day review timeframe) for an original or Category II supplemental approval.

CVM encourages sponsors to contact their assigned ONADE Project Manager (PM) prior to submission of an H submission for written feedback to determine if this H submission process is appropriate/applicable for the sponsor's situation. The H 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 new animal drug application (ANADA) project that will culminate in a Category II supplemental approval that may require safety and/or effectiveness data/information;
- In lieu of a PSC for a 60-day ADAA combination product;
- To submit information in support of a protocol (H > Support Protocol (SP)) as part of development plan feedback.

If a sponsor includes Early Information (EI) or other additional supportive information (e.g., extensive background information, references, data summaries) not appropriate for this H submission, the PM, in consultation with the PM's team leader, will determine the appropriate action (i.e., continue review with 100-day review timeframe or void).

III. INITIAL PROCESSING OF THE H SUBMISSION

Requests by sponsors seeking written feedback on their development plans are coded as a specialized H submission to an INAD file in the Submission Tracking and Reporting System (STARS; INAD > General Information/Data [H] > Request for Written Feedback on Development Plan [OT]). This submission will be differentiated in STARS from other H submissions by the Purpose of Submission field:

- Request for Written Feedback on Development Plan (OT)-Development plan feedback
- Request for Written Feedback on Development Plan (OT)-Non-admin (180-day) NADA

- Request for Written Feedback on Development Plan (OT)-Other

H submissions for written feedback on development plans are assigned to the PM responsible for the sponsor's projects. Upon receipt of the H submission, the PM will review 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 information in support of a protocol, 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.

This H submission will have a 60-day review timeframe. However, due to current limitations in STARS, the STARS due date will show the standard H submission due date of 100 days. As such, the PM will track the review of this type of H submission outside of STARS and provide a timeline to the reviewers for reference.

IV. REVIEW OF THE H SUBMISSION

Review of the H submission will involve at least one representative from each team involved in the review of technical sections selected by the sponsor in the eSubmitter administrative cover sheet and will allow for confirmation of requirements across all applicable technical sections.

- The PM will have 2 days from the assignment of the H submission to review the submission for completeness/appropriateness and issue consult requests to all members of the review team.[3] The PM will share a timeline for review of the submission for reviewers' reference, because this submission has a shorter review timeframe (60 days) then what will be reflected in STARS (100 days) due to current STARS limitations.

- Team leaders will assign consults within 3 days from the date that the consult is sent.

- The assigned consulting reviewer (CR) should confirm the status of their technical section and identify any concerns with the sponsor's proposed development plan. The CR should notify 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, will determine whether additional action is needed, such as:

    - Advising the sponsor that an H submission is not the appropriate submission type;

    - Requesting an amendment with additional information from the sponsor; or

[3] See section IV, part A of P&P 1243.3024 Scheduling and Holding Meetings with Outside Parties, for details about creation and assignment of consults.

- Scheduling an internal meeting of the review team to discuss the submission and CVM's response.

- The CR determines technical section 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 technical section, the review team will determine whether:[4]

  - No new submission is required (e.g., the technical section is not affected by a supplemental change; or the sponsor has appropriately referenced, including justification, a completed technical section from another application in their proposed development plan);

  - New submission(s) is required to complete the technical section, and whether the sponsor's proposal for completing the technical section is acceptable, including any recommendations/feedback from the CR; or

  - 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 technical section.

- If after sufficient review of the materials in the H submission, a CR has significant concerns about one or multiple technical section(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 technical section requirements of concern with CVM. Review of the H 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 technical sections of concern, including clarification of the CVM's concerns, will be reflected in the H submission acknowledgement letter.

V. CONTENT OF THE ACKNOWLEDGEMENT LETTER AND INTERNAL DOCUMENTATION

A. Acknowledgement Letter

CVM will provide written feedback, including confirmation of the status of each major technical section (including technical sections considered complete), in an acknowledgement letter to the sponsor using the appropriate office template.[5]

[4] See P&P 1243.3050 Determining Technical Section Requirements for New Animal Drug Product Approval
[5] Sponsor Development Plan Feedback (H Submission) Acknowledgement Letter Template.docx on the ONADE Templates SharePoint site
Internal information redacted.

The PM will prepare the acknowledgement letter, including any comments provided by the review team to be relayed to the sponsor.[6] Documentation of reviewer concurrence with the acknowledgment letter language is defined below in Section B.

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

- For technical sections or components (in the case of the Human Food Safety technical section) that the sponsor identifies in eSubmitter as complete, CVM will provide feedback in the H submission acknowledgement letter that CVM agrees, disagrees, or that CVM cannot confirm the sponsor's assessment.

- For any technical sections 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 technical section complete letter when they submit their NADA for approval.[7]

- 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 H submission. CVM's feedback may be modified in the future if substantiated scientific requirements essential to the determination of safety or effectiveness arise after the review of the H submission, including new scientific issues/information.[8]

B. Submission Summary and CR Reviews

The PM will document 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 H submission need to be documented, or if information related to the H 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.[9]

[6] Refer to P&P 1243.3025 Preparing Meeting Documentation (i.e., Memorandum of Conference, Acknowledgement Letter, Other Review Documentation), for reviewer instructions on providing information to the sponsor in an acknowledgement letter.

[7] Refer to P&P 1243.3025 Preparing Meeting Documentation (i.e., Memorandum of Conference, Acknowledgement Letter, Other Review Documentation), for reviewer instructions on providing information to the sponsor in an acknowledgement letter.

[8] Refer to 21 CFR 514.5(g) - Modification of presubmission conference agreements.

[9] See P&P 1243.3009 Format and Style Conventions for Reviews and Submission Summaries, for information on format and style conventions for a scientific review.

VI. TIMEFRAMES FOR PREPARING AND REVIEWING SUBMISSION DOCUMENTATION

CVM has **60 days** from the received date to issue the acknowledgement letter to the sponsor. Because the times allotted for preparing, circulating, and concurring or commenting on the documentation, and closing out the H submission, are relatively brief, it requires a collaborative effort. Individuals are expected to provide their text and concurrence or comment within the timeframes below.

A. Consulting Reviewer Initial Comments and Review

1. The CR(s) will notify the PM of any concerns with the submission, if applicable, by **day 10**.

2. The CR will provide draft text to the designated lead consultant, when applicable. If the CR is providing text to the lead consultant (e.g., biostatistician may be providing text to a target animal division reviewer), this text is sent by **day 29**.

3. The CR(s) will provide the PM comments to be included in the letter by **day 40**. The CR(s) will provide comments they want communicated to the sponsor in the acknowledgement letter no later than 40 days from the received date of the H submission. The text provided to the PM must be cleared using the established procedures of the CR's division. The comments can be sent through email or provided in a written consulting review by day 40.

4. The CR(s) will close out the consulting review request through Appian by **day 40**. All consulting reviews will be returned through Appian no later than 40 days after the received date of the H submission.[10]

B. Review of and Concurrence on the Acknowledgement Letter

1. The PM will prepare and provide access to the draft acknowledgement letter to the CR(s) by **day 47**. The PM will draft the acknowledgement letter, as described above, incorporating the sections and comments written by the CR(s). The PM will clear the draft letter through the PM's team leader and then make it available to the CR(s) for concurrence and comment. The documentation will be posted in a shared location so that comments can be entered directly into the draft(s).

2. CR(s) will concur on the acknowledgement letter by **day 54**. The CR(s) will provide comment, work through revisions, and concur on the acknowledgement letter by day 54.

C. Closing Out the Submission

1. The PM will finalize the letter by **day 60**. The PM will work through all the submitted edits and compile all of the concurrences from the CR(s), before finalizing the acknowledgement letter and submission summary. The PM will

[10] These procedures will be consistent with P&P 1243.3029 Closing Out a Consulting Review for STARS Submissions.

follow their team's established procedures for clearing the final action package for the H submission through their team leader and closing it out in Appian by day 60.

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

VIII. VERSION HISTORY

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