OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

REFUSE TO FILE AND REFUSE TO REVIEW

I. PURPOSE

This document describes when the Office of New Animal Drug Evaluation (ONADE) may "refuse to file" (RTF) an application or "refuse to review" (RTR) a submission and provides instructions for using the office letter templates to notify the sponsor (or applicant) of our decision.

II. REFUSE TO FILE

A. Applicability

We may RTF an original or supplemental new animal drug application (NADA) or an abbreviated NADA (ANADA) and reactivations of applications (see 21 CFR 514.110). RTF only applies to applications; we may not RTF a submission to a pioneer or generic investigational new animal drug file (INAD or JINAD).

B. Making the Decision

The intent of refusing to file is to ensure that the sponsor provides complete and high-quality information. If any of the criteria below apply, consult with your team leader (TL) and division director (DD) on whether to refuse to file or to request an amendment to the application. If you decide to RTF, then seek concurrence from the Office Director. It is the Office Director who signs RTF letters. Refer to P&P 1243.3100 for a description of the basic assessment of applications to determine when to RTF an application of insufficient quality.

C. Criteria

We RTF a NADA or ANADA if any of the following criteria apply.

- The application does not contain complete and accurate English translations of any pertinent part in a foreign language.
- The application is incomplete on its face in that it is not properly organized and indexed.
- The information concerning the required matter is so inadequate that the application is clearly not approvable.

- The new animal drug is to be manufactured, prepared, propagated, compounded, or processed in whole or in part in any State in an establishment that has not been registered or exempted from registration under the provisions of section 510 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 USC 360.[1]

- The sponsor does not reside or maintain a place of business within the United States and the application has not been countersigned by an attorney, agent, or other representative of the applicant, which representative resides in the United States and has been duly authorized to act on behalf of the applicant and to receive communications on all matters pertaining to the application.

- The new animal drug is a drug subject to licensing under the Virus-Serum-Toxin Act (VSTA) (21 USC 151, et seq.).[2]

- The application fails to include, with respect to each nonclinical laboratory study contained in the application, either a statement that the study was conducted in compliance with the good laboratory practice regulations set forth in 21 CFR Part 58, or, if the study was not conducted in compliance with such regulations, a brief statement of the reasons for the non-compliance.

- The applicant fails to submit a complete environmental assessment under 21 CFR 25.40 or fails to provide sufficient information to establish that the requested action is subject to the categorical exclusion under 21 CFR 25.30 or 21 CFR 25.33.

D. Communicating the Decision with the Sponsor

If we determine that an application is not acceptable for filing, we must notify the applicant of the reasons for our refusal within 30 days of receiving the application [see 21 CFR 514.110(c)]. Although the regulations do not explicitly require that we provide this notification in writing, it is our policy to do so. Use the appropriate office template to write the letter and document the decision in a review.

E. Filing Over Protest

An applicant may file over protest if it disputes our decision that the application is not acceptable for filing [see 21 CFR 514.110(d)]. The applicant must submit a written request that we file the application over protest. When we file an application over protest, the application has its original due date in our Submission Tracking and Reporting System (STARS). In this case, conduct a complete review that is as detailed as possible considering the quality and level of detail of the submission and document the deficiencies in your review and letter to the sponsor.[3]

[1] The Division of Veterinary Product Safety assigns establishment numbers to each person who registers an establishment under section 510 of the Act. For questions about an establishment number, contact the Marketed Product Information Team.

[2] Typically, the Office of Surveillance and Compliance in CVM assesses whether a product is subject to the FFDCA or VSTA before filing an NADA. As such, this criterion seldom provides a basis for refusing to file a submission.

[3] The regulations do not specify a timeframe in which a sponsor must file over protest. In most cases, we would expect the sponsor to file over protest in a relatively short timeframe. When a sponsor files over protest, we file the application as of the day originally received. This means that the application has the original due date. In the rare event that a sponsor files an application over protest such that you have a short timeframe to review the application, notify your DD, who is responsible for notifying the Office Director. Conduct a complete review of the application. The DD and Office Director will discuss any ADUFA timeframe implications.

III. REFUSE TO REVIEW

A. Applicability

We may RTR any INAD or JINAD submission that is of insufficient quality [see 21 CFR 514.110(b) and Guidance for Industry (GFI) #119].

B. Making the Decision

The intent of refusing to review a submission is to ensure that the sponsor provides complete and high-quality information. Use the criteria in Section III.C below when deciding to RTR an INAD or JINAD submission. If you think we should RTR a submission, talk to your TL and DD to get their concurrence. DDs sign RTR letters. Refer to P&P 1243.3100 for a description of the basic assessment of submission to determine when to refuse to review a submission of insufficient quality.

C. Criteria

In general, the criteria for refusing to review a submission are similar to those for refusing to file applications (see Section II.C.). In addition, we may RTR submissions where the number and types of errors in the submission cause us to question the quality of the entire submission [see 21 CFR 514.110(b) and GFI #119]. For example:

- missing data sets or missing components in the submission,
- lack of detail in a study protocol,
- discrepancies between electronic data sets and the paper copy,
- conflicting information between sections of the submission, and
- absence of important information.

D. Communicating the Decision to the Sponsor

When we decide to RTR a submission, we notify the sponsor in writing within 60 days of our receipt of the submission (see GFI #119). Our letter states that we did not accept the submission for review and summarizes the reason(s) for our decision. We also document the decision in a review.

IV. COMPLETING THE FINAL ACTION PACKAGE

Prepare the final action package using procedures in P&P 1243.3030. The list of Final Action codes may be accessed in STARS through the Quality Control > Printed Reports > Action Codes report. Do not use the STARS action code 063 (“Refuse Acc”, “Refuse to accept submission for filing; acct in arrears; letter sent”) for RTF or RTR actions. This code is only for use by ONADE’s Business Informatics Team when we refuse to accept a submission because the sponsor is not current on the fees owed under the provisions of the Animal Drug User Fee Act (ADUFA) or the Animal Generic Drug User Fee Act.

RTF final action letters are signed by the Office Director and are routed through the Quality Assurance Team, except that the Division of Manufacturing Technologies DD may sign RTF letters for manufacturing chemistry supplements. RTR letters are signed by DDs. We require Office-level authority on RTF generally because it has more substantial impact on the application and its sponsor.

V. REFERENCES

Code of Federal Regulations (Title 21)

Part 514 – New Animal Drug Applications

§514.110, Refuse to file

CVM Guidance for Industry

GFI #119, "How the Center for Veterinary Medicine Intends to Handle Deficient Submissions Filed During the Investigation of a New Animal Drug."

CVM Program Policy and Procedure Manual

1243.3010 - Format and Style Conventions for Letters

1243.3030 - Completing Final Action Packages for STARS Submissions

1243.3100 - ONADE Refuse to Review (RTR) and Refuse to File (RTF) Assessment of Submissions and Applications.

VI. VERSION HISTORY

December 13, 2005 – original version

April 26, 2010 – Updated to incorporate the ERA process. The document was also revised to reflect current ONADE processes.

August 14, 2017 – Updated to remove the ERA process.

November 26, 2018 – Removed reference to the retired P&P 1243.3022 entitled Implementing the Animal Drug User Fee Act of 2003.

September 10, 2019 – Updated to include that ONADE can now refuse to file reactivations of applications.

May 20, 2020 – Updated to include information about signature authorities in Section IV.

August 1, 2022 – Quality systems review for minor formatting updates.

May 24, 2023 - Quality system review conducted of the document and no updates or revisions were necessary at this time. 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.