

J-P-BQ/Bioequivalence Technical Section tab of A-A-OT eSubmitter Template

Note that this template relies on information obtained in the separate eSubmitter "7.0
Product Description" tab.

Template questions are written in **bold text**
Hints for the user are designated by **HINT: text**
Programming instructions are provided by *<italic text>*
Upload prompts are indicated by **Upload: text**

Table of Contents

J-P-BQ/Bioequivalence Technical Section tab of A-A-OT eSubmitter Template	1
1.0 GENERAL INFORMATION	3
2.0 ADDITIONAL PRODUCT DESCRIPTION.....	4
3.0 INFORMATION TO SUPPORT BIOEQUIVALENCE TECHNICAL SECTION.....	4
4.0 BIOEQUIVALENCE DATA/INFORMATION	11
5.0 COMMENTS.....	26

<All content will be present in both J-P-BQ template and BQ TS of A-A-OT unless otherwise indicated>

1.0 GENERAL INFORMATION

When attaching files, please review the specifications for file attachments in the **CVM eSubmitter File Specification Quick Guide**. When submitting.pdf file(s), CVM prefers a single bookmarked .pdf file in place of multiple .pdf files.

<Disable next question for A-A-OT>

Please select the final action letter you are requesting from CVM with this submission.

HINT: Select one of the following options.

- Submitted Information Acceptable; Technical Section Incomplete
- Technical Section Complete

Is this in response to a previous CVM Technical Section Incomplete Letter?

- YES
 - <If "YES":>
 - Please provide the CVM Submission Number associated with the referenced Technical Section Incomplete Letter. <Click here to enter text. 4 characters>
 - <Disable item for A-A-OT> In the Technical Section Incomplete Letter referenced above, did CVM offer you a shortened review time with the resubmission of this Technical Section?
 - YES
 - NO
 - Are there any additional CVM Submission Numbers associated with your CVM Technical Section Incomplete Letter(s)?
 - YES
 - <If "YES":> Include the CVM Submission Number(s) associated with your CVM Technical Section Incomplete Letter(s). <Click here to enter text. 4 characters. Item allows for multiple entries.>
 - NO
 - Please provide a description of the updates included as part of your response to the Technical Section Incomplete Letter(s). Include any impacted Bioequivalence Studies in 4.0 "Bioequivalence Data/Information" only providing updates to section 4.1 through 4.11, as needed.
Upload a single PDF file that contains the description of the updates as part of your response to the Technical Section Incomplete Letter(s).
- NO

Provide a brief summary of the information provided in this Bioequivalence technical section submission.

HINT: The brief summary aids the reviewer in quickly identifying the purpose of the submission. It is represented in the administrative cover form received by CVM and is used to populate the CVM database. There is an 80 character limit to this response. For example, "Blood level bioequivalence study in dogs."

Additional information may be provided as a PDF attachment in the next response to upload a submission summary and/or cover letter. *<Click here to enter text. 80 characters>*

Upload your submission summary or cover letter.

2.0 ADDITIONAL PRODUCT DESCRIPTION

Has a suitability petition been granted for the proposed generic product? this in response to a previous CVM Technical Section Incomplete Letter?

- YES
 - *<If "YES":> Provide the suitability petition number, the date on which it was granted, and a description of the applicable change(s). <Click here to enter text. 500 characters>*
- NO

3.0 INFORMATION TO SUPPORT BIOEQUIVALENCE TECHNICAL SECTION

This section will inform CVM of your overall plan for the Bioequivalence technical section by identifying all relevant components supporting the technical section and their status with respect to submission to CVM. This supporting information includes bioanalytical method validation reports, all relevant studies, communications with CVM, and All Other Information. If the documentation requested in this section is included in the FSR you will be uploading under this submission, please reference its location in the FSR instead of uploading a duplicate copy when prompted.

In the next eSubmitter section (Section 4), you will be prompted to upload your FSR(s) and raw data. Please do not attach this information until prompted. Also note that Section 4 allows you to submit data from multiple studies (if applicable).

Are there bioanalytical method validation report(s) applicable to this Bioequivalence technical section submission?

- YES
 - *<If "YES" activate 3.1>*
- NO

3.1 Bioanalytical Method Validation

HINT: You should include all analytical method validation reports to support the data you are submitting. For example, if you are submitting two blood level bioequivalence data studies, one in dogs and one in cats, CVM would expect two analytical method validation reports, one for dog plasma and one for cat plasma.

Provide a brief description of the report. *<Click here to enter text. 100 characters>*

What is the status of the bioanalytical method validation report submission? HINT: *Select one of the following options.*

- **The bioanalytical method validation report submission has been reviewed by CVM and found acceptable.**
 - *<If selected> Enter the submission number. <Click here*

to enter text. 50 characters>

- **The bioanalytical method validation report has been submitted to CVM and is under review.**
<If selected> Enter the submission number. HINT: Enter "to be determined" if the submission number is not yet known. <Click here to enter text. 50 characters>
- **The bioanalytical method validation report has not been submitted to CVM.**
<If selected> You may upload the method validation report OR provide the location of the bioanalytical method validation report in your FSR. HINT: Select one of the following options.
 - **The bioanalytical method validation report will be uploaded now. Upload the bioanalytical method validation report.**
 - **The location of the bioanalytical method validation report in the FSR will be provided now. HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>**

As you indicated within the Product Description tab, are you seeking approval for multiple uses of this product (multiple dosage forms, routes of administration, and/or species)? HINT: If in the Product Description tab you indicated that the product is proposed for use in multiple dosage forms, routes of administration and/or species, please select YES.

- **YES**
 - *<If "YES" activate 3.2>*
- **NO**

3.2 Bioequivalence studies for each proposed use of product

The list below is populated with each of the combinations of dosage form, route of administration, and target animal you entered under the Product Description tab. Please select and provide the bioequivalence study status for each combination listed.

Select each combination of dosage form, route of administration, and target animal for which you are seeking approval:

<User will be able to select from pick list and provide BE study status for each of the combinations previously entered in the Product Description tab.>

- **Bioequivalence Study Status**
HINT: Select one of the following options.
 - **Included in this submission**
 - **Previously submitted**
<If selected> Enter submission number and final outcome. <Click here to enter text. 500 characters>
 - *<Disable for A-A-OT>* **Pending or planned**
<If selected> Enter details. <Click here to enter text. 500 characters>
 - **Other**
<If selected> Enter details. <Click here to enter text. 500 characters>

Are you requesting a waiver from the requirement to perform in-vivo blood level bioequivalence study(s) for additional generic drug product strength(s) based on comparative dissolution data??

- **YES**

- <If "YES" activate 3.3>
- **NO**

3.3 Comparative Dissolution Studies

Provide the following information.

- **Additional strength(s):** <Click here to enter text. 25 characters>
- **Dissolution method validation status:**
HINT: Please note that the dissolution method validation report is typically submitted in the Chemistry, Manufacturing and Controls technical section. Select one of the following options.

<Options for A-A-OT (Dissolution method validation status)>

- **The dissolution method used for comparative dissolution studies supporting bioequivalence is the same dissolution method used to support the Chemistry, Manufacturing and Controls (CMC) technical section. The dissolution method validation report will be included in this submission as part of the CMC technical section.**
- **The dissolution method used for comparative dissolution studies supporting bioequivalence is NOT the same dissolution method used to support the Chemistry, Manufacturing and Controls (CMC) technical section. The dissolution method validation report will be included in this submission as part of the Bioequivalence technical section.**

<If selected> You may upload the dissolution method validation report OR provide the location of the dissolution method validation report in your FSR.

HINT: Select one of the following options.

- **The dissolution method validation report will be uploaded now. Upload the dissolution method validation report.**
- **The location of the dissolution method validation report in the FSR will be provided now. HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>**
- **The dissolution method validation report was previously submitted.**
<If selected> **Enter submission number and final outcome. <Click here to enter text. 500 characters>**
- **Other**
<If selected> **Enter details. <Click here to enter text. 500 characters>**

<Options for J-P-BQ (Dissolution method validation status)>

- **The dissolution method validation report was previously submitted.**
<If selected> **Enter submission number and final outcome. <Click here to enter text. 500 characters>**
- **The dissolution method validation report will be submitted at a later date.**
<If selected> **Enter details. <Click here to enter text. 500 characters>**

- **The dissolution method used for comparative dissolution studies supporting bioequivalence is NOT the same dissolution method used to support the Chemistry, Manufacturing and Controls (CMC) technical section. The dissolution method validation report will be included in this submission.**
<If selected> You may upload the dissolution method validation report OR provide the location of the dissolution method validation report in your FSR.
HINT: Select one of the following options.
 - **The dissolution method validation report will be uploaded now. *UPLOAD the dissolution method validation report.***
 - **The location of the dissolution method validation report in the FSR will be provided now. HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>**
- **Other**
<If selected> **Enter details.** <Click here to enter text. 500 characters>

<This item is for both J-P-BQ and A-A-OT>

- **Comparative dissolution study report (including individual vessel dissolution data and representative HPLC printout):**
HINT: Please note that the dissolution method validation report is typically submitted in the Chemistry, Manufacturing and Controls technical section. Select one of the following options.
 - **Included in this submission.**
<If selected> You may upload the comparative dissolution study report OR provide the location of the comparative dissolution study report in your FSR.
HINT: Select one of the following options.
 - **The comparative dissolution study report will be uploaded now. *Upload the comparative dissolution study report.***
 - **The location of the comparative dissolution study report in the FSR will be provided now.**
HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>
 - **Previously submitted.**
<If selected> **Enter submission number and final outcome.** <Click here to enter text. 500 characters>
 - <De-activate for A-A-OT> **Pending or planned**
<If selected> **Enter details.** <Click here to enter text. 500 characters>

<For A-A-OT, disable following tissue residue study question and display the following statement:>

The following question pertaining to tissue residue studies is not available as part of the A-A-OT template because human food safety is separately addressed in Section 3.6 of the A-A-OT template.

Is a tissue residue study (or studies) applicable to this generic drug product?

- YES

- *<If "YES" activate 3.4.>*
- **NO**

3.4 Tissue Residue Studies

The list below is populated with each of the target animals you entered under the Product Description tab. Please select and provide the tissue residue study status, if applicable, for each target animal listed.

Select each target animal for which you are seeking approval:
<User will be able to select from pick list and provide tissue residue study status for each of the target animals entered in the Product Description tab.>

- **Tissue Residue Study Status**
HINT: Select one of the following options.
 - **Previously submitted**
<If selected> Enter submission number and final outcome. <Click here to enter text. 500 characters>
 - **Pending or planned**
<If selected> Enter details. <Click here to enter text. 500 characters>
 - **Not applicable (A tissue residue study is not required for this target animal.)**

3.5 Meeting/Informal Communication with CVM

Have you had a meeting with CVM regarding the study (or studies) performed for this generic drug product?

- **YES**
 - *<If "YES"> Enter the submission identification and date of the Memorandum of Conference. <Click here to enter text. 25 characters>*
- **NO**

Have you had any informal communication (via email or telephone) with CVM regarding the study (or studies) performed for this generic drug product?

- **YES**
 - *<If "YES"> Provide the following information.*
 - **Provide a description of any telephone conversations, including the dates the conversation(s) occurred and the names of CVM personnel with whom you spoke.**
HINT: Enter "N/A" if not applicable. <Click here to enter text. 500 characters>
 - **If applicable, upload documentation of email communication. *UPLOAD documentation of email communication.***
- **NO**

3.6 All Other Information

As part of the Bioequivalence technical section, CVM requires that All Other Information (AOI) pertaining to bioequivalence for the proposed product be submitted.

HINT: Select one of the following options.

- **AOI pertaining to bioequivalence for the proposed product will be submitted now. This should be selected even if AOI was provided as part of a previously submitted data submission.**
 - *<If selected>*
 - **Have any previous studies evaluating this proposed generic drug product been conducted that were intended to serve as a pivotal study, yet failed to demonstrate bioequivalence?**
 - **YES**
 - *<If selected>* **Did you previously provide a summary of information related to the study(s) to CVM?** *<Click here to enter text. HTML>*
 - **YES**
 - *<If selected>* **Enter the submission number under which this information was previously provided to CVM and, if applicable, any associated comments.** *<Click here to enter text. 500 characters>*
 - **NO**
 - *<If selected>* **Please provide the following summary information related to the previous study(s): a description of the study design, dates of study, study location, study outcome. Additionally, please provide a justification for conducting a subsequent bioequivalence study (i.e., evidence of flawed study design or implementation in the previous study and/or subsequent product reformulation).** *<Click here to enter text. HTML or>* **UPLOAD document containing this information.**
 - **NO**
 - **Is this proposed generic drug product currently marketed or has it previously been marketed in countries outside the United States?**
 - **YES**
 - *<If selected>* **Have any concerns regarding adverse events and/or lack of efficacy been reported?**
 - **YES**
 - *<If selected>* **Did you previously provide all information related to this concern(s) to CVM?** *<Click here to enter text.>*
 - **YES**
 - **Enter the submission number under which this information was previously provided to CVM and, if applicable, any associated comments.** *<Click here to enter text. 500 characters>*
 - **NO**
 - **Please provide a thorough description of the concern and a justification for pursuing the current approval.** *<Click here to enter text. HTML or>* **UPLOAD document containing this information.**
 - **NO**
 - **NO**

- **NO**
- **CVM requests that sponsors perform a literature search for any publications (manuscripts, proceedings, etc.) related ONLY to BIOEQUIVALENCE of the active pharmaceutical ingredient(s) (API) under evaluation. This search should be conducted using the combined search terms of each API and the term "bioequivalence". If it has been 6 months since you last performed this search, CVM requests that you repeat the search.**

Did you identify any concerns related to bioequivalence of the API(s) under evaluation in your literature search?

- **YES**
 - *<If selected>* **Did you previously provide all information related to these concerns to CVM?** *<Click here to enter text. HTML>*
 - **YES**
 - *<If selected>* **Enter the submission number under which this information was previously provided to CVM and, if applicable, any associated comments.** *<Click here to enter text. 500 characters>*
 - **NO**
 - *<If selected>* **Please provide a thorough description of the concerns, the associated publications, and a discussion of the impact of the concerns on your Bioequivalence technical section.** *<Click here to enter text. HTML or>* **UPLOAD document containing this information.**
 - **NO**
- **Are you aware of any other applicable information related to bioequivalence, safety, and/or efficacy that should be considered by CVM for this proposed generic drug product?**
 - **YES**
 - *<If selected>* **Did you previously provide this information in its entirety to CVM?** *<Click here to enter text. HTML>*
 - **YES**
 - *<If selected>* **Enter the submission number under which this information was previously provided to CVM and, if applicable, any associated comments.** *<Click here to enter text. 500 characters>*
 - **NO**
 - *<If selected>* **Please provide a thorough description of the information, and a discussion of the impact of the information on your Bioequivalence technical section.** *<Click here to enter text. HTML or>* **UPLOAD document containing this information.**
 - **NO**
- *<Disable for A-A-OT>* **A Bioequivalence technical section complete letter is not being sought with this submission, and AOI pertaining to bioequivalence for the proposed product will**

be submitted as part of a future submission to CVM.

<If selected> **Enter a description of the future submission which will contain AOI pertaining to bioequivalence for the proposed product.** *<Click here to enter text. 500 characters>*

- **Other**

<If selected> **Enter details.** *<Click here to enter text. 500 characters>*

<The following section 4.0 is formatted to allow for entry of multiple studies (tabular format). All content will be available for each submitted study.>

4.0 BIOEQUIVALENCE DATA/INFORMATION

What type of study/information are you submitting?

HINT: Select the study type that most closely matches your study. The use of "Other" should be avoided unless necessary. We recommend contacting CVM prior to completing the template with any questions about which study to select.

- **Blood Level Bioequivalence Study (*In-vivo*)**
- **Clinical Endpoint Study (*In-vivo*)**
- **Pharmacological Endpoint Study (*In-vivo*)**
- **Dissolution Study**
- **Other**

<If Dissolution Study is selected.> **Is the dissolution study intended to support a waiver from the requirement to perform in vivo bioequivalence studies (biowaiver) for additional strengths of the generic drug product?**

- **YES**
- **NO**

<If selected> **Explain the purpose of the dissolution study.** *<Click here to enter text. 200 characters>*

What is the study number?

<Click here to enter text. 25 characters>

What is the title of the study?

<Click here to enter text. 250 characters>

What was the objective of the study?

HINT: The objective should include the intent to assess the bioequivalence of the generic drug product with the reference listed new animal drug (RLNAD). Include the species, generic/test article, RLNAD/control article and dose in this section.

<Click here to enter text. HTML question>

<Disable following question if Dissolution Study submission.>

Did study personnel collect any information regarding *in-vivo* study procedures (e.g., drug accountability records, animal feeding, animal dosing, sample collection) or clinical observations (e.g., body weights, physical examination findings, post-dose observations, daily clinical observations) by manual entry into an Electronic Data Capture (EDC) system (as opposed to manual entry onto paper data collection forms)?

HINT: If you are submitting a blood level bioequivalence study, and an EDC system was used for bioanalysis of incurred samples and/or clinical pathology (complete blood count, serum chemistry, urinalysis) only, enter "NO". If an EDC system was used to collect in-vivo or clinical data (e.g., physical examination findings, body weights, dosing times, blood sampling times, clinical observations, post-dose observations), enter "YES".

- YES
- NO

<If user previously indicated submission is in response to TS INC letter, enable following two questions.>

Have you submitted this study previously?

- YES
 - *<If "YES":>* Select the section(s) to be updated for this study in response to the previous CVM Technical Section Incomplete Letter:
 - Final Study Report (FSR)
 - Protocol
 - Test and Control Article Characterization
 - Standard of Conduct/Regulatory Standards
 - Electronic Data Capture (EDC) Systems
 - ReadMe File
 - Data Files
 - Program Files
 - Contributing Scientist Reports
 - Other Study Related Information
- NO

4.1 Final Study Report (FSR)

Please review the specifications for file attachments in the [CVM eSubmitter File Specification Quick Guide](#).
Links to [GLP](#) and [GCP](#) FSR references. For additional questions, contact CVM.

<Only enable confirmation box through end of list (#15) if Blood Level BE Study submission.>

Confirm agreement:

- The Final Study Report (FSR) to be uploaded below contains a detailed table of contents providing the page numbers/locations for each of the items listed below.
<If box is NOT checked> Explain why you did not check the box to confirm agreement with the statement above.
<Click here to enter text. 1000 characters>

1. Name and address of the facility performing the study and the dates on which the study was initiated and completed.
2. Objectives and procedures stated in the approved protocol, including any changes in the original protocol. This includes descriptions of amendments to and deviations from the original protocol.
3. Statistical methods employed for analyzing the data.
4. The test and control articles identified by name, dosage form, chemical abstracts number or code number, batch numbers, expiration dates (if applicable), strength, purity, and composition or other appropriate characteristics. Summary of conditions under which test and control articles were stored. Excursions or deviations from maintenance storage conditions should be described along with a discussion of any perceived impact on the pivotal study data as a result. Raw data for storage conditions is not required as part of this submission. Description of reserve samples that were retained. Commitment that final formulations were used in the study.

5. **Stability of the test and control articles under the conditions of administration.**
6. **A description of the methods used during the in vivo portion of the study. (The bioanalytical methods are discussed under number 12, below.)**
7. **A description of the test system used. Where applicable, the final report shall include the number of animals used, sex, body weight range, source of supply, species, strain and substrain, age, and procedure used for identification. A description of the animal housing environment (temperature, relative humidity, ventilation, lighting) should be provided along with a discussion of any impact from excursions or deviations to the animal housing environment during the study.**
8. **A description of the dosage, dosage regimen, route of administration, and duration.**
9. **A description of all circumstances that may have affected the quality or integrity of the data.**
10. **The name of the study director, the names of other scientists or professionals, and the names of all supervisory personnel, involved in the study.**
11. **A description of the transformations, calculations, or operations performed on the data, a summary and analysis of the data, and a statement of the conclusions drawn from the analysis.**
12. **The signed and dated reports of each of the individual scientists or other professionals involved in the study, including the stand-alone bioanalytical phase and statistical reports.**

The complete, signed bioanalytical phase report should include any amendments (if applicable). The appendix to the bioanalytical phase report should include raw data associated with sample analysis, including but not limited to the following:

- **sample analysis (sequence/batch/run summary (accepted and rejected), reasons for failure, tables of calibration standards and QCs, study sample results, 20% of chromatograms, reasons for re-integration (if applicable), original and re-integrated chromatograms)**
- **re-assay (reasons for reanalysis, original and re-assay results)**
- **Incurred Sample Reproducibility (original and ISR data table, % difference, % passed, failure investigation if applicable)**

The appendix to the bioanalytical phase report may also include:

- **sample tracking records (dates of receipt, sample condition on receipt, analytical site storage condition, total duration of sample storage, a description of the planned storage conditions and any excursions or deviations from those conditions)**
- **communication records (records related to any issue that required investigation during sample analysis such as investigation reports, notes to file, email correspondences, etc.)**

If any of the bioanalytical phase report appendix content items listed above are not included in the FSR, they may be uploaded in Section 4.8.10 "Other Data Files" below.

13. The locations where all specimens, raw data, and the final report are to be stored.
14. Quality Assurance Unit (QAU) statements for the in-life and analytical phases of the study. The QAU statements should verify the study was independently audited, and the observations reported to the Study Director and Test Facility Management. The statement should include a list of audits performed, audit dates, and dates results were reported to study director and testing facility management. The QAU statements should be signed by the QAU officials.
15. Descriptions of how the attributes of ALCOA (Attributable, Legible, Contemporaneous, Original and Accurate) were maintained for the collected data. Additionally, if an Electronic Data Capture (EDC) system(s) (as defined in Section 4.0) was used, descriptions of how the attributes of ALCOA were maintained within the EDC system(s).

UPLOAD a single PDF that contains the Final Study Report.

4.2 Protocol/Standard Test Procedure

Did you previously submit a protocol/Standard Test Procedure for concurrence by CVM? *HINT: A protocol is applicable to an in vivo study or a comparative dissolution study. A standard test procedure is applicable only to comparative dissolution studies.*

- YES
 - *<If "YES">*
 - Please provide the CVM Submission Number associated with the referenced protocol submission. *<Click here to enter text. 25 characters>*
 - Did you receive CVM concurrence on your protocol?
 - YES
 - NO
- NO

Did you include your signed protocol/Standard Test Procedure (used for conducting the study) in the Final Study Report?

- YES
 - *<If "YES">* Provide the location of your signed protocol/Standard Test Procedure in the FSR. *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
- NO
 - *<If "NO">* **UPLOAD signed protocol/Standard Test Procedure.**

<The following section 4.3 is formatted to allow for multiple entries (tabular format). All content will be available for each submitted test/control article.>

4.3 Test and Control Article Characterization

Select the characterization type.

- **Test Article**
- **Control Article**

Provide the article identifier used during the study and reflected in the final study report. *<Click here to enter text. 200 characters>*

< If "Test Article" is selected above, display following section.>

Enter the Test Article Details:

- **Confirm agreement: The test article formulation is the same as your proposed final formulation.**
- **Provide the lot number(s) for the test article used for this study.** *<Click here to enter text. 100 characters>*
- **Did you include the certificates of analysis (COAs) for the test article in the FSR?**
 - **YES**
 - *<If "YES">* **Provide the location of the test article COAs in the FSR. HINT: Include page numbers and section title as it appears in the table of contents. You will be able to upload additional raw data associated with the test article (e.g., accountability, receipt, and storage records) in Section 4.8.** *<Click here to enter text. 250 characters>*
 - **NO**
 - *<If "NO">* **UPLOAD test article COAs.**

< If "Control Article" is selected above, display following section.>

Enter the Control Article Details:

- **Provide the lot number(s) for the control article used for this study.** *<Click here to enter text. 100 characters>*
- **Did you obtain certificates of analysis (COAs) for the control article?**
 - **YES**
 - *<If "YES">* **Did you include the COAs for the control article in the FSR?**
 - **YES**
 - *<If "YES">* **Provide the location of the control article COAs in the FSR. HINT: Include page numbers and section title as it appears in the table of contents. You will be able to upload additional raw data associated with the control article (e.g., accountability, receipt, and storage records) in Section 4.8.** *<Click here to enter text. 250 characters>*
 - **NO**
 - *<If "NO">* **UPLOAD control article COAs**
 - **NO**
 - *<If "NO">* **Describe how you ensured that the potency of the test and control articles used in the *in vivo* bioequivalence study were within $\pm 5\%$?** *<Click here to enter text. 250 characters>*

4.4 Protocol Amendments and/or Protocol Deviations

Protocol Amendments

Were protocol amendments implemented in the study?

- **YES**
 - *<If "YES">*

- **For all protocol amendments, were descriptions and discussions of associated study impact included in the FSR?** *<Select one>*
 - **Description and discussion of the impact of protocol amendments are included in the FSR and their location within the FSR will be provided now.** *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
 - **Description and discussion of the impact of protocol amendments will be submitted now. *UPLOAD a description and discussion of the impact of protocol amendments.* OR Provide a description and discussion of the impact of protocol amendments.** *<Click here to enter text. HTML>*
- **Were original documentation of all protocol amendments included in the FSR?** *<Select one>*
 - **Original documentation of protocol amendments are included in the FSR and their location within the FSR will be provided now.** *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
 - **Original documentation of protocol amendments will be uploaded now. *UPLOAD original documentation of protocol amendments.***
- **NO**

Protocol Deviations

Did any protocol deviations occur during the course of the study?

HINT: Note that this question specifically pertains to deviations from the information specified in your study protocol rather than deviations from GLP standards. Although there may be study occurrences that require discussion under both sections, you will be prompted to specifically discuss any GLP deviations, if applicable, in Section 4.5 Standard of Conduct/Regulatory standards.

- **YES**
 - *<If "YES">*
 - **For all protocol deviations, were descriptions and discussions of associated study impact included in the FSR?** *<Select one>*
 - **Description and discussion of the impact of protocol deviations are included in the FSR and their location within the FSR will be provided now.** *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
 - **Description and discussion of the impact of protocol deviations will be submitted now. *UPLOAD a description and discussion of the impact of protocol deviations.* OR Provide a description and discussion of the impact of protocol deviations.** *<Click here to enter text. HTML>*
 - **Were original documentation of all protocol**

deviations included in the FSR? *<Select one>*

- **Original documentation of protocol deviations are included in the FSR and their location within the FSR will be provided now.** *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
- **Original documentation of protocol deviations will be uploaded now.** ***UPLOAD original documentation of protocol deviations.***
- **NO**

4.5 Standard of Conduct/Regulatory Standards

<Enable link and following question if NOT Blood Level BE Study submission>

Links to **GLP** and **GCP** references.

What quality standard was used to conduct the study? *<Select one>*

- **Good Laboratory Practices (GLP) 21 CFR Part 58**
- **Good Clinical Practices (GCP)**
- **Other**
 - *<If "Other">* **Please describe the quality standard used to conduct the study.** *<Click here to enter text. 1000 characters>*

<Enable following parent question and "NO" follow-up only if Blood Level BE Study submission.>

Was the study conducted according to Good Laboratory Practices (GLP) 21 CFR Part 58?

- **YES**
- **NO**
 - *<If "NO">*
 - **List all alternate standard(s) (e.g., OECD) that were used.** *<Click here to enter text. 1000 characters>*
 - **Provide a detailed description and justification of all differences between 21 CFR Part 58 and the standards used in the study, including an assessment of the impact on the study and/or data for each difference; or, provide the location of this description in the FSR.** *HINT: If providing a location, include page numbers and section title as it appears in the table of contents. If this information is not contained within the FSR, provide your detailed description of all differences here. <Click here to enter text. HTML>*

<If "YES" to above parent question, or "GLP" is selected for "What quality standard was used to conduct the study?" enable rest of node>

Provide your sponsor GLP compliance statement. *HINT: A sponsor GLP compliance statement is expected to 1) affirmatively state what specific elements of the study the sponsor has assured itself were conducted in compliance with 21 CFR 58, 2) briefly state the reasons for any noncompliance, 3) explicitly describe all observed differences (preplanned differences and deviations) between the practices used in the study and 21 CFR 58, and 4) be signed and dated by the sponsor. **Upload***

sponsor GLP compliance statement.

Have GLP compliance statements from all relevant laboratories been included in the Final Study Report? *<Select one>*

- **GLP compliance statements from relevant laboratories are included in the FSR and their location within the FSR will be provided now.** *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
- **GLP compliance statements from relevant laboratories will be uploaded now.** ***UPLOAD GLP compliance statements from relevant laboratories.***

Did your GLP compliance statement(s) describe any preplanned differences or deviations from GLP? *HINT: Note that this question specifically pertains to deviations from GLP standards rather than deviations from the information specified in your study protocol. Although there may be study occurrences that require discussion under both sections, you were prompted to specifically discuss any deviations from the information specified in your study protocol in Section 4.4 Protocol Amendments and/or Protocol Deviations.*

- **YES**
 - *<If "YES">*
 - **Were original documentation of all preplanned differences or deviations from GLP included in the FSR?** *<Select one>*
 - **Original documentation of preplanned differences or deviations from GLP are included in the FSR and their location within the FSR will be provided now.** *HINT: Include page numbers and section title as it appears in the table of contents. <Click here to enter text. 250 characters>*
 - **Original documentation of preplanned differences or deviations from GLP will be uploaded now.** ***Upload files associated with original documentation of preplanned differences or deviations from GLP.***
- **NO**

Describe how the attributes of ALCOA (Attributable, Legible, Contemporaneous, Original, Accurate) were maintained for collected data during the time between its receipt from study director and submission to CVM. *<Click here to enter text. 1000 characters>*

<4.6 is enabled only if user indicated in 4.0 that an Electronic Data Capture (EDC) system(s) was used for data collection.>

<The following section 4.6 is formatted to allow for multiple entries (tabular format). All content will be available for each EDC system used during the study.>

4.6 Electronic Data Capture (EDC) Systems

In section 4.0 you indicated that you used an EDC system(s). Each EDC system entered within this section will be available within section 4.8 "Data Files" as a reference to associate data files with the EDC system used to collect the data.

Identify the EDC system. <Click here to enter text. 250 characters>

Enter a brief description of the type of data collected with the EDC system (e.g., physical examination findings, body weights). <Click here to enter text. 250 characters>

<For Dissolution Study submissions de-activate 4.7>

4.7 ReadMe File

Please review the specifications for file attachments in the CVM eSubmitter File Specification Quick Guide.

ReadMe File

Your submission should include a comprehensive “README” file (PDF), including a listing and description/purpose of each data file and program file submitted. For each data file, include a list of all variables, abbreviations if used, columns in the data file, and units of measure. See GFI #197 for more information on what to include within a ReadMe file for this study.

UPLOAD a single PDF file that contains the ReadMe file for this study.

<For dissolution studies de-activate 4.8>

4.8 Data Files

Copies of raw data submitted to CVM should be provided in the same format as it was originally collected, either in paper or electronic, as described next.

For raw data collected in paper format, provide PDF copies. The PDF files should meet the specifications as described in the CVM eSubmitter File Specification Quick Guide.

Provide electronic data files (including electronically captured raw data) in non-proprietary eXtensible Markup Language (XML) or SAS Transport (XPT) format. If necessary, electronic data files of other formats may be copied into the above acceptable file formats using validated software. All copied data should be imported exactly as they appear in the original format (e.g., no column changes or calculations). If files are converted, the program used to make the conversion should be provided to CVM in XML format. Additionally, we encourage you to evaluate/analyze the data using the same file format that you submit to CVM.

In this section, please upload data files applicable to this submission that haven't already been included as part of the FSR uploaded above or a previous data submission. Raw data for test and control article storage conditions (temperature and humidity, if applicable), animal housing environmental conditions (temperature, relative humidity, ventilation, lighting) is not required for this submission unless excursions or deviations from maintenance have occurred.

CVM prefers that bioequivalence study data files be uploaded according to categories defined below (reference and test article, environment: animal housing, feed, water, baseline data, inclusion/exclusion, etc.). If you elect to upload raw data accordingly, you will be provided with the list and description of data file categories below. You will be able to select the categories for which you would like to upload data files. The final category is titled "Other data files" to allow for uploading of data files that do not fit into any of the predefined categories.

If you are unable to upload data files according to predefined categories, you have the option of performing multiple data file uploads according to your preferred method of organization by selecting "Sponsor Organized Files" and providing a description of the data collected within the data set.

Please select the category for the set of data files to be uploaded (see the question hint for description of each category). [HINT: For sections that are selected, the option to upload data files will follow.](#)

<Select all relevant options. The hints for each of these categories are provided below this selection list.>

- **4.8.1 Reference and Test Article**

<Enable next item for Blood Level BE submissions only>

- **4.8.2 Environment: animal housing, feed, water (Blood Level BE Studies)**

<Enable next item for Clinical Endpoint and Pharmacological Endpoint submissions only>

- **4.8.2 Environment: animal housing, feed, water**

<Enable next item for Blood Level BE submissions only>

- **4.8.3 Baseline Data (Blood Level BE Studies)**

<Enable next item for Clinical Endpoint and Pharmacological Endpoint submissions only>

- **4.8.3 Baseline Data**

- **4.8.4 Inclusion/Exclusion**

- **4.8.5 Administration/Dosing**

<Enable next item for Blood Level BE submissions only>

- **4.8.6 Sampling**

<Enable next item for Clinical Endpoint and Pharmacological Endpoint submissions only>

- **4.8.6 Bioequivalence Endpoint Data**

- **4.8.7 Clinical Observations and Adverse Events**

- **4.8.8 Euthanasia and Necropsy**

- **4.8.9 Statistical Methods and Bioequivalence Analysis**

- **4.8.10 Other Data Files**

- **Sponsor Organized Files**

<For each category selected, the following content is displayed>

<Activate the following question if user previously indicated in 4.0 and 4.6 that an EDC system(s) was used.>

Was any of the data associated with this section collected using an EDC system?

- **YES**

- *<If "YES">*
 - **Select the associated EDC.** *<User is provided list of EDC systems that were previously entered in section 4.6.>*
 - **For each selected EDC system, describe which component(s) of the raw data were collected using that EDC System.** *<Click here to enter text. 500 characters >*
 - **When possible, a single electronic data file should be submitted that includes the recorded data and audit trail (non-proprietary XML of XPT file format) from the study. However, if the audit trail information can only be submitted in a separate file, that information should be submitted as an electronic data file (non-proprietary XML or XPT format). See GFI #197 for information related to audit trails.**

Upload data files.

<Activate the following question if user previously indicated that in 4.0 and 4.6 an EDC system(s) was used.>

Do audit trails exist outside the data files?

- **YES**
 - *<If "YES">*
 - **Do you have any non-proprietary XML or XPT file format audit trail files to attach?**
 - **YES**
 - *<If "YES"> Upload audit trail files. You have the option to submit a single or multiple eXtensible Markup Language (.xml) or SAS SYSTEM XPORT (.XPT) files.*
 - **NO**
 - **Do you have PDF file format audit trail files to attach?**
 - **YES**
 - *<If "YES"> Upload audit trail files. You have the option to submit a single or multiple .pdf files.*
 - **NO**
 - **Do you have audit trail information from the electronically collected data that cannot be submitted to CVM in either non-proprietary XML, XPT, or PDF file formats?**
 - **YES**
 - *<If "YES"> Explain why this audit trail information cannot be submitted in any of these file format options. <Click here to enter text. 1000 characters>*
 - **NO**
- **NO**

<For each raw data category selected, the associated hint will be displayed at UPLOAD prompt>

4.8.1 Reference and Test Article

In this section, you will upload raw data pertaining to the reference and test articles, including but not limited to the

following:

- **COAs/Potency (data that was not already uploaded in section 4.3)**
- **shipping and receiving records**
- **excursions or deviations for storage conditions**
- **accountability records (including storage check-in, dispensing, and disposal records)**

<Enable next item for Blood Level BE submissions only>

4.8.2 Environment: animal housing, feed, water (Blood Level BE Studies)

In this section, you will upload raw data pertaining to animal housing, maintenance (non-medicated) feed and water, including but not limited to the following:

- **housing diagram**
- **significant excursions or deviations to the animal housing environment (temperature, relative humidity, ventilation, lighting) that are expected to have impacted the study**
- **animal feeding records**
- **records documenting availability of water to animals**
- **feed label (for commercial feeds)**
- **food analysis**
- **water analysis**

<Enable next item for Clinical Endpoint or Pharmacological Endpoint submissions only>

4.8.2 Environment: animal housing, feed, water

In this section, you will upload raw data pertaining to animal housing, maintenance (non-medicated) feed and water, including but not limited to the following:

- **housing diagram**
- **animal housing environment records (temperature, relative humidity, ventilation, lighting)**
- **housing cleaning and sanitation records**
- **animal feeding records**
- **records documenting availability of water to animals**
- **feed label (for commercial feeds)**
- **food analysis**
- **water analysis**

<Enable next item for Blood Level BE submissions only>

4.8.3 Baseline Data (Blood Level BE Studies)

In this section, you will upload raw baseline data, including but not limited to the following:

- **body weight measurement forms**
- **physical examination forms**
- **blood sampling (for CBC and serum chemistry) forms**
- **CBC raw data results**
- **serum biochemistry raw data results**

<Enable next item for Clinical Endpoint or Pharmacological Endpoint only>

4.8.3 Baseline Data

In this section, you will upload raw baseline data, including but not limited to the following:

- **body weight measurement forms**
- **scale calibration forms**
- **physical examination forms**
- **blood sampling (for CBC and serum chemistry) forms**
- **CBC raw data results**
- **serum biochemistry raw data results**

4.8.4 Inclusion/Exclusion

In this section, you will upload raw data associated with inclusion/exclusion of animals and animal enrollment.

4.8.5 Administration/Dosing

In this section, you will upload raw data associated with reference and test article administration, including but not limited to the following:

- **dosing records**
- **post-dose vomit check records (if applicable)**
- **dosing failure documentation (if applicable)**

<Enable next item for Blood Level BE submissions only>

4.8.6 Sampling

In this section, you will upload raw data associated with pharmacokinetic sampling, including but not limited to the following:

- **sample collection forms**
- **sample processing records**
- **sample storage records**
- **sample inventory records**
- **records of shipment of samples to bioanalytical laboratory (including excursions or deviations related to the temperature logger record and documentation of any associated email correspondences)**

<Enable next item for Clinical Endpoint or Pharmacological Endpoint only>

4.8.6 Bioequivalence Endpoint Data

In this section, you will upload raw data associated with bioequivalence endpoints.

4.8.7 Clinical Observations and Adverse Events

In this section, you will upload raw data associated with clinical observations and adverse events, including but not limited to the following:

- **daily clinical observation forms**
- **post-dosing clinical observation forms**
- **adverse event documentation forms**
- **forms documenting follow-up clinical evaluation or**

treatment of animals

- **removal of enrolled animals**
- **concurrent medications, medical treatment or vaccinations, including but not limited to the following:**
 - **documentation of treatment administration**
 - **for medications, include medication name, lot/batch number, expiration date, dose, frequency, and route of administration**

4.8.8 Euthanasia and Necropsy

In this section, if applicable you will upload raw data associated with necropsies performed following unanticipated animal deaths, including but not limited to the following:

- **euthanasia records**
- **records of necropsy procedure including name(s) of individual(s) that performed necropsy**
- **reports of gross necropsy findings**
- **tissue sample storage and shipment records (if applicable)**
- **histopathology records and records from any additional tests performed on samples (if applicable)**

4.8.9 Statistical Methods and Bioequivalence Analysis

In this section, you will upload data files associated with the statistical methods and bioequivalence analysis, including but not limited to the following:

- **individual animal time/concentration data (This item applies to blood level bioequivalence studies. For other study types, upload the relevant individual animal data used for bioequivalence analysis.)**
- **randomization records for sequence assignment (XML format)**
- **if applicable, other randomization records (XML or PDF format)**

4.8.10 Other Data Files

In this section, if applicable, you may upload additional *in vivo* raw data or records not already uploaded in one of the other categories above.

As stated in Section 4.1, you may also upload bioanalytical phase raw data or records that are not already included in your FSR.

Sponsor Organized Files

If you elect to proceed with uploading data using your preferred method of organization, the data should be logically organized, complete, and consistent to avoid CVM refusing to review the submission. For each data file (or set of related data files) you attach below, provide a brief categorical description of the contents.

The raw data files associated with this study can be attached

using multiple items within this tabular screen. This allows you to logically group raw data files, such as by the EDC system used to collect the data (if applicable), or by the type of data collected.

Enter a brief description to help identify the contents of the raw data file items added for this study.

<For Dissolution Study submissions de-activate 4.9>

4.9 Program Files

See **GFI #197** for information related to program files.

<Enable following item if NOT Blood Level BE Study submission.>

Upload program files related to statistical methods and bioequivalence analysis (.xml). You have the option to submit a single or multiple eXtensible Markup Language (.xml) files.

<Enable remainder of node if Blood Level BE Study submission.>

Upload program files related to statistical methods and bioequivalence analysis (.xml), including but not limited to the following:

- **Calculation of AUC, C_{MAX}, T_{MAX}, etc.**
 - **Transformations**
 - **Analysis of endpoints**
 - **Calculation of bioequivalence bounds**
- You have the option to submit a single or multiple eXtensible Markup Language (.xml) files.**

4.10 Contributing Scientist Reports

Do you have any contributing scientist reports associated with this study?

- YES
 - <If "YES">
 - **Were any contributing scientist reports included in the FSR?**
 - YES
 - <If "YES"> **Provide the location(s) of the contributing scientist report(s) in the FSR. HINT: Include page numbers and section title as it appears in the table of contents.**
<Click here to enter text. 250 characters>
 - NO
 - **Do you have any contributing scientist reports (that were not included in the FSR) to upload now?**
 - YES
 - <If "YES"> **Upload contributing scientist reports.**
 - NO
- NO

4.11 Other Study Related Information

Upload other study related information supporting bioequivalence (e.g., CVM letter granting biowaiver, study

files, etc.) files for this study.

5.0 COMMENTS

If you have additional comments that you would like to include in this submission, enter below or attach a single PDF that contains the information.