COMPLIANCE

CVM BIORESEARCH MONITORING PROGRAM - GENERAL PROCEDURES FOR THE PREPARATION AND ASSIGNMENT OF BIORESEARCH MONITORING (BIMO) INSPECTIONS

I. PURPOSE

The purpose of this document is to describe the interoffice processes for preparing, submitting, and assigning requests for Bioresearch Monitoring (BIMO) inspections within the Center for Veterinary Medicine (CVM). It is applicable to the premarket new animal drug review process conducted by the Office of New Animal Product Evaluation (ONAPE, NADA), the abbreviated new animal drug review process conducted by the Office of Generic Animal Drugs (OGAD, ANADA), and the reviews related to food additives conducted by the Office of Surveillance and Compliance (OSC), Division of Animal Food Ingredients.

II. BACKGROUND

The Food and Drug Administration's (FDA) BIMO program is a comprehensive program of on-site inspections and data audits designed to monitor all aspects of the conduct and reporting of FDA-regulated research. FDA's BIMO Program was established to assure the quality and integrity of data submitted to the agency in support of new product approvals and marketing applications, as well as to provide for the protection of the rights and welfare of the thousands of human subjects and animals involved in FDA regulated research. It is a cornerstone of the FDA pre-approval process for new drugs, medical devices, food and color additives, veterinary products, and new tobacco products.[1]

CVM considers BIMO inspections to be an integral part of our regulatory decision-making process for new animal products and animal food additives to ensure that the data and reports submitted are accurate and reliable.

[1] https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/fda-bioresearch-monitoring-information/bioresearch-monitoring-program-information

The CVM BIMO program involves a three-stage process as follows:

- Stage 1. Pre-inspection – process from initial interest in requesting a BIMO inspection to submission of the assignment to OII.
- Stage 2. Inspection – process from receipt of the assignment in OII to receipt of the Establishment Inspection Report (EIR) in CVM.
- Stage 3. Post-inspection – process from receipt of the EIR in CVM to final classification, including post-inspectional correspondence.

CVM has two designated BIMO Coordinators to help facilitate and monitor this process. One coordinator, the CVM BIMO Requests Coordinator (BRC), resides in the ONAPE and is responsible for facilitating the inspection request process within CVM's review divisions. The other coordinator, the CVM BIMO Inspections Coordinator (BIC), resides in the OSC and is responsible for facilitating the inspection assignment process with FDA OII's Office of Bioresearch Monitoring Inspectorate (OBMI) and CVM's BIMO and CGMP Branch.

During the pre-market review process, a reviewer may request a BIMO inspection of one or more entities involved in the conduct of a regulated study. A reviewer may be

III. BIMO INSPECTION REQUEST PROCESS – SPONSOR AND CONTRACT RESEARCH ORGANIZATION INSPECTIONS

Contact the CVM BRC to get assistance with sponsor and contract research organization (CRO) inspection requests.

IV. BIMO INSPECTION REQUEST PROCESS – GLP AND CI INSPECTIONS

When a reviewer is considering a BIMO inspection request for a clinical investigator (CI) or Good Laboratory Practice (GLP) entity, they should use the procedures in this section. If a reviewer is unsure which compliance program applies to the inspection, they should contact the CVM BIMO Coordinators. Throughout this document, the term requestor is used for a reviewer who has requested an inspection.

Throughout the document, calendar due dates are used, but a due date may fall on weekends or holidays. In these cases, the due date will be on the next expected agency working day.

A. Early Discussions

When a reviewer is considering a BIMO inspection request for a CI or GLP entity, they should contact their supervisor to discuss the potential request. If the supervisor agrees that the request should be considered, the requestor will complete Section A of the CVM BIMO Request Form in SharePoint®.[2] Upon completion, the requestor clicks the Submit to CVM BIMO Requests Coordinator button on the form to send an email alert to the CVM BIMO Coordinators, requestor, requestor's supervisor, requestor's DD, and the BIMO and CGMP Branch Chief.

[2] This is an electronic form that resides in SharePoint throughout its use and should be opened and completed in Google Chrome to ensure optimal functionality.

If CVM requests an employee accompany the field investigator on a BIMO inspection, the requestor will complete the associated questions within Section A. The CVM BIMO Coordinators will guide the attendee through the process of attending BIMO inspections. See CVM SOP 1240.234.003 CVM Subject Matter Expert (SME) BIMO Inspection Attendance.

Please note: When a reviewer is requesting an inspection due to suspected significant study quality and integrity issues, they should contact the CVM BRC immediately so that discussions can begin as soon as possible, and appropriate personnel can be involved.

Within **3 calendar days**[3] (this time may be slightly longer for foreign inspections) of receipt of a completed request form from the review division, the CVM BRC will:

- Review entity inspection history (both CVM and other centers).

  If the most recent inspection has not yet been closed out the CVM BRC will discuss next steps with the CVM BIC.

- Review pending inspection requests for the entity from CVM.

  If adequate time remains prior to the inspection start date, the new request may be added to the pending inspection request. The CVM BRC will discuss the new request with the CVM BIC to determine acceptability.

- Determine if other divisions or branches may also be interested in an inspection of the entity.

  The CVM BRC will work with any other divisions or branches to determine if other studies should be added to the inspection. For further information about this process, contact the CVM BRC.

- Provide the date by which the review division can expect to receive the EIR. This date presumes that the inspection request will progress through the remainder of the process in the times outlined in this document and summarized in Appendix 2. This would mean that the CVM BRC would submit the request to the CVM BIMO Requests Mailbox within **17 calendar days** after Section A was submitted to the CVM BRC.

  - Discuss the potential inspection request with the requestor, if necessary.

  - For foreign inspections, contact the CVM BIC for the items below. The CVM BIC will provide a response within **5 calendar days**[4], that includes the following:

    - Guidance on the process for inspecting facilities in the applicable country.

    - Inspectional history for the foreign facility.

[3] Please note that, throughout the document, calendar due dates may fall on weekends or holidays. In these cases, the due date will be on the next expected agency working day.

[4] For foreign inspections, the CVM BIMO Inspections Coordinator needs to coordinate with the Foreign Inspection Cadre Leader in OII OBIMO.

The CVM BRC will complete Section B of the CVM BIMO Request Form, that includes the information above as well as space to provide recommendations. This information, provided by the CVM BRC, is intended to assist the division in determining whether a BIMO inspection request should proceed. The CVM BRC will click the Return to Division button to submit the completed section. This triggers an email notification to the requestor and the CVM BRC.

B. Division Deliberations

Following review of the information provided by the CVM BRC, the requestor should discuss the potential request with their division management. After discussion with management and within **2 calendar days** of receiving the SharePoint email notification referenced above, the requestor will convey the division's decision whether they will proceed with the request or not and complete the Division Decision section of the CVM BIMO Request Form as follows:

- If the division chooses to stop the request, the requestor will select the Stop Request button to cancel the request. This triggers an email alert to the CVM BRC, the requestor, and the requestor's supervisor. Once the requestor clicks the Stop Request button, no further action is required for the request.

- If the division chooses to continue the request, the requestor will select the Submit Request button. This triggers an email alert to the CVM BRC and the requestor. At this time, the requestor will be able to complete Section C of the request form as directed in Section C below.

C. Completion of Inspection Request

The requestor should complete Steps 1-3 below within **9 calendar days** of receiving the SharePoint email notification referenced above. The requestor is responsible for preparing the inspection request and providing appropriate documents as described below.

1. The requestor will complete Section C of the CVM BIMO Request Form. The request form will prompt for additional information that will help OII to complete the inspection and the field investigator to focus on the areas of the study the requester is interested in inspecting. Follow the directions in the form and contact the CVM BRC with any questions.

2. Because OII investigators do not have access to CVM databases, CVM must provide copies of all documents relevant to completion of the inspection (e.g., field investigators do not have access to CVM's Corporate Document Management System (CDMS)). The BIMO Request Form will prompt for some required documents, and other documents should be provided based on any concerns to be addressed during the inspection. The requestor will place all necessary documents in the appropriate SharePoint folder for the request. Sections a-i below provide further instructions for the requestor when providing necessary documents. Contact the CVM BRC for assistance when determining documents to be provided. The link to the appropriate SharePoint folder will have been provided in the automated SharePoint email referenced in Step B above. Contact the CVM BRC for assistance in finding the appropriate SharePoint folder.

In the Supporting Documents section of the request form, the requestor will list each document provided in the SharePoint folder and check the box for Added to SharePoint. Use the file naming conventions provided in parentheses below for each type of document. Additional documents may be included if relevant to specific issues identified in the CVM BIMO Request Form. When these documents are provided, they should be referenced in the Objectives for BIMO Inspection Request document (further details regarding this document are provided below).

a. Study protocol (naming convention: I123456_StudyIdentifierProtocol.pdf)

- If CVM has received a copy of the signed final protocol in a submission, the requestor should provide a copy of the signed final protocol. If CVM has not received a copy of the signed final protocol but has previously concurred upon the protocol, the requestor should provide a copy of the concurred upon protocol. If CVM does not have a copy of the protocol, the requestor should include a request for the field investigator to collect a copy of the protocol during the inspection in the Objectives for Bioresearch Monitoring Inspection Request document.

- For clinical investigator inspections, the requestor should ensure that the signed copy of the protocol provided includes the investigator's signature. If the investigator's signature is provided in a separate document, the requestor should provide this investigator signature page.

  Please note: Having the protocol helps the field investigator understand the study, including methods and objectives, before arriving at the inspection site.

  Additionally, field investigators may compare the copy of the protocol provided by CVM to the original at the inspection site and determine if there are differences.

b. Protocol amendments and deviations (naming convention: I123456_StudyIdentifier Amendments.pdf, I123456_StudyIdentifierDeviations.pdf)

- The requestor will provide a copy of all protocol amendments.

- The requestor will also provide a copy of all deviations from the protocol and standard of conduct relevant to the entity to be inspected.

  Please note: The protocol, amendments, and deviations need not be provided in separate documents but rather may be provided as a part of other documents. For example, in some cases, these documents are provided with the final study report (FSR). When this occurs, the requestor should clearly state in the Supporting Documents section of the BIMO Request Form where each of the document types can be found, including page numbers and filename for each document type.

  Sometimes deviations are described in the report, but a separate copy of each signed deviation is not provided. In this case, the requestor should

refer to the section of the report (including page number and section identification) where the deviations are discussed.

For clinical investigator inspections, the requestor should only provide or reference page numbers for deviations that are specific to the site to be inspected.

c. Product shipment information for each study identified (naming convention: I123456_StudyIdentifierNCIE.pdf)

- Product shipment information is required for all clinical studies and for any GLP studies for which Notice of Claimed Investigational Exemptions (NCIE) were submitted to CVM.
- The requestor will prepare a table that depicts the amount of product shipped on each date to the inspected entity, based on the NCIEs submitted. The requestor should not include copies of NCIEs with the table.

  Please note: The field investigator may compare the quantity of product shipped on the NCIEs to the quantity of product received on the product shipment records at the inspection site.

d. Informed consent (naming I123456_InformedConsent.pdf)

- For all field effectiveness studies using client-owned animals, the requestor should provide the most up-to-date version of the informed consent form (i.e., if the informed consent is amended, provide the copy in the most recent amendment).
- For other types of studies, the requestor should provide the informed consent form if it was provided to CVM.

  Please note: The field investigator may compare the informed consent **received** in the submission against the informed consent documents at the site.

e. Final study report (FSR) (naming convention: I123456_StudyIdentifierFSR.pdf)

- The requestor will provide a copy of the final study report and all amended reports submitted to CVM, if the FSR was amended.
- The FSR allows the field investigator to become familiar with the study before arriving at the inspection site.
- Additionally, the field investigator may compare the copy of the final study report submitted to CVM with the report on site during the inspection, if applicable.
- Please note for a clinical investigator inspection, the final study report may not be present at the clinical investigator site.

- See note above about providing FSR, protocol, amendments, and deviations in combined files.

f. Objectives for Bioresearch Monitoring Inspection Request document (naming convention: I123456_StudyIdentifierBIMOObjectives.pdf)

- The requestor will provide this document in all cases where the requestor has specific concerns for the field investigator to address during the BIMO inspection.

- In Section A of the request form, requestors select specific circumstances causing interest in requesting an inspection. Some of these circumstances may not require further explanation (e.g., when the entity has never been inspected or enrolled a significant percentage of animals on study), but for most of these circumstances, an explanation is necessary in order for the field investigator to understand and investigate our concerns. If the requestor is not sure whether an explanation is necessary for your circumstances, they should contact the CVM BRC.

- For each circumstance that requires an explanation, the requestor will provide this explanation using the Objectives for Bioresearch Monitoring Inspection Request template. This template provides directions for providing thorough explanations for each concern. The requestor will provide any files to support the issue in the appropriate SharePoint folder and also ensure that they are listed in the Supporting Documents section. For each document provided in support of the objectives document, under the Document Specifics and Why is it included? sections of the form, the requestor should state “See Objectives for Bioresearch Monitoring Inspection Request.”

g. Data listing (e.g., line listings/results) (naming convention: I123456_StudyIdentifierSASData.pdf)

- For these file types, the requester must provide the reason for each file being included in the Objectives for Bioresearch Monitoring Inspection Request document; so that the BIMO compliance staff member and the field investigator understand the purpose of each file.

- The requestor should be judicious when providing data listings and copies of raw data for the field investigators. The requester should provide only the data that is relevant to the inspection and does not need to provide all copies of raw data and all data listings. For example, a requestor may want the field investigator to compare the raw data to some data listings during the inspection. In this case, the requestor should provide the relevant data listing(s) and describe the data to be compared in the Objectives for Bioresearch Monitoring Inspection Request document.

- When providing data, the requestor should:

  - Only provide data that are specific to the site to be inspected.

- Organize the data by data elements (Option A) or by subjects (Option B).
- Refer to OBMI WI-000036 (Standardized Format Options for Site-Specific Study Data) for further information on this topic. This document can be located on the OII OBMI Documents page included in References below.

h. For GLP studies, the sponsor compliance statement (naming convention: I123456_StudyIdentifierGLPSCS.pdf)

- The field investigator may compare the noncompliances identified on the sponsor compliance statement to those identified by the study director.

i. Other documentation that may be useful to the field investigator in completing the assignment.

- For these file types, the requester must provide the reason for each file being included on the form in the Objectives for Bioresearch Monitoring Inspection Request document so that the BIMO compliance staff member and the field investigator understand the purpose of each file.
- The requestor should contact consulting reviewers for the submission to request a list of concerns to be addressed during the BIMO inspection. The requestor may choose to provide relevant consulting reviews or excerpts from them when the field investigator will need this information to understand specific concerns. In these cases, the requestor should reference the additional documents and information in the Objectives for Bioresearch Monitoring Inspection Request document discussed above.

3. Upon completion of Section C of the BIMO Request Form, the requestor will click the Send to BRC button to send the request form to the CVM BRC. Clicking the button sends an email alert to the CVM BRC and the requestor.

4. The CVM BRC will then complete the CVM BRC Concurrence section of the CVM BIMO Request Form. If the package is not acceptable, the CVM BRC will note areas that the requestor needs to address in the Comments section and click the Return Package to Division button. This will trigger an email alert to the requestor. The requestor will make corrections and click the Return to BRC button, which will trigger an alert to the CVM BRC.

5. If the package is acceptable, the CVM BRC will click the Submit Request to BIMO Mailbox button and an email notification will be sent to the CVM BIMO Mailbox Internal information redacted. , copying the requestor, requestor's supervisor, and the CVM BIMO Coordinators. If multiple divisions will be providing request forms for a single inspection request, the CVM BRC will wait until all forms are ready from all divisions and will submit all requests at one time.

6. The CVM BRC will also email the CVM BIMO Requests Mailbox and include the following information:

- Requestor's name and division

- Name of the entity to be inspected
- Compliance program for inspection
- Inspection type (i.e., in-life, data)
- Whether the inspection is for cause
- Inspection due date
- A link to the package in SharePoint

7. Once the CVM BRC sends the submission to the CVM BIMO Requests Mailbox, the BIMO and CGMP Branch will begin working on the request. This process is described in sections V-VIII below.

8. If the requestor needs to update the request based on new or changed information (e.g., the requestor changes, the review team finds useful information while reviewing the data, etc.), they will:

   - Contact the CVM BIMO Coordinators (email both coordinators), copying the BIMO compliance staff member (if a BIMO compliance staff member has been assigned), and provide the reason for modification. The BIMO Coordinators will work together to ensure that the changes are properly incorporated.

     NOTE: To cancel an inspection request following submission to BIMO and CGMP Branch, contact both CVM BIMO Coordinators for further direction.

V. BIMO AND CGMP BRANCH RECEIPT OF BIMO INSPECTION ASSIGNMENT REQUESTS

1. The BIMO and CGMP Branch Chief or CVM BIC checks the CVM BIMO Requests mailbox Internal information redacted. at least once daily.

2. When an inspection request is received in the mailbox, within **4 calendar days**, the CVM BIC will review the request package, including a quality assessment of the request to determine whether we have sufficient information for assignment to a BIMO compliance staff member.

   If the package is not acceptable, the CVM BIC will provide comments to the CVM BRC, copying the requestor. The CVM BRC will work with the requestor to amend the request, as needed, and will alert the CVM BIC when the amended package is ready for review.

   If the package is acceptable, the CVM BIC will alert the BIMO and CGMP Branch Chief that the package is ready for assignment to a BIMO compliance staff member.

3. After the CVM BIC reviews the request, within **2 calendar days**, the BIMO and CGMP Branch Chief or designee responds to the requestor and copies the CVM BRC, CVM BIC, and the requestor's branch chief. The email acknowledges receipt of the request and identifies the BIMO compliance staff member who will be handling the request.

VI. ASSIGNMENT MEMO CREATION AND PROCESSING

The BIMO compliance staff member develops the assignment memo within **10 calendar days** of being assigned the request. The BIMO and CGMP Branch Chief is responsible for clearing the memo within **5 calendar days**. Steps for these procedures are below:

1. The BIMO compliance staff member establishes a BIMO control number in the BIMO database. Please note: When a request originates from multiple divisions, the CVM BRC should be the Originator in the BIMO database.

2. The BIMO compliance staff member determines whether an FDA Establishment Identifier (FEI) number exists and if not, requests a number from OII's Official Establishment Inventory (OEI) Coordinator (refer to OII WI-000033).

3. The BIMO compliance staff member determines if there are open inspections associated with the inspected entity/firm.

4. The BIMO compliance staff member selects and completes the current assignment memo template (i.e., Inspection Assignment Memo (IAM) General info Section Template Form-000450). The BIMO compliance staff member will name the memo using the BIMO control number, inspected entity name, and compliance program number identifier (ex. 2020-200 John Research 808).

5. The BIMO compliance staff member develops the assignment memo to include any additional relevant inspectional history not covered previously, background information, inspection instructions, and other concerns.

6. The BIMO compliance staff member consults with the requestor, as needed, and includes the BIMO Coordinators in any communications.

7. The BIMO compliance staff member completes the draft assignment memo and emails the BIMO and CGMP Branch Chief with the link to the memo in SharePoint for review and clearance.

8. The BIMO and CGMP Branch Chief reviews and clears the assignment memo within 3 calendar days of receipt.

9. If the draft memo is acceptable to the BIMO and CGMP Branch Chief, the BIMO compliance staff member will complete the steps in Section VIII. If the draft memo is not acceptable, the BIMO and CGMP Branch Chief returns it to the BIMO compliance staff member with suggested changes.

VII. ASSIGNMENT MEMO/PACKAGE FINALIZATION

Once the BIMO compliance staff member receives the draft memo from the BIMO and CGMP Branch Chief, the BIMO compliance staff member finalizes the assignment memo within **3 calendar days** by completing the following:

1. Updating the assignment memo with any remaining edits from the BIMO and CGMP Branch Chief.

2. Establishing an eNSpect Operation ID and adding it to the assignment memo and BIMO database.

3. Recording the appropriate inspection due date from eNSpect in the assignment memo and the BIMO database.

4. Ensuring the document clearance chain and distribution list are complete and correct. Verifying that the date in the date field in the assignment memo is the same as the Issue Date in the BIMO database and the Date EIR due to center field in the assignment memo is the same as the target completion date field in eNSpect.

5. Converting the assignment memo document into PDF using Adobe Acrobat and then signing the PDF document electronically.

VIII. CVM TO OII INSPECTION ASSIGNMENT TRANSFER

A. Prepare the Inspection Package

The BIMO compliance staff member starts the inspection package process by completing the following:

1. Establishing an Enterprise Content Management System (ECMS) folder according to OII naming convention per WI-000144.

2. Uploading the inspection package material provided by the review division along with the signed assignment memo into the ECMS folder.

3. Informing OII OBMI of the inspection request via e-mail to OII BIMO point of contact mailbox per WI-000079, and cc BIMO Coordinators, BIMO and CGMP Branch Chief and requestor.

B. The Final Processing Steps

The BIMO compliance staff member will:

1. Send the final assignment memo to the requestor and other appropriate individuals identified in the ec (email copy) or cc (carbon copy) list of the memo.

2. Upload the assignment memo and inspection package material into the BIMO Database.

IX. REFERENCES

CVM BIMO Request Form

Internal information redacted.

CVM BIMO Selection Tool

Internal information redacted.

CVM Standard Operating Procedures

1240.184.001 – Using the BIMO Selection Tool

1240.234.003 – CVM SME BIMO Inspection Attendance

OII Resources

WI-000033 – Instructions for Filling Out BIMO Inspection Assignment (General Information Section)

FORM-000450 – IAM General Information Section Template

WI-000144 – Work Instruction for Naming Convention for Assignment Packages Issued by the Centers and Importing Assignments into ECMS

WI-000079 – Instructions for ECMS Electronic Mail (Email) Subject Line and Body for Issuance of Inspection Assignment Information and Corresponding Communication(s)

OII OBMI Documents, Templates and Associated Process Maps:

Internal information redacted.

X. VERSION HISTORY

December 16, 2024 – Original Version – Document has been developed jointly by OSC and ONADE as a cross-office replacement for ONADE P&P 1243.8215 “Requesting a Bioresearch Monitoring (BIMO) Inspection”.

APPENDIX 1. GLOSSARY

Some of the terms, abbreviations, and acronyms that are used in this document are defined below.

BIMO – Bioresearch Monitoring – Describes a comprehensive, agency-wide program of site inspections and data audits designed to monitor all aspects of the conduct and reporting of FDA-regulated research.

BIMO and CGMP Branch – The branch resides in the Division of Drug Compliance in OSC and is primarily responsible for requesting BIMO inspections of regulated entities and taking compliance actions when appropriate.

BIMO and CGMP Branch Chief – The person responsible for designating the BIMO Compliance Staff Member to issue inspection assignments, review inspection assignments, and who provides general oversight on the direction of BIMO and CGMP Branch resources and operations.

BIMO compliance staff member – Is a staff member within BIMO and CGMP Branch who is responsible for preparing and monitoring BIMO inspection assignments and coordinating any BIMO compliance and follow-up actions.

CDMS – Corporate Document Management System – CVM's Documentum-based document repository

CP – Compliance Program – CVM participates in three agency-wide bioresearch monitoring programs developed to provide uniform guidance and specific instructions for inspections. They are: Good Laboratory Practice (Nonclinical Laboratories) (CP 7348.808), Sponsors/CROs/Monitors (CP 7348.810), and Clinical Investigators (CP 7348.811).

CI – Clinical investigator – As defined in 21 CFR 511.3 "an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. 'Subinvestigator' includes any other individual member of that team."

CRO – Contract research organization – As defined in 21 CFR 511.3, "Contract research organization means a person that assumes, as an independent contractor with the sponsor, one or more of the obligations of a sponsor, e.g., design of a protocol, selection or monitoring of investigations, evaluation of reports, and preparation of materials to be submitted to the Food and Drug Administration."

Most clinical investigators and GLP laboratories do not fit this definition, because being a clinical investigator or laboratory is not an obligation required in the regulation.

CVM BIMO Coordinators – These individuals are responsible for coordinating and monitoring CVM's BIMO inspection program. The CVM BIMO Coordinators work collaboratively and reside in ONAPE or OGAD and OSC. When regulatory action is necessary, the CVM BIMO Coordinators collaborate to ensure a consistent message and approach from CVM across all review and compliance divisions.

CVM BIMO Requests Coordinator – This individual resides in ONAPE in the Quality Assurance Branch in the Division of Business Information Science and Management and collaborates with the CVM BIMO Inspections Coordinator. The CVM BIMO Requests Coordinator is responsible for coordinating and monitoring BIMO requests coming from CVM's review divisions in ONAPE, OGAD, and OSC, including request preparation and subsequent review of EIRs by the review divisions.

CVM BIMO Inspections Coordinator – This individual resides in OSC on the BIMO and CGMP Branch in the Division of Drug Compliance and collaborates with the CVM BIMO Requests Coordinator. The CVM BIMO Inspections Coordinator is responsible for coordinating and monitoring BIMO inspections, including assignment memorandum preparation, inspection procedures and progress by OII, and subsequent review of the inspection materials by the BIMO and CGMP Branch.

ECMS – Enterprise Content Management System – A computer application (Documentum) that is designed to serve as a storage/archival space for inspection documents for OII.

eNSpect – A web-based application used by the BIMO and CGMP Branch, OII and other Centers to create new inspection assignments, view active assignments, and maintain completed assignments for OII.

EIR – Establishment Inspection Report – A report of an inspection that is completed by a FDA field investigator or if applicable, FDA inspection team. The EIR is comprised of endorsement section (coversheet), an investigator's narrative report, attachments, and exhibits.

Entity – Includes all entities subject to BIMO inspection, including the following: sponsors, CROs (including monitors), clinical investigators, and nonclinical laboratories. Nonclinical laboratories include testing facilities and test sites (analytical laboratories, histopathology laboratories, clinical pathology laboratories, etc.).

Field investigator – A staff person located in FDA's Office of Inspections and Investigations, Office of Bioresearch Monitoring Inspectorate (OBMI) who is responsible for scheduling and conducting inspections or investigations, including writing an EIR or memorandum of investigation.

For Cause Inspection Assignments – Inspection assignments issued to assess or evaluate allegations of data integrity issues, research misconduct, or serious public health concerns.

GLP – Good Laboratory Practice – A set of requirements under 21 CFR Part 58 that provides a framework within which nonclinical laboratory studies are planned, performed, monitored, reported, and archived.

Inspection – A careful, critical, official examination of an to determine its compliance with FDA laws and regulations and/or to facilitate regulatory decision making. Inspections may be used to obtain evidence to support legal action when violations are found, or they may be directed to obtain specific information such as a firm's compliance with applicable regulations including those in 21 CFR Part 58 (good laboratory practices), 21 CFR Part 511 (new animal drugs for investigational use), 21 CFR Part 514 (new animal drug applications), 21 CFR Part 570 (investigational food additives), and 21 CFR Part 571 (food additive petitions).

NCIE – Notice of Claimed Investigational Exemption – Also known as a drug or product shipment notice, this permits an investigational new animal drug to be legally shipped in interstate commerce for clinical investigation. See 21 CFR 511.1(b).

OBMI – Office of Bioresearch Monitoring Inspectorate (formerly Office of Bioresearch Monitoring Operations/OBIMO) – OII's BIMO Program office. This office is the custodian of all BIMO harmonized documents.

OII – FDA's Office of Inspections and Investigations – OII performs, among other things BIMO inspections and investigations, and was formerly known as the Office of Regulatory Affairs (ORA).

QASR – Quality Assurance Study Reviewer – Personnel within the ONAPE Quality Assurance Branch who perform data quality and integrity reviews for data submitted to CVM.

Raw data – Raw data for GLP studies is defined in 21 CFR 58.3, which states "*Raw data* means any laboratory worksheets, records, memoranda, notes, or exact copies thereof, that are the result of original observations and activities of a nonclinical laboratory study and are necessary for the reconstruction and evaluation of the report of that study. In the event that exact transcripts of raw data have been prepared (e.g., tapes which have been transcribed verbatim, dated, and verified accurate by signature), the exact copy or exact transcript may be substituted for the original source as raw data. *Raw data* may include photographs, microfilm or microfiche copies, computer printouts, magnetic media, including dictated observations, and recorded data from automated instruments."

Raw data for GCP studies is described in Guidance for Industry 85, Good Clinical Practice, which states "Any original worksheets, calibration data, records, memoranda and notes of first-hand observations and activities of a study that are necessary for the reconstruction and evaluation of the study. Raw data may include, but are not limited to, photographic materials, magnetic, electronic, or optical media, information recorded from automated instruments, and hand-recorded datasheets. Facsimile transmissions and transcribed data are not considered raw data."

Reviewer – Reviewer is a general term used to refer to any CVM staff member who reviews pending submissions made to FDA as part of the regulatory decision-making process (e.g., submissions related new animal drug applications, food-additive petitions, etc.) and who may desire additional information gathered by a BIMO inspection to help facilitate that decision.

SAS – A statistical software suite developed by SAS Institute.

Sponsor – Sponsor is defined in various locations in FDA regulations (21 CFR 511.3, 58.3(f), and 510.3(k)). In general terms, sponsor means a person who takes responsibility for, initiates, and supports clinical investigations or nonclinical laboratory studies. The sponsor is the entity who actually submits information to FDA in support of an approval.

WI – Work instruction – Is a document type used by OII that describes how to complete specific tasks and activities which may be at a more detailed level than an SOP.

APPENDIX 2. PRE-INSPECTION TIMELINE

Task Name	Task Days	Cumulative Days
Requestor submits completed Section A to CVM BIMO Requests Coordinator	0	0
CVM BIMO Requests Coordinator reviews request and completes Section B	3	3
Division determines whether to go forward with request and completes Division Decision section	2	5
Requestor prepares BIMO request and sends to CVM BIMO Requests Coordinator	9	14
CVM BIMO Requests Coordinator reviews package and provides comments to requestor for resolution; CVM BIMO Requests Coordinator sends package to BIMO & CGMP Branch following resolution of comments	3	17
CVM BIMO Inspections Coordinator reviews package and provides comments for resolution	4	21
BIMO & CGMP Branch Chief or designee triages assignment request, responds to request email and assigns to BIMO compliance staff member	2	23
BIMO compliance staff member reviews materials and develops draft assignment memo	10	33
BIMO & CGMP Branch Chief clears assignment memo	5	38
BIMO compliance staff member finalizes and issues the assignment to OII	3	41