OFFICE OF NEW ANIMAL PRODUCT EVALUATION REVIEWER'S CHAPTER

IMPLEMENTING SHORTENED REVIEW TIMES FOR NEW ANIMAL DRUG APPLICATION (NADA) REACTIVATIONS AND INVESTIGATIONAL NEW ANIMAL DRUG (INAD) FILE RESUBMISSIONS USING eSUBMITTER

I. PURPOSE

This document describes the Office of New Animal Product Evaluation's (ONAPE) procedures for implementing shortened review time (SRT) for reactivations of new animal drug applications (NADAs) and resubmissions to an investigational new animal drug (INAD) file.

II. BACKGROUND

On October 1, 2014, CVM implemented a SRT process for NADA reactivations and INAD resubmissions as outlined in the Animal Drug User Fee Act (ADUFA) Reauthorization Performance Goals and Procedures – Fiscal Years 2014 through 2018 (ADUFA III Goals Letter). Refer to Section IV of this document for the criteria to determine whether an application or submission may qualify for SRT when reactivated or resubmitted. Appendix 1 also provides the list of the criteria.

III. APPLICATION/SUBMISSION TYPES THAT MAY QUALIFY FOR SRT WHEN REACTIVATED OR RESUBMITTED

In the ADUFA III Goals Letter, CVM identifies the four types of NADA and INAD submissions that may qualify for SRT when reactivated or resubmitted. Table 1 summarizes these submission types and their associated review timeframes.

Table 1. CVM ONAPE Review Times

Submission type: ADUFA III Goals Letter terminology	Submission type: CVM ONAPE terminology	Initial submission: normal review time	Reactivation or resubmission: SRT
Non-administrative new animal drug applications	Non-administrative original NADA	180 days Submission code: A	135 days Submission code: E
Non-manufacturing supplemental new animal drug applications	Non-administrative B1 supplemental NADA	180 days Submission code: C	135 days Submission code: R
INAD study submission[1]	Technical section (TS) submission	180 days Submission code: P	60 days Submission code: P
INAD protocol without data submission	Protocol	50 days Submission code: E	20 days Submission code: E

IV. CRITERIA FOR SHORTENED REACTIVATION OR RESUBMISSION REVIEW TIMES

CVM generally offers the shortened reactivation and resubmission times where possible. We expect sponsors to continue to submit high-quality submissions to facilitate review by ONAPE. If we decide to issue an application incomplete, TS incomplete, or protocol non-concurrence letter, reviewers should confirm that all of the following criteria are met in their decision to offer a SRT for a future NADA reactivation or INAD resubmission.

1. The sponsor submitted the initial application or submission using eSubmitter.
2. We can clearly identify and communicate to the sponsor the changes and/or submission of additional information that could reasonably be expected to complete the application or submission.
3. We can complete review of the NADA reactivation or INAD resubmission and make the review decision within the SRT.
4. All consulting reviews and the primary review, when taken as a whole, support the decision to offer the SRT.

Based on the criteria above, CVM states in the incomplete or non-concurrence letter whether the future NADA reactivation or INAD resubmission may qualify for SRT and indicates the appropriate review timeframe. The letter outlines the criteria to qualify for SRT.

Because the decision to offer the SRT is situation-dependent, the determination of whether to offer it when issuing an incomplete or non-concurrence letter involves the judgment of the primary reviewer (PR) in conjunction with the consulting reviewers (CRs). As necessary, the PR keeps the branch chief (BC), CRs, and project managers (PMs) informed to assure consistency across ONAPE.

[1] The shortened SRT process does not apply to stand-alone Human Food Safety – Microbial Food Safety Hazard Characterization TS submissions (100-day review time).

V. MEETINGS TO DISCUSS INCOMPLETE OR NON-CONCURRENCE LETTERS

If a sponsor wants to discuss proposals to address the deficiencies in the incomplete or non-concurrence letter, they can do so informally or formally within 120 days of receiving CVM's non-concurrence or incomplete letter. Informal communication occurs by email or telephone and does not result in a memorandum of conference (MOC). For example, CVM can address appropriately minor questions and clarifications of CVM's comments in an informal meeting.

If the sponsor wants a formal meeting with an MOC, there is time within the 120-day response window to accomplish this. The sponsor should submit a formal meeting request (submission type code Z) as described in P&P 1243.3024.

VI. EVALUATION OF THE REACTIVATION OR RESUBMISSION

The PR examines the NADA reactivation or INAD resubmission, once received, to confirm it qualifies for the SRT. An NADA reactivation or INAD resubmission qualifies for the SRT if it meets the following criteria.

1. The sponsor submits it using eSubmitter within 120 days of CVM's dated incomplete or non-concurrence letter.
2. The sponsor certifies that no additional information beyond the scope of addressing the comments/deficiencies was included in the NADA reactivation or INAD resubmission. CVM determines that the sponsor only included information that adequately addresses the comments and deficiencies stated in the initial incomplete or non-concurrence letter.
3. When resubmitting a protocol, the sponsor highlighted the changes within the text of the protocol, including minor modifications that were necessary during the incorporation of the requested changes (e.g., section numbering, pagination). The sponsor also should provide a written response to each CVM comment and written certification (either in the cover letter or in eSubmitter) that, with the exception of the highlighted protocol changes, the text of the protocol found in the resubmission is identical to the text of the initial protocol. Additionally, sponsors should state that they did not make other text changes beyond those highlighted.

VII. HANDLING SUBMISSIONS THAT ARE DEFICIENT OR CONTAIN UNSOLICITED ADDITIONAL INFORMATION

A. Utilizing the Review Time Change Process

If the sponsor includes unrequested information in the parent submission, it may no longer qualify for SRT. When we determine a reactivation or resubmission does not qualify for SRT, we change the review time to the normal review and notify the sponsor. When we change the review time, the review time is changed to the normal review time (refer to Table 1 for normal review times).

The PR follows the instructions in the Appian User Guide to change the review timeframe using the 'Review Time Change' Appian Workflow. Before changing the review time, the PR prepares the Review Time Change notification letter using the template in the ONAPE Template SharePoint to be sent to the sponsor advising them

of the new CVM due date. The PR uploads the letter in Appian during the 'Review Time Change' Appian Workflow.

B. Utilizing the Reset the Clock Process

When we request an amendment during the SRT process, we have determined we need information and have already determined that if the sponsor can submit that information in the agreed timeframe, we can complete our review in the SRT established timeframe. It is important to note that if we receive an unsolicited amendment, an amendment that contains unrequested information, or a major amendment during the SRT without the sponsor having a prior conversation with us, we will utilize the reset the clock process if the review team determines the information is not minor in nature and there isn't sufficient time to complete the review of the submission within the SRT. When we reset the clock (per P&P 1243.3026) on a reactivation or resubmission, we will base its new due date upon the amendment received date, change the review timeframe to the normal review time associated with the submission type, and notify the sponsor.

C. Utilizing Another SRT

If, after review of the submitted information, we find that a reactivation or resubmission is still incomplete, we issue another incomplete or non-concurrence letter to the sponsor, respectively. Using the same criteria above, we determine if we can offer another shortened reactivation or resubmission review time in the next review cycle. There is no limit on the number of review cycles a reactivation or resubmission may qualify for SRT. If we determine that a reactivation or resubmission does not qualify for the SRT in the next review cycle, it will be assigned the normal review time (refer to Table 1 for the normal review times).

VIII. ACTIONS ON NADA/INAD SUBMISSIONS AND REACTIVATIONS/RESUBMISSIONS

The following tables summarize the Appian actions available to reviewers and include the new Final Action Codes for offering shortened review. The actions apply to non-administrative original NADA, non-administrative B1 supplemental NADA, and INAD technical section submissions and protocols. The available actions in the tables below also apply to NADA reactivations and INAD resubmissions.

Table 2. Appian Actions for Non-administrative NADAs (sub types: C, A, R, E)

Appian Action	Description
Refuse to File	Refer to P&P 1243.2050
Withdraw of Pending Supplement	If the sponsor submits an amendment requesting to withdraw the pending supplement, we discontinue the review of the application and issue an acknowledgement letter.
Application Complete (Approvable)	If we consider the application complete based on the submitted information, we issue the appropriate approval letter.
Application Incomplete	If we consider the application incomplete based on the submitted information and SRT upon reactivation is **not** possible, we issue an incomplete application letter.
Application Incomplete, Shortened Review Reactivation Offered	If we consider the application incomplete based on the submitted information but a SRT upon reactivation is possible, we issue an incomplete application, SRT offered letter. FINAL ACTION CODE: (INC APP SR) INCOMPLETE APPLICATION; SHORTENED REVIEW REACTIVATION OFFERED; LETTER SENT

Table 3. Appian Actions for INAD TSs (sub type code: P)

Appian Action	Description
Refuse to Review	If we consider the submission wholly incomplete on its face, we issue a RTR letter within 60 days of receipt.
Stop Review	If the sponsor submits an amendment requesting we stop review, we discontinue the review of the submission and issue an acknowledgement letter.
Technical Section Complete	If we consider the submission acceptable and it completes a TS based on the submitted information, we issue a TS complete letter.
Submitted Information Acceptable, Technical Section Incomplete	If we consider the submitted information acceptable but other aspects of the TS remain incomplete, we issue a submitted information acceptable, TS incomplete letter.
Technical Section Incomplete; Submitted Information Not Acceptable	If we consider any of the submitted information unacceptable, the TS is incomplete, and we do **not** offer SRT. We will issue a TS incomplete letter.
Technical Section Incomplete, Shortened Review Resubmission Offered	If we consider the TS incomplete based on the submitted information but a shortened review upon resubmission is possible, we issue a TS incomplete, SRT offered letter. FINAL ACTION CODE: (TS INC SR) TECHNICAL SECTION INCOMPLETE; SUBMITTED INFORMATION NOT ACCEPTABLE; SHORTENED REVIEW RESUBMISSION OFFERED; LETTER SENT

Table 4. Appian Action for INAD Protocol Submissions **(sub type code: E)**

Appian Action	Description
Refuse to Review	If we consider the submission wholly incomplete on its face, we issue a RTR letter within 60 days of receipt.
Stop Review	If the sponsor submits an amendment requesting we stop review, we discontinue the review of the submission and issue an acknowledgement letter.
Protocol Concurrence	If we can concur on the submitted protocol, we issue a protocol concurrence letter.
Protocol Non-concurrence	If we cannot concur on the submitted protocol and it does not qualify for SRT, we issue a protocol non-concurrence letter.
Protocol Non-concurrence, Shortened Review Resubmission Offered	If we cannot concur on the submitted protocol but a shortened review upon resubmission is possible, we issue a protocol non-concurrence, SRT offered letter. FINAL ACTION CODE: (PROT NC SR) PROTOCOL NOT ACCEPTABLE AS SUBMITTED; SHORTENED REVIEW RESUBMISSION OFFERED; LETTER SENT

As stated in Section III, the shortened resubmission review process does not apply to stand-alone Human Food Safety – Microbial Food Safety Hazard Characterization technical section (Submission Type Code P) submissions (100-day review clock).

A. Initial Submission – Normal Review Time

When a sponsor submits the initial submission, STARS assigns the normal review timeframe to the submission. CVM's Electronic Submission System (ESS) generates a submission receipt advising the sponsor of the CVM due date. This receipt is sent via the Electronic Submissions Gateway (ESG). The PR follows conventional CVM review procedures to review and close out the submission in Appian within the normal review timeframe (see Table 1). Refer to Tables 2, 3, and 4 for the available actions.

B. Reactivation or Resubmission

If CVM offered a shortened reactivation or resubmission review time in their incomplete or non-concurrence letter, reviewers follow the process outlined in Section 1 below. If CVM did not offer shortened reactivation or resubmission review time in their incomplete or non-concurrence letter, reviewers follow the process outlined in Section 2 below.

1. CVM offered the sponsor SRT for their reactivation or resubmission in the incomplete or non-concurrence letter to the initial submission.

    a. Sponsor submits the reactivation or resubmission 'on or after day **121**'

    If the sponsor submits the reactivation or resubmission 'on or after day **121** of CVM's dated incomplete or non-concurrence letter,' STARS will assign the normal review timeframe to the submission. The sponsor will receive a submission receipt via the ESG advising them of the CVM due date. The PR follows conventional CVM review procedures to review and close out the

submission in Appian within the normal review time. The PR should refer to Table 2, 3, and 4 for the available final actions on a submission. There is no limit on the number of review cycles that we can offer SRT on qualifying reactivations or resubmissions.

b. Sponsor submits the reactivation or resubmission 'on or before day **120'**

If the sponsor submits the reactivation or resubmission 'on or before day **120** of CVM's dated incomplete or non-concurrence letter,' STARS will assign the shortened review timeframe. The sponsor receives a submission receipt via the ESG advising them of the CVM due date.

If CVM determines at any point during the review, using the criteria in Section IV, that the submission does not meet the criteria for SRT, we will change the review time to the normal review timeframe (see table 1). Refer to Section VII for the Review Time Change Process. The PR follows conventional CVM review procedures to review and close out the submission in Appian either within the SRT or normal review time.

2. CVM did not offer the sponsor SRT in their incomplete or non-concurrence letter.

When a sponsor submits the reactivation or resubmission, STARS assigns the normal review timeframe to the submission. The sponsor receives a submission receipt via the ESG advising them of the CVM due date.

The PR follows conventional CVM review procedures to review and close out the submission in Appian within the normal review timeframe (see Table 1). Refer to Table 2, 3, and 4 for the available final actions.

C. INAD Phased Review Process - Impact of Last Pending Technical Section Submission (Submission Type Code P)

During the end game (as described in P&P 1243.3051), the 'last technical section submission' (frequently referred to as the last P) under review is the TS with the latest CVM due date, regardless of its review time; the last TS can have a 180-day, 100-day, or 60-day review time. The most recently submitted TS may not necessarily be the last P. The PM maintains a detailed project timeline to help determine the last P within a project.

1. Initial Submission - Normal 180-day review time

The due dates for the Labeling TS and All Other Information (AOI) TSs (submission type code M; referred to as minor TSs and described in P&P 1243.4080) and the Freedom of Information (FOI) Summary (submission type code Q; described in P&Ps 1243.5761 and 1243.5762) assume the due date of the last pending TS (submission type code P). The PM reminds the sponsor to submit the minor TSs no later than 80 days into the review of the last TS. The review time for the minor TSs is usually around 100 days, but it can be longer or shorter depending on when the sponsor submits the Labeling and AOI TSs. If the sponsor is late in submitting the minor TSS, the PR, BC, and PM assign an appropriate due date that may not be reflected in STARS but is communicated to the sponsor. The PM looks at the pending P submissions and ensures that any

pending M submission references the 'last P' submission. The FOI Summary Q should be created when the minor TSs arrive.

If we incomplete one or more of the pending P submissions, we continue a thorough review of the minor TS commensurate with the information available at that time and include our review findings in the Labeling and AOI TS incomplete letters.

EXAMPLE: The Chemistry, Manufacturing, and Controls (CMC) TS is the last pending TS. The M submissions (FOI and AOI) are submitted and given the same due date as the CMC P submission. All other TSs, including Effectiveness and Target Animal Safety, are complete. The Division of Manufacturing Technologies notifies the target animal reviewer that it will incomplete the CMC submission. The target animal reviewer continues the review of the minor TSs, allowing time for the primary and consulting reviews (such as the Office of Surveillance and Compliance). The target animal reviewer includes CVM's comments in the Labeling and AOI TS incomplete letters. The target animal reviewer indicates in the Labeling incomplete letter that CVM might make additional changes to the labeling when the labeling is reviewed as a whole. The reviewer instructs the sponsor to incorporate our comments before resubmitting the minor technical sections in the next review cycle.

If there is an open Q submission for the FOI Summary, the PR completes the Q commensurate with the information available to permit more efficient preparation of the FOI Summary later and follow the procedures in P&P 1243.5761.

2. Resubmission - Shortened 60-day review time (Last P)

   The due dates for the minor TSs and the FOI Summary Q assume the due date of the last pending TS (submission type code P). The PM reminds the sponsor, prior to the resubmission of the last P, to resubmit the minor TSs at the same time as the last P submission. If the sponsor submits the minor TSs late, the PR, BC, and PM assign an appropriate due date that may not be reflected in STARS but is communicated to the sponsor. The PM looks at the pending P submissions and ensure that any pending M submission references the 'last P' submission. The FOI Summary Q should be created when the last P submission arrives to ensure that reviewers have at least 60 days to write the FOI Summary.

IX. REFERENCES

ADUFA III Goals Letter

https://www.fda.gov/media/85724/download

Appian User Guide

Internal information redacted.

CVM Program Policies and Procedure Manual – ONAPE and OGAD Reviewer's Chapter

1243.2050 - Refuse to File and Refuse to Review

1234.3024 - Scheduling and Holding Meetings with Outside Parties

1243.3026 – Assessing Submission Quality and Amending and Resetting the Clock on Submissions

1243.3051 - Verifying Scope and Technical Status for Phased Review Investigational New Animal Drug (INAD) Projects in the End Game

1243.4080 - Labeling and All Other Information Technical Sections (Minor Technical Section or M Submissions)

1243.4085 - All Other Information

1243.5761 - Freedom of Information (FOI) Summary for Original and Supplemental New Animal Drug Applications (NADA)

1243.5762 - Freedom of Information (FOI) Summary for an Animal Drug Availability Act (ADAA) Medicated Feed Combination New Animal Drug Application

X. VERSION HISTORY

October 1, 2014 – Original version.

March 15, 2017 – Reformatted to current format for P&Ps and corrected broken link to ONADE Template page in SharePoint

March 07, 2019 – Updated to include a link to the ADUFA III goals letter, include language about shortened review timeframe certifications that will be included in cover letters and eSubmitter, referenced end game information. Information on the Appian workflow was removed from the body of the P&P and the Appian User Guide included in the references. Updated references in the reference sections and other minor edits and corrections for clarity.

July 16, 2019 – Updated FDA.gov URL links to new directed links due to migration of new FDA.gov Website. No other updates needed.

July 2, 2020 - Updated all internal links for SharePoint sites because FDA has migrated this information to a new version of SharePoint.

September 23, 2020 - Created a new section on handling submissions that are deficient or contain unsolicited information. Clarified information on resetting the clock and changing the review time to distinguish that the two are different and are utilized in different circumstances with different impacts on review due dates.

February 2, 2022 – Updated to fix minor grammar errors and updated section VII B to add language to be consistent with P&P 1243.3026 Amending and Resetting the Clock on Submission Tracking and Reporting System (STARS) Submissions.

March 24, 2022 – Revised table 2 to include Appian action of withdraw of supplement. Revised tables 3 and 4 to include stop review. Revised table 3 to add information to the Appian action for Technical Section Incomplete to include “Submitted Information not Acceptable”. Revised the description to state if any of the submitted information in the

technical section is unacceptable, the technical section is incomplete. Revised reference section.

July 18, 2022 – Quality systems review for minor formatting updates.

March 12, 2025 – Quality systems review for minor formatting updates. The Office of New Animal Drug Evaluation (ONADE) has reorganized into the Office of New Animal Product Evaluation (ONAPE) and the Office of Generic Animal Drugs (OGAD). Updated all reference of ONADE to ONAPE. Updated all HFV codes to the new abbreviation.

July 30, 2025 – Updated to add Office of Generic Drugs (OGAD) to the header and footer.

September 23, 2025 – Updated to remove OGAD from the header and footer. A decision was made to use only the offices that the P&P apply to in the header and footer.

APPENDIX 1 CRITERIA FOR SHORTENED REACTIVATION/RESUBMISSION REVIEW TIMES

CVM uses the below criteria to determine if an application or submission qualifies for shortened reactivation or resubmission timeframe.

1. The sponsor submits the initial NADA or INAD submission on or after October 1, 2014, using the eSubmitter electronic submission tool.
2. CVM offered a shortened reactivation or resubmission review time in their incomplete or non-concurrence letter.
3. The sponsor submits the NADA reactivation or INAD resubmission using eSubmitter within 120 days of CVM's incomplete or non-concurrence letter.
4. The sponsor only includes information that adequately addresses the comments and deficiencies stated in the initial incomplete or non-concurrence letter.
5. The sponsor certifies that no additional information beyond the scope of addressing the comments/deficiencies was included in the NADA reactivation or INAD resubmission.
6. The sponsor highlights changes within the text of the protocol.
7. The sponsor provides a written response to each CVM comment and written certification that, with the exception of the highlighted protocol changes, the text of the protocol found in the resubmission is identical to the text of the initial protocol.