
OFFICE OF NEW ANIMAL DRUG EVALUATION
REVIEWERS' CHAPTER

BIMO INSPECTION REQUEST PROCESS

I. PURPOSE

The purpose of this guide is to describe the process in ONADE for nominating a study for inspection under the Bioresearch Monitoring (BIMO) program.

In the Office of New Animal Drug Evaluation, inspection requests for the conduct of the BIMO inspections are initiated at the team/reviewer level and progress through the Division Director, the Center Bioresearch Monitoring and Administrative Action Team (BIMO Team) in the Division of Compliance, to the field district investigational branches or Office of Regulatory Affairs foreign investigation unit.

II. APPLICABILITY

The agency monitors the conduct of animal drug studies with three compliance programs:

Good Laboratory Practice Compliance Program (CP)	CP 7348.808
Sponsors, Contract Research Organizations, and Monitors	CP 7348.810
Clinical Investigators	CP 7348.811

These compliance programs help to assure the integrity of scientific testing and the reliability of test data submitted to FDA. The inspection request process initiated in ONADE divisions allows the agency to assess, through audit procedures and real-time inspections, whether data submitted to FDA in specific studies will permit sound judgments regarding the safety and effectiveness of regulated drug products.

The regulations that pertain to investigational animal studies are codified in 21 CFR 511.1 and 21 CFR 58. The sponsors of studies are required to notify the Center by means of a "notice of claimed investigational exemption" of 511.1 (b) clinical studies conducted under an INAD. The notice of claimed investigational exemption is also known in the Center as a "notice of drug shipment."

This guide applies to studies that are submitted to FDA in support of new animal drug applications (including abbreviated new animal drug applications) or supplemental new animal drug applications.

III. INSPECTION REQUEST PROCESS

A. Target Animal Divisions

Target Animal Divisions (HFV-101 Staff, HFV-110, HFV-120, HFV-130) are responsible for target animal safety and effectiveness studies. They also:

- review sponsor's study protocols,
- manage investigational drug products through the various preclearance stages, and
- evaluate studies and data submitted following completion of studies.

Target Animal Divisions are best able to initiate the BIMO inspection request for target animal safety and effectiveness studies. For studies conducted under

511.1 (b), non-GLP studies, the Document Control Unit (DCU) sends a copy of the "Notice of Drug Shipment," indicating a clinical investigation is to be conducted, to the responsible division/team (CVM Policy and Procedures Guide 1240.3020, Processing Amendments to an Investigational New Animal Drug Application).

The target animal division reviewer determines which studies are critical to making scientific decisions; a subset of these studies should be nominated for inspection under the BIMO program. The Division Director, or a designated appointee, prioritizes the inspection requests within the division (if necessary). Each division determines if the receipt of a "Notice of Drug Shipment" will result in inspection of the investigation(s). A Notice of Drug Shipment is marked File No Reply (FNR), and then the reviewer has the following options:

1. the investigation(s) is nominated for inspection, or

2. the primary reviewer enters an explanation for not nominating the investigation(s) for inspection on the FNR copy, or

3. the Notice of Drug Shipment is marked FNR (without explanation) and the notice is filed to the DCU.

In identifying studies for inspection, a reviewer should use the following criteria. If the reviewer answers "yes" to one of these questions, then they should consider an inspection of that investigation.

1. Is the study identified by the sponsor as being pivotal? (i.e., will the Agency rely on this study to make a decision?) A "pivotal" study is a study that is considered by CVM to be an essential part of the basis for the approval of a new animal drug.

2. Has it been a while since the investigator has been inspected? Has the investigator been inspected before and was the outcome anything other than "No Action Indicated"?

3. Is there a specific cause for concern necessitating an inspection?

4. Is the product a new entity (or is it a new delivery system)? Or is it not a well-studied drug?

5. Have we had previous problems with the investigator or the study location?

6. Is the study to be used for a major decision?

7. Are there a limited number of replicates?

8. Is the study pivotal and is it significantly more critical than others in helping the Agency to reach a conclusion?

9. Is the study pivotal but we are **not** postponing a decision on whether to inspect until the data are submitted?

Reviewers may choose not to nominate a study for BIMO review if, for example, an adequate inspectional history exists for the investigator or laboratory, or if the study is one of a series of trials in which others have been selected for inspection. A determination of the adequacy of inspectional history includes, among other considerations, how much time has elapsed since the last inspection, and previous classifications of inspections. Such a determination may require consultation with the Division Director and the BIMO Team. The Division also determines if the presence of a headquarters reviewer is necessary when the inspection is conducted.

Information on inspectional history is available to the reviewer from the ONADE folder **S:\Division\Bimo\ Bimo_inv**. It is also available by sending a request for a status/investigational history check to the Bioresearch Monitoring and Administrative Action Team (HFV-234) and including the relevant information (clinical investigator and location; sponsor name and INAD/NADA number; or laboratory and location).

When a request for BIMO inspection is generated, it is sent directly to the Center's BIMO Team where an initial review is performed. The BIMO Team then:

- assures that all the necessary information has been provided,
- accesses a record of requests and Center actions on each site inspection assignment,
- concurs or discusses any duplicative requests with the Division,
- assigns a control number if an inspection is assigned, or informs Division if an assignment will not be issued,
- issues the inspection request to the appropriate field office, or if a foreign inspection, to the FDA Office of Regulatory Affairs, and
- maintains extensive records and the Center's BIMO database and makes information available to assist divisions in ONADE.

B. Specialty Divisions

The Division of Human Food Safety or the Division of Manufacturing Technologies reviewer may obtain a status check for toxicology, residue, pharmacokinetic submissions, and environmental submissions involving review of Good Laboratory Practices (GLP) studies that are submitted in support of an application.

If, during the specialty review process, any cause is found that might indicate an inspection is warranted, the primary reviewer will then typically request the inspection.

The reviewer may obtain information on inspectional history by referencing a current listing of establishments such as the "White List" or CDER's "List of Inspected Tox Labs" available in the Quality Assurance Team (HFV-102) and

HFV-234. For certain veterinary drug establishments and investigators, the reviewer may obtain information by referencing the BIMO Investigator listing in the BIMO Investigator folder on the **S:drive (S:\division\Bimo\Bimo_inv)**.

The request memo is forwarded to the BIMO Team, and is assigned as described in paragraph III.A. above.

NOTE:
The standard FORMAT for a memorandum requesting a BIMO Inspection can be found in the BIMO Inspection Request FORMAT folder **S:\Division\Bimo\Bimo_Req**. A reviewer may use the standard FORMAT, or may choose to use alternative formats that are currently in common use.

IV. REFERENCES

FDA Compliance Program (CP) Guidance Manual: CP 7348.808, Good Laboratory Practice

CP 7348.810, Sponsor, Contract Research Organizations, and Monitors; CP 7348.811, Clinical Investigators

Code of Federal Regulations 21 CFR 511.1; 21 CFR 58