# REQUESTING A QUALITY ASSURANCE STUDY REVIEW FROM THE QUALITY ASSURANCE TEAM



## I. PURPOSE

This document describes the procedure to request a Quality Assurance (QA) Study Review from a QA study reviewer (QASR) on the Office of New Animal Drug Evaluation's (ONADE) QA Team (HFV-184). A QA Study Review is requested for submissions with safety, effectiveness, and bioequivalence data. These submissions are typically Submission Tracking and Reporting System (STARS) P submissions to a (generic) investigational new animal drug ((J)INAD) file or in a traditional or abbreviated new animal drug application ((A)NADA).[1] This document also describes how the QASR conducts their review and provides timeframes associated with the process steps.

## II. QUALITY ASSURANCE STUDY REVIEW PROCESS

A QASR on the QA Team performs the QA Study Review on a submission that contains effectiveness, safety (target animal safety or human food safety), or bioequivalence studies with data. The QASR consulting review begins after the Refuse to Review/Refuse to File (RTR/RTF) assessment is completed by the primary review division (PR) and the QASR is notified that the submission is acceptable for further review (see Policies and Procedures (P&Ps) 1243.3100 and 1243.2050 for details on RTR/RTF). Appendix 1 contains a flow chart summarizing the process for the QA Study Review of a data submission including timeframes for each step.

Before initiating the review, the QASR notifies the primary reviewer (PR) that the QA Study Review is starting. The PR can discuss any issues or concerns with the QASR. Regular communication will continue throughout the review process. The QA Study Review is conducted in two parts: the submission screen and the full study review.

### A. Part 1: Submission Screen

Screening the submission is the first phase of the QA Study Review. This screen is conducted to confirm that all necessary documents and data are included for each study in the submission or application that will be used to support scientific and regulatory decisions. The QASR selects the appropriate submission screen template depending on the type(s) of studies included in the submission or application and their stated standards of conduct (i.e., Good Clinical Practice (GCP) or Good Laboratory

[1] Note: Per current processes ,P submissions received by the Division of Animal Bioengineering and Cellular Therapies do not undergo a quality assurance study review.

Practice (GLP)). Although there is occasional variation, typically submissions with STARS subclass codes of EF have studies conducted in accordance with the GCP guidance (Guidance for Industry (GFI) #85) and submissions with STARS subclass codes of TS, HF, and BE typically have studies conducted in accordance with the GLP regulations (21 CFR part 58). If the submission contains a mixture of studies (e.g., a traditional (A)NADA), the QASR modifies the screen as appropriate to accommodate the submitted studies. While conducting the screen, the QASR:

1. reviews each final study report and study protocol in the submission to verify they are present and reasonably complete and that all relevant categories of raw data copies and contributor reports are included in the submission (per the study protocol and ONADE policy regarding requirements for raw data); and

2. identifies the data collection method(s) and appropriate corresponding information or data files in the submission.

The screen target completion date is Day 50 of the review clock. If significant deficiencies are identified, the QASR provides Transmit to Sponsor comments and asks the PR to request an amendment. Data submissions with a shortened review time (SRT) do not undergo a screen and only a full study review is performed.

It is possible that the number and nature of the significant deficiencies found may prompt the QASR reviewer to request the submission be RTR/RTF. If this situation arises, the determination for how to move forward is discussed and agreed upon by the review team.[2] If a technical section determined to be incomplete by the review team, the QASR provides Transmit to Sponsor comments to the PR for the technical section incomplete letter.

## B. Part 2: Full Study Review

The full study review is started only if the submission is determined to be acceptable for further review. For submissions with SRT, the QA Study Review process is modified to meet the required consulting timelines. The QASR reviews the submission and any amendments. In this phase, the QASR:

1. confirms that the final study report accurately describes the study conduct, the study was conducted in accordance with the protocol, and any amendments or deviations were documented;

2. confirms the final study report accurately reflects the copies of raw data (study documentation) submitted;

3. confirms the standard of conduct (typically GLP or GCP) stated in the protocol appears to have been followed; and

4. provides an assessment of study and data quality and identify any issues of the study or data quality that should be further evaluated via a Bioresearch Monitoring (BIMO) inspection or addressed by the submission of additional information by the sponsor.

[2] For the purposes of this process, the review team is the PR and all consulting reviewers involved in the review of the submission, including the QASR.

The QASR performs a complete data quality review, but the QASR's Transmit to Sponsor comments focus on the following five critical areas:

1. drug accountability;
2. dosage to animal;
3. animal accountability and enrollment;
4. study endpoints and critical variables; and
5. adverse events.

Issues outside of these five areas of focus are discussed in the QA Study Review but will not result in Transmit to Sponsor comments unless the issues are egregious and impact the quality and integrity of the study or data. In addition, any protocol deviation identified by a QASR but not discussed in any manner in the submission will result in a Transmit to Sponsor comment, asking the sponsor to provide documentation for the deviation that includes:

- the date the deviation occurred;
- a description/explanation of the deviation;
- any corrective or mitigating action that was undertaken to address the deviation, if appropriate; and
- the impact of the deviation on the study.

The documentation of the deviation should meet the basic standards expected for all raw data: attributable, legible, contemporaneous, original, and accurate (ALCOA). Often, the QASR recommends that quality issues be evaluated by appropriate review team members to determine their impact on the acceptability of the study and the necessity of any further action by the Center for Veterinary Medicine (CVM) or the sponsor.

## III. QUALITY ASSURANCE STUDY REVIEW REQUEST: GENERAL INFORMATION

### A. QASR Responsibilities

While conducting a QA Study Review, the QASR:

1. reviews the submission for study and data integrity issues using team Standard Operating Procedures (SOPs), templates, and checklists specific to the type of study being reviewed;
2. assesses the quality and credibility of the data and final study report; and
3. communicates with other members of the review team if issues are identified.

It is important to note that the QASR utilizes his or her QA expertise to assess the submission quality. Critical gaps in data quality will result in Transmit to Sponsor comments. Other data quality issues are identified for the PR to assess when

determining whether issues found impact the study(ies) acceptability to support the approval of the new animal drug.

**B. Contacting the Quality Assurance Team Leader**

The PR emails the QA Team Leader (TL) and requests a consult for a QA Study Review. This request is made before a formal consult is requested in Appian. The email subject line specifies the request for a QASR consulting review and the submission identifier as follows “Request for QASR Consult; X-XXXX-X-XXXX (XX).” Any pertinent background information or special considerations are included in the email request.

The QA TL reviews the STARS pending lists of the team and determines whether the resources are available to accept a consult. Within three (3) business days, the QA TL responds to the requester’s email. In special cases where study and data quality are of specific concern, the PR contacts the QA TL to discuss the package and timing of the QA Study Review.

**C. Creating the QASR Request Consult in Appian**

Once the PR receives confirmation that the QA Team can accept a consult, the PR requests a formal QASR consult in Appian according to the procedures in P&P 1243.3200. The PR provides any critical information about the in the instructions section of the consult.

**D. Assignment of the QASR Consults**

Once the QA TL receives the Appian notification for the request for a QASR consult, he or she will assign the consult to a QASR.

**E. Review of the QASR’s Draft Review**

When the QASR sends the draft review to the QA TL, the QASR also sends a copy of the draft review to the PR and any other members of the review team designated by the PR. The review is identified as draft by a watermark that says DRAFT. The QASR schedules a meeting with the PR and additional attendees determined by the PR to discuss the QASR’s findings and address questions or concerns. If the QASR determines that a BIMO inspection is needed, the QASR and PR coordinate the completion of the necessary request forms (see P&P 1243.8215). Every effort is made by the QASR to schedule this meeting before the QASR review is finalized. At the meeting, the review team discusses the QASR’s findings and any potential revisions to the QA Study Review.

**F. Returning the QASR Consult**

Once the QA Review is completed and ready to finalize, the QASR uploads the review and returns the consult to the PR in Appian (see P&P 1243.3029). The final QASR review is returned by Day 130 as per the consulting due date established in STARS for data submissions.

## IV. REFERENCES

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

1243.2050-Refuse to File and Refuse to Review

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

1243.3100- Refuse to Review (RTR) and Refuse to File (RTF) Assessment of Submissions and Applications That Contain Data

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

## V. VERSION HISTORY

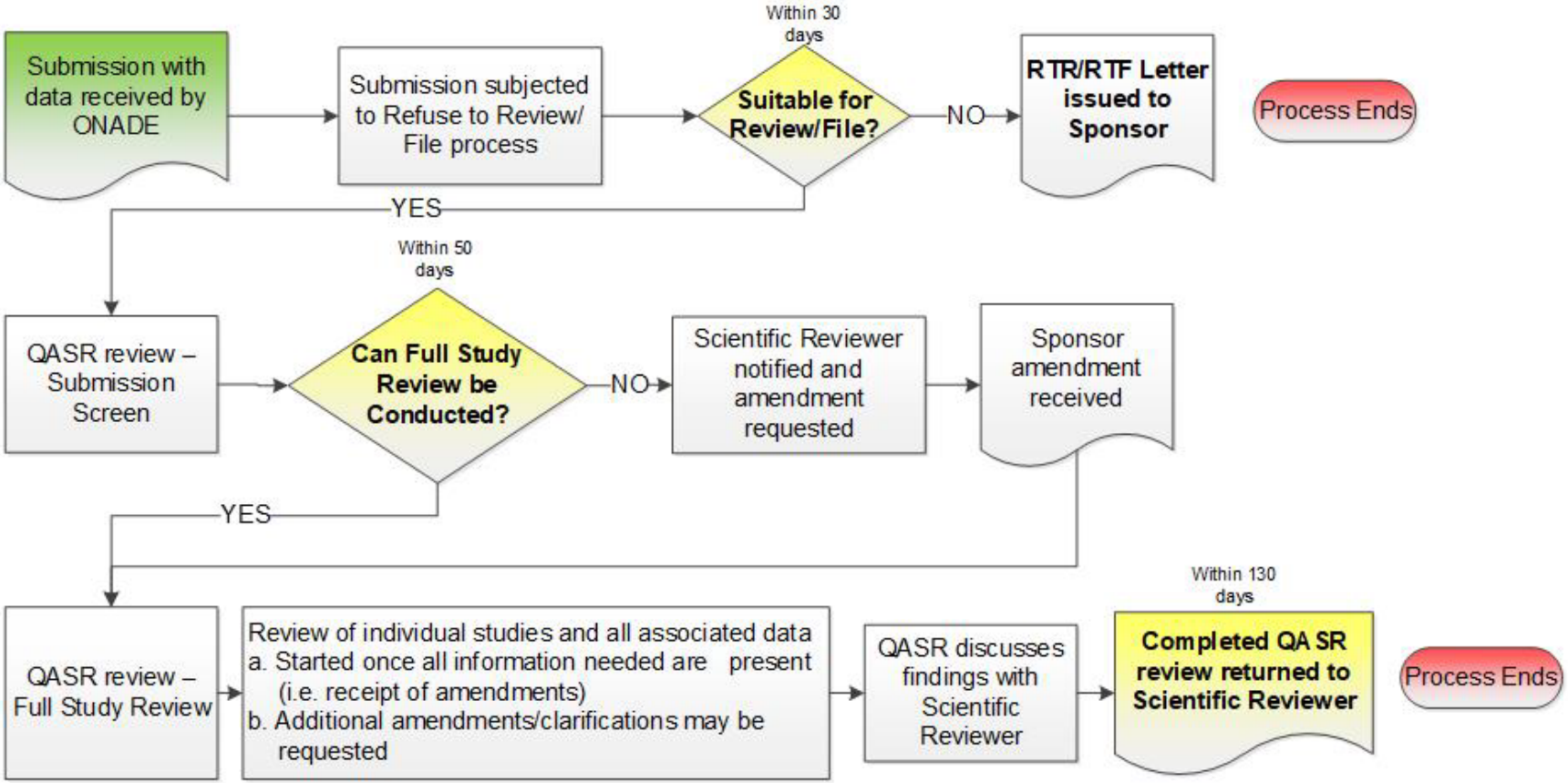
October 11, 2018 – Original version.

May 6, 2021 – Updated titles in the reference section and reflect that there is now a Division of Animal Bioengineering and Cellular Therapies.

July 15, 2022 – Quality systems review for minor formatting updates.

October 19, 2023 – Quality system review and minor formatting updates made. The document was placed in the most recent template. In addition, to align ONADE documentation with the agency's Visual Identity program, the font was changed from Verdana 10-point to Arial 11-point font.

## APPENDIX 1. QUALITY ASSURANCE STUDY REVIEWER (QASR) REVIEW PROCESS FLOWCHART




October 19, 2023