OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

PROCESSING A REQUEST TO OPEN AN INVESTIGATIONAL (INAD) OR GENERIC INVESTIGATIONAL NEW ANIMAL DRUG (JINAD) FILE

I. PURPOSE

The purpose of this document is to explain:

- what an (J)INAD file is,
- how to process and review the A-0000 submission, and
- how to process A-0000 submissions containing multiple requests.

II. WHAT IS A (J)INAD FILE?

The investigational new animal drug (INAD) file contains correspondence and submissions that may be used to support a new animal drug application (NADA) (i.e., phased review submissions). Regulations governing unapproved new animal drugs intended for investigational use are in 21 CFR 511. When a sponsor plans to begin clinical studies, they will submit the information required to maintain their investigational exemption.[1]

The generic investigational new animal drug (JINAD) file is the investigational file for generic animal drugs. The information submitted to the file may be used to support an abbreviated new animal drug application (ANADA).

The submission made by a sponsor to request an investigational file, regardless of whether it is intended to support an NADA or an ANADA, is an A-0000 submission.

III. WHEN DOES A SPONSOR REQUEST A (J)INAD FILE?

Sponsors of new animal drugs typically submit a request to open an INAD file when they have enough pilot data to start discussing the development process and/or they want to begin shipping drug for use in investigational studies. If the sponsor is

[1] See P&P 1243.4065 Requirements for Investigational New Animal Drug Exemptions.

pursuing a supplemental approval, we may request that the sponsor establish a new (J)INAD file so we can better administer review of the data.[2] Sponsors of generic products typically submit a request to open a JINAD file after they have researched and identified a reference listed new animal drug (RLNAD) they intend to copy.

IV. INITIAL ROUTING AND PROCESSING OF A (J)INAD FILE REQUEST

A. Requests Made in Paper

The Document Control Unit (DCU) receives all paper requests to establish (J)INAD files. The Records and Information Management (RIM) Team will date stamp the submission, record its receipt, cross-check records to verify that it is an original submission, prepare a draft acknowledgement letter with a tentative (J)INAD file number, and enter pertinent information into our Submission Tracking and Reporting System (STARS). The submission is then delivered to the appropriate target animal division (TAD) director, who performs an informal cursory review. If the division director believes it is appropriate to open a new (J)INAD file, they initial the copy of the acknowledgement letter prepared by the RIM Team and return the submission to the DCU. The RIM Team then mails the acknowledgement letter to the sponsor confirming receipt of the request and informing the sponsor of the (J)INAD file number. The RIM Team then creates the A-0000 submission.

If the division director does not believe it is appropriate to open a new (J)INAD file, they will instruct the RIM Team to convert the file to a General Correspondence (GC). The respective TAD will then prepare the necessary documentation for this GC submission.

B. Requests Made Electronically

All requests to establish (J)INAD files that are received via eSubmitter result in an investigational file being automatically created. The sponsor is notified that their file has been created by an acknowledgement issued from the Electronic Submission Gateway. The acknowledgement will contain the (J)INAD file number. If, once the TAD director receives the submission, they do not believe it is appropriate to open a new (J)INAD file, they should request that the submission be voided and notify the sponsor of this action.

C. The A-0000 and the User Fee Check

After the RIM Team creates the A-0000 submission for the request, they route the submission to the STARS Evaluation Queue for the Business Informatics (BI) Team to evaluate. If this is the first filing of a (J)INAD by the sponsor, they will be subject to a sponsor fee under either the Animal Drug User Fee Act (ADUFA) or the Animal Generic Drug User Fee Act (AGDUFA), whichever is applicable. Once the BI Team has confirmed the sponsor's user fee status is current, the submission is routed to the TAD for review.

[2] See Guidance for Industry 191 Changes to Approved NADAs-New NADAs vs. Category II Supplemental NADAs.

V. REVIEWING THE SUBMISSION

The primary reviewer reviews the submission and identifies any areas in which it is deficient. The primary reviewer may contact the sponsor to get clarification on the information submitted or request they provide additional information through an amendment. The primary reviewer should request consulting reviews,[3] if appropriate, within two working days of receipt of the submission.

If the sponsor provides user safety information, the primary reviewer should conduct an initial human user safety assessment following the process described in CVM ONADE Scientific Resource Document 1243.130.001. Typically, this is not done for generic new animal drugs.

If the product identified in the A-0000 submission contains nanomaterials or otherwise involves the application of nanotechnology, the primary reviewer should follow the early identification and information collection procedures described in P&P 1243.2600.

If the product identified in the A-0000 submission is protein-based, the sponsor may need to address immunogenicity concerns. See the ONADE Scientific Reference Document 1243.135.001 and ProTech/Immunomodulators Focus Group (PI FG) SharePoint page for current procedures, including boilerplate language for the A-0000 letter and adding the proposed product to the PI FG spreadsheet.[4]

If the product identified in the A-0000 submission is an oncology drug, the sponsor may need to address human user safety concerns. See the Oncology SOP on the Division of Therapeutic Drugs for Non-Food Animals inside.FDA website for current procedures, including boilerplate langage for the A-0000 letter.[5]

If applicable, the primary reviewer should send a consulting review request to the Clinical Pharmacology Team as described in ONADE SOP 1243.166.001.

A. Information That We Generally Receive in an A-0000 Submission

1. Sponsor information including the sponsor name, address, telephone number(s), e-mail address, and contact person or, if they are a foreign sponsor, US agent information.

2. Drug identification information. This may include the drug/chemical name or other unique identifier, the pharmacological category, and the dosage form.

3. Species and if applicable, class of animals

4. Dosage regimen, if this information is known (e.g. the route of administration, dose, frequency, and duration of treatment administration).

[3] See P&P 1243.3200 for information on how to request a consulting review.
[4] Internal information redacted.
[5] Internal information redacted.

5. Indication, if this information is known. Often, only a high-level description of the indication (e.g., "respiratory disease") is provided in the A-0000 for an INAD. It is understood that the final indication wording (e.g., "treatment of bovine respiratory disease associated with [specific pathogens]) will be developed (and often revised) as the project moves forward and the data supporting the indication are evaluated.

For products with novel indications, use the evaluation described in the ONADE SOP 1243.100.001.

If the sponsor requested that information in the INAD be publicly available, the submission should detail the scope of the disclosure.

Request an amendment or ask the sponsor to clarify if you determine that the submission does not address or include the above information.

B. Labeling

The sponsor is not required to submit investigational labeling along with their request to open an (J)INAD file. The acknowledgement letter informs the sponsor of their obligations regarding investigational labeling and "Notices of Claimed Investigational Exemption for a New Animal Drug," in accordance with 21 CFR 511.1.

VI. ADDITIONAL INFORMATION FOR SUBMISSIONS REQUESTING A JINAD FILE

Requests to establish a JINAD file should include the information in section V above and also contain the following information:

1. Reference listed new animal drug (RLNAD) information: Sponsors are required to identify the RLNAD for their proposed generic drug, including trade name (and/or established name), dosage form, strength(s), sponsor name, and (A)NADA number;

2. Patent information: Sponsors should list any patents applicable to the RLNAD, and their expiration dates. Verify the patent information submitted by using the FDA Green Book. Note: If the time to patent expiration is greater than 5 years, consult your team leader for guidance on how to proceed;

3. Marketing exclusivity information: Sponsors should indicate if there are any marketing exclusivities applicable to the RLNAD, and their expiration dates. Verify the accuracy of the marketing exclusivity information submitted by the sponsor using the FDA Green Book. Note: If the period for marketing exclusivity is 5 years, consult your team leader for guidance on how to proceed; and

4. If the sponsor indicates that a suitability petition was previously submitted for the proposed generic product, and their request was granted, a copy of the letter approving the petition should be included with their JINAD request. If the proposed generic drug product has a different dosage form, strength, route of administration, and/or active ingredient (in a combination drug product), and a suitability petition has not been submitted, document this in the primary (AA)

review and notify the sponsor they must have an approved suitability petition for the proposed differences from the RLNAD before proceeding with their application.

VII. COMBINED REQUESTS OR THE SUBMISSION OF OTHER INFORMATION WITH THE A-0000

Sponsors sometimes include other requests in their request to establish an investigational file (or A-0000). Examples include requests for an investigational food-use authorization (FUA), protocol review, meeting, bioequivalence waiver, environmental claims (e.g., categorical exclusion), and expedited review.[6] If additional requests are made within the A-0000 submission:

1. contact the sponsor informally (e.g., by phone or email) and inform them that the request to open the (J)INAD will be reviewed but the additional requests will not be reviewed under the A-0000 submission. Also instruct them to resubmit each additional request separately under the appropriate submission code(s);

2. document in your A-0000 review that the additional requests were not reviewed under the A-0000 submission and that the sponsor was contacted; and

3. include the template language regarding additional requests in the A-0000 acknowledgement letter.

VIII. PREPARING THE FINAL ACTION PACKAGE

Prepare a review and an acknowledgement letter using the specific office templates. Follow the procedures described in P&P 1243.3005 and P&P 1243.3030 to prepare clean electronic documents and assemble the final action package.

IX. REFERENCES

Code of Federal Regulations

Part 511 – New Animal Drugs for Investigational Use

CVM Program Policies and Procedure Manual

1243.2200 - Submission and Review of Early Information (EI) Prior to Presubmission Conferences and Protocol Review

1243.3005 – Creating Clean Electronic Files

1243.3030 – Completing Final Action Packages for STARS Submissions

1243.3200– Routing a Request to Obtain a Review of an INAD, JINAD, ANAD, NADA, or VMF Submission

1243.4065 – Requirements for Investigational New Animal Drug Exemptions

[6] Submission of early information or other background materials to facilitate CVM's understanding of the project is acceptable. See P&P 1243.2200.

1243.2600 - Review of ONADE Regulated Products that Contain Nanomaterials or Otherwise Involve the Use of Nanotechnology

ONADE Standard Operating Procedures and Scientific Resource Documents

CVM SOP 1243.100.001 - ONADE Process for Determining Whether a Proposed Indication (Claim) is Valid

CVM SOP 1243.166.001 - Clinical Pharmacology Team (HFV-166) Involvement and Communications During the Project Lifecycle

CVM SRD 1243.130.001 – Human User Safety Assessment

CVM Guidance for Industry

Guidance 191 – Changes to Approved NADAs-New NADAs vs. Category II Supplemental NADAs.

FDA Green Book

X. VERSION HISTORY

March 31, 2009 – Beta test version

June 30, 2009 – Revised Beta test version

March 15, 2010 – Final Version

December 5, 2011 – Revised version to address bundled submissions

August 30, 2017 - Revised to incorporate electronic review processes, expand discussion of bundled submission procedures, and reference the SOP on valid indications

March 9, 2018 – Revised to provide instructions regarding user safety assessments, clinical pharmacology assessment, and process for products that may contain nanomaterials.

January 17, 2019 – Updated references to reflect the P&P 1243.4090 for human user safety assessment is now a CVM ONADE Scientific Resource Document and is found on the ONADE Standard Operating Procedures and Resource Documents SharePoint page.

May 8, 2019 – Revised section V to include information about investigational files being opened for protein-based and oncology new animal drug prooducts and links to resources for them.