OFFICE OF NEW ANIMAL DRUG EVALUATION REVIEWER'S CHAPTER

UNITED STATES (U.S.)-BASED EMPLOYEE AND U.S. AGENT REPRESENTATION OF FOREIGN SPONSORS

I. PURPOSE

This document describes ONADE's procedures for working with the representatives of foreign sponsors and includes:

- the definitions of a U.S.-based employee and a U.S. agent and the differences between these roles;
- when a U.S. agent is required and the administrative process for a foreign sponsor to appoint a U.S. agent;
- the role of consultants; and
- communication responsibilities.

II. BACKGROUND

Sponsors who do not reside or maintain a place of business within the U.S. are commonly referred to as foreign sponsors. Foreign sponsors must be represented[1] in the U.S. in their interactions with CVM by either a U.S.-based employee of the foreign sponsor, or U.S. agent.

III. DEFINITIONS, ROLES AND RESPONSIBILITIES

The roles described below are very different identities, legally speaking, because their relationships to the sponsor are different and distinct.

A. Responsible Official

The responsible office is any individual who is authorized to make legal representation on behalf of the firm before the FDA (see CFR §514.1(a)). For U.S.-

[1] 21 CFR § 514.1(a): "Applications to be filed under section 512(b) of the act…must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of, and must be countersigned by, an authorized attorney, agent, or official residing or maintaining a place of business within the United States."

based companies, this can be any employee of the firm or an authorized consultant. For foreign sponsors with a U.S.-based subsidiary or branch, this can be any employee of the U.S.-based subsidiary or an authorized consultant based in the U.S. For non-U.S. companies without a U.S.-based subsidiary, this must be the U.S. Agent.

B. U.S.-Based Employee

A U.S.-based employee is a person who is employed by a U.S. subsidiary or branch of a foreign sponsor. U.S. subsidiaries of foreign sponsors must maintain a place of business within the U.S. The name of the U.S. subsidiary may or may not be the same as the foreign sponsor. Frequently, the subsidiary's name is a variation of the foreign sponsor's name. The U.S.-based employee is not identified in the Freedom of Information (FOI) summary (per 1243.5761).

C. U.S. Agent

A U.S. agent is a person who resides or maintains a place of business within the U.S. and serves as the responsible official for a foreign sponsor. The U.S. agent must be available for contact by email and/or telephone during regular business hours. The U.S. Agent is identified by name in the FOI summary (if applicable).

D. Submitter

The submitter is the person who is registered with the FDA's Electronic Submission Gateway (ESG) and CVM's Electronic Submission System (ESS) and transmits the submission to CVM. This individual should not sign the eSubmitter package unless this person is the same as the responsible official and is legally responsible for the content of the submission. All CVM responses are sent back to the account of the individual who submitted the information to the Agency unless the submission is amended to request it to be redirected to another user who holds ESG and ESS accounts.[2]

Note: In the review documentation we prepare, we will identify when a sponsor has a U.S. agent or a U.S.-based employee working on their behalf. This means that in review summaries, submission summaries, and in letters to the sponsor we include their name, title, and address (where applicable). For approvals letters, we address the letter to the U.S. agent or U.S.-based employee working on the sponsor's behalf. We also identify and include the address of the U.S. agent in the memorandum recommending approval (MRA) and Freedom of Information Summary (FOI). However, we do not identify a U.S.-based employee or provide their address in the MRA and FOI because the individual is considered an employee of the sponsor.[3]

IV. SUBMISSION REQUIREMENTS

A. Submission to Investigational and Application File Types

Investigational and application file types consist of (generic) investigational new animal drug ((J)INAD) files and (abbreviated) new animal drug applications

[2] eSubmitter Resources page: https://www.fda.gov/industry/fda-esubmitter/cvm-esubmitter-resource-center

[3] While U.S. agents are encouraged for Veterinary Master Files, they are not required.

((A)NADAs). Electronic (eSubmitter) submissions to these files must have the Administrative Cover Sheet signed[4] by one of the following:

- for foreign sponsors with U.S.-based employees, either a U.S.-based employee or an authorized consultant[5] based in the U.S.; or

- for foreign sponsors with no U.S.-based employees, a U.S. agent, or their representative (a colleague from the U.S. agent's company (same company name)).

ONADE extends this requirement to all submissions to (J)INAD files because under the phased review process, we are making application-level decisions about the acceptability of data or information submitted. Phased review submissions are intended to support a future decision to approve an application. For simplicity, ONADE applies this requirement to all investigational submissions rather than specifying the representation required for each individual submission type.

A foreign sponsor can make submissions that are countersigned by a U.S. agent. Because of eSubmitter limitations, electronic submissions cannot be countersigned in eSubmitter right now; therefore, submissions to (J)INAD and (A)NADA files must be signed by the U.S. agent or their representative.

Submissions to (J)INAD files and (A)NADAs for foreign sponsors with U.S.-based employees do not need to be countersigned when they are submitted by a U.S.-based employee or an authorized U.S.-based consultant. In this situation CVM requires that submitters select in eSubmitter the "U.S.-based employee" option.

Electronic submissions to these files that are not signed by an authorized representative (as specified above) are closed out with the final action Refuse to Review (RTR) or Refuse to File (RTF) per P&P 1243.2050. Paper submissions made by a foreign sponsor and countersigned by a U.S. agent are processed for review.

B. Submissions to Type VIII Veterinary Master Files (Import Tolerance Requests)

Import tolerance requests (per SOP 1243.150.009) under a Type VIII Veterinary Master File (VMF) require the requester, if they do not reside or have a place of business within the U.S., to furnish the name and address of an authorized attorney, agent, or official residing or maintaining a place of business within the U.S. (21 CFR § 510.205(d)). As with (J)INAD and (A)NADA submissions described above, electronic import tolerance requests must have the Administrative Cover Sheet signed by one of the following:

- for foreign requesters with U.S.-based employees, either a U.S.-based employee or an authorized consultant based in the U.S.; or

- for foreign requesters with no U.S.-based employees, a U.S. agent or their representative as defined above.

[4] Instructions for digitally signing the Administrative Cover Sheet externally from eSubmitter, when the Responsible Official is not the one packaging the submission, are available in https://www.fda.gov/media/139159/download?attachment.

[5] An authorized consultant is one for whom we have a signed letter from the sponsor in the file permitting the consultant to interact with CVM on the sponsor's behalf.

C. Submissions to Other File Types

A U.S.-based employee or a U.S. agent is not required for submissions to files other than (J)INADs, (A)NADAs, and Type VIII VMFs. Submissions to other files, such as General Correspondence (GC) or other VMF types, do not need to be countersigned by a U.S. agent and may be signed by a foreign sponsor.

Note: Foreign manufacturing facilities are required to designate a U.S. agent, and ONADE encourages them to identify the U.S. agent in their VMF using the process below (see P&P 1243.2400 and 21 CFR § 510.205(d)).

V. ADMINISTRATIVE PROCESS FOR A FOREIGN SPONSOR TO APPOINT A U.S. AGENT[6]

A sponsor or requester may appoint only one U.S. agent to a file at a time. When the initial submission (A-0000) to establish a file is made by the U.S. agent, the U.S. agent should include a signed letter from the foreign sponsor stating that they are appointing (person or company) as their U.S. agent (see P&P 1243.4000). The U.S. agent may be a specific person or a company (for example, “John Smith” or “John Smith Consulting”). The letter appointing the U.S. agent should also contain their contact information, including email address, phone number, and mailing address.

The U.S. agent for a foreign sponsor may be changed through a general correspondence (G) submission to all applicable files; the G submission should include a signed letter from the foreign sponsor as outlined above. Foreign sponsors may appoint different U.S. agents to different files; therefore, a record is needed in each file to document the identity of the U.S. agent. Ideally with any change in U.S. agent, the current U.S. agent submits a G submission notifying ONADE of the identity of the new U.S. agent taking responsibility from that point on. If a U.S. agent relationship terminates without a new U.S. agent being identified, the current U.S. agent submits a G submission stating that they are no longer serving as the U.S. agent from that point on. If the current U.S. agent is unable to make this submission, we would accept this notification directly from the foreign sponsor. **Note**: before ONADE can accept further submissions to a (J)INAD, (A)NADA, or Type VIII VMF, the foreign sponsor or requester must appoint a new U.S. agent and that agent must submit a G submission (as described above) informing ONADE they are the U.S. agent.

The G submission is assigned to the project manager (PM) for a pioneer (INAD or NADA) sponsor. G submissions to other file types are assigned to the appropriate review division. If we receive a linked G submission across diverse file types, the submission is assigned according to the majority of impacted files. The primary reviewer assigned to the G submission closes it out with final action code 007, SUBMISSION FILED WITH NO REVIEW DOCUMENTATION; NO LETTER SENT (FNR).

For all affected files, the primary reviewer of the G submission will email Internal information redacted. that the ADUFA invoice should be addressed to the new contact, providing the new contact’s information, from the submission, in the following format:

Title First Name Last Name
Company Name

[6] No administrative process is needed for U.S.-based employees.

Address Line 1
Address Line 2
City State Zip Code Country
Email Address
Primary Phone Number
Secondary Phone Number

VI. COMMUNICATION RESPONSIBILITIES

ONADE copies the U.S. agent or U.S.-based employee when emailing a foreign sponsor or consultant. While we encourage foreign sponsors and consultants to include the U.S. agent or U.S.-based employee in formal meetings and any informal communication, we do not monitor this. It is the responsibility of the foreign sponsor and their representatives to effectively manage communication among themselves.

VII. ROLE OF CONSULTANTS

A foreign sponsor may engage consultants in addition to their U.S.-based employees or U.S. agent. Authorized U.S.-based consultants can sign the Administrative Cover Sheet for electronic submissions to (J)INADs, (A)NADAs, and Type VIII VMFs (import tolerance requests) on behalf of foreign sponsors or requesters with U.S.-based employees. However, for foreign sponsors or requesters with no U.S.-based employees, all electronic submissions to (J)INADs, (A)NADAs, and Type VIII VMFs must have the Administrative Cover Sheet signed by the U.S. agent or their representative, and any paper submissions must be countersigned by the U.S. agent, as discussed above. Submissions to other file types, as described above, may be made signed by a consultant.

VIII. REFERENCES

Title 21 Code of Federal Regulations

Part 510 – New Animal Drugs

Subpart C - Import Tolerances for Residues of Unapproved New Animal Drugs in Food §§510.201 -510.213

Part 514 – New Animal Drug Applications

§514.1 Applications

Part 207 - Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs, and the National Drug Code

§207.69 What are the requirements for an official contact and a United States agent?

CVM Program Policy and Procedures Manual – ONADE Reviewer's Chapter

1243.2050 - Refuse to File and Refuse to Review

1243.2400 - Veterinary Master Files with Manufacturing Information

1243.4000 - Processing a Request to Open an Investigational (INAD) or Generic Investigational New Animal Drug (JINAD) File

1243.5761 – Freedom of Information (FOI) Summary for Original and Supplemental NADAs

ONADE Standard Operating Procedure

1243.150.009 - Procedures for Processing and Reviewing Import Tolerances

IX. VERSION HISTORY

May 28, 2020 – Original version. This document takes ONADE policy and formalizes it in this policy and procedure document.

October 28, 2021 – Updated language in Section III to include the requirement for a U.S. Agent for import tolerance requests

December 22, 2021 – Updated to include information about roles and responsibilities of the Responsible Official, U.S. agent, U.S.-based employees, and submitters. A table summarizing the roles of U.S. agents and U.S.-based employees was placed in an appendix.

February 14, 2022 – Updated language to reflect that the U.S.-based employee may not be the responsible official, to clarify that VMF Type VIII (import tolerance) submission requirements are the same as for (J)INADs and (A)NADAs, and to revise communication expectations.

July 26, 2022 – Quality systems review for minor formatting updates.

September 8, 2022 – Update to distinguish which officials are identified by name in the FOI summary. References updated to include 1243.5761.

May 11, 2023 – Updated section III to include a note with specific information on where we include information about the U.S. agent and U.S.-based employee in the review documentation we prepare. 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.

September 27, 2023 – Language about electronic submission requirements updated to specify who must sign the Administrative Cover Sheet rather than who must make the submission.

February 15, 2024 – Updated to add information that says the PR of the G submission needs to email the ADUFA billing mailbox to let them know the address for sending the invoice.

APPENDIX 1. SUMMARY TABLE OF U.S. AGENT AND U.S.-BASED EMPLOYEE INFORMATION

Information	U.S. agent	U.S.-based employee
Definition	The person who serves as the responsible official for a foreign sponsor in their interactions with CVM.	A person who is employed by a U.S. subsidiary or branch of a foreign sponsor.
Requirements	Must reside or maintain a place of business within the U.S.	U.S. subsidiaries of a foreign sponsors must maintain a place of business within the U.S.
	Must be available for contact by email and/or telephone during regular business hours.	The name of the U.S. subsidiary may or may not be the same as the foreign sponsor. Frequently, the subsidiary's name is a variation of the foreign sponsor's name.
	A sponsor may appoint only one U.S. agent to a file at a time (1:1 ratio of US agent to a file).	A foreign sponsor may have more than one U.S-based employee, just like U.S.-based sponsors.
Electronic Submissions to (J)INAD, (A)NADA, and Type VIII VMF (import tolerance request)	Must be signed by a U.S. agent or their representative (a colleague from the U.S. agent's company (same company name)).	Must be signed by either a U.S.-based employee or an authorized consultant based in the U.S.
Consultants	All electronic submissions to (J)INADs, (A)NADAs, and Type VIII VMFs must be signed by the U.S. agent or their representative.	Authorized U.S.-based consultants can sign electronic submissions to (J)INADs, (A)NADAs, and Type VIII VMFs on behalf of a foreign sponsor or requester with U.S.-based employees.