REFUSE TO FILE AND REFUSE TO REVIEW

I. PURPOSE

This document:

- Describes when we (ONADE) may "refuse to file" an application or "refuse to review" 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 refuse to file an original or supplemental new animal drug application (NADA) or an abbreviated NADA (ANADA).[1] Refuse to file only applies to applications. Therefore, we may not refuse to file 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, you should consult with your team leader and division director on whether to refuse to file or to request an amendment to the application. If you decide to refuse to file, you should then seek concurrence from the Office Director. It is the Office Director who signs Refuse to File letters.

Refer to P&P 1243.3100 for a description of the basic assessment of applications to determine when to refuse to file an application of insufficient quality.

C. Criteria

We will refuse to file an NADA or ANADA if any of the following criteria apply:

[1] See 21 CFR 514.110

- 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.[2]
- 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 (21 USC 151, et seq.).[3]
- 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.[4] 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. We should also document the decision in a review.

[2] The Division of Surveillance assigns establishment numbers to each person who registers an establishment under section 510 of the Act. If you have questions regarding an establishment number, you should contact the Marketed Product Information Team.

[3] Typically, the Office of Surveillance and Compliance in CVM assesses whether a product is subject to the Federal Food, Drug, and Cosmetic Act or the Virus-Serum-Toxin Act before the filing of an NADA. As such, this criterion will seldom provide a basis for refusing to file a submission.

[4] See 21 CFR 514.110(c).

E. Filing over protest

An applicant may file over protest if it disputes our decision that the application is not acceptable for filing.[5] The applicant must submit a written request that we file the application over protest. When we file an application over protest, the application will have its original due date in our Submission Tracking and Reporting System (STARS). In this case, you should 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.[6]

III. REFUSE TO REVIEW

A. Applicability

We may refuse to review any INAD or JINAD submission that is of insufficient quality.[7]

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 refuse to review an INAD or JINAD submission. If you think we should refuse to review a submission, talk to your team leader and division director to get their concurrence. Division directors sign Refuse to Review 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 refuse to review submissions where the number and types of errors in the submission cause us to question the quality of the entire submission,[8] for example:

- Missing data sets or missing components in the submission,
- Lack of detail in a study protocol,

[5] See 21 CFR 514.110(d).

[6] 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 will file the application as of the day originally received. This means that the application will have the original due date. In the rare event that a sponsor files an application over protest such that you have a short time frame to review the application, you should notify your division director who will be responsible for notifying the Office Director. You will conduct a complete review of the application. The Division Director and Office Director will discuss any ADUFA timeframe implications.

[7] See 21 CFR 514.110(b) and GFI #119.

[8] See 21 CFR 514.110(b) and GFI #119.

- 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 refuse to review a submission, we will notify the sponsor in writing within 60 days of our receipt of the submission.[9] Our letter should state that we did not accept the submission for review and summarize the reason(s) for our decision. We should 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 refuse to file or refuse to review 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. Refuse to File final action packages are signed by the Office Director and should be routed through the Quality Assurance Team.

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.

[9] See GFI #119.

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.