## Table 1 Submission Summary*

| | |
|---|---|
| **Drug Product Name** | |
| **Strength(s)** | |
| **Applicant Name** | |
| **Address** | |
| **Point of Contact**<br>**Name**<br>**Address**<br>**Telephone Number**<br>**Fax Number** | |

Or, please provide an electronic copy of Form 356H.

* This information is needed for a complete Bioequivalence review and, although required for the archival copy submitted to the Agency, it is frequently not readily available in the Bioequivalence Submission. The Division of Bioequivalence prefers that this information be submitted as a electronic Form 356H. If this is not possible, then please complete Table 1.

**Table 2 Summary of Bioavailability Studies**

| Study Ref. No. | Study Objective | Study Design | Treatments (Dose, Dosage Form, Route) [Product ID] | Subjects (No. (M/F) Type Age: mean (Range) | Mean Parameters (+/-SD) | | | | | | Study Report Location |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Cmax (units/mL) | Tmax (hr) | AUC0-t (units) | AUC∞ (units) | T1/2 (hr) | Kel (hr-1) | |
| Study # | Fasting study title | Randomized single-dose crossover | Test product strength Tab./Cap./Susp p.o. [Batch #]<br><br>Ref. product strength Tab./Cap./Susp p.o. [Batch #] | # completing (#M/#F) Healthy subjects or patients mean age (range) | M (%CV)<br><br>M (%CV) | Median (Range)<br><br>Median (Range) | M (%CV)<br><br>M (%CV) | M (%CV)<br><br>M (%CV) | M (%CV)<br><br>M (%CV) | M (%CV)<br><br>M (%CV) | Vol.# p.# |
| Study # | Fed study title | Randomized single-dose crossover | Test product strength Tab./Cap./Susp p.o. [Batch #]<br><br>Ref. product strength Tab./Cap./Susp p.o. [Batch #] | # completing (#M/#F) Healthy subjects or patients mean age (range) | M (%CV)<br><br>M (%CV) | Median (Range)<br><br>Median (Range) | M (%CV)<br><br>M (%CV) | M (%CV)<br><br>M (%CV) | M (%CV)<br><br>M (%CV) | M (%CV)<br><br>M (%CV) | Vol.# p.# |

**Table 3A Statistical Summary of the Comparative Bioavailability Data for Unscaled Average BE Studies**

| Reference Scaled Average Bioequivalence Approach Used | ☐ Yes | ☐ No | | | | |
|---|---|---|---|---|---|---|
| If No, then complete Table 3A only | | | | | | |
| If Yes, then complete Tables 3A and 3B | | | | | | |
| Drug (No of subjects completed= )<br>Dose (# x mg)<br>Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals | | | | | | |
| Fasting Bioequivalence Study (Study No.) | | | | | | |
| **Parameter** | **Test** | **N** | **RLD** | **N** | **Ratio** | **90% C.I.** |
| AUC0-t | | | | | | |
| AUC∞ | | | | | | |
| Cmax | | | | | | |
| | | | | | | |
| Drug (No of subjects completed= )<br>Dose (# x mg)<br>Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals | | | | | | |
| Fed Bioequivalence Study (Study No.) | | | | | | |
| **Parameter** | **Test** | **N** | **RLD** | **N** | **Ratio** | **90% C.I.** |
| AUC0-t | | | | | | |
| AUC∞ | | | | | | |
| Cmax | | | | | | |

**Table 3B Statistical Summary of the Comparative Bioavailability Data for Reference-Scaled Average BE Studies**

| Parameter | T/R Ratio | Lower 90% CI | Upper 90% CI | s2wr | sWR | Criteria Bound | Method Used | Outcome |
|---|---|---|---|---|---|---|---|---|
| LAUCT | | | | | | | | |
| LAUCI | | | | | | | | |
| LCMAX | | | | | | | | |

## Table 4 Bioanalytical Method Validation

| Information Requested | Data |
|---|---|
| **Bioanalytical method validation report location** | Provide the volume(s) and page(s) |
| **Analyte** | Provide the name(s) of the analyte(s) |
| **Internal standard (IS)** | Identify the internal standard used |
| **Method description** | Brief description of extraction method; analytical method |
| **Limit of quantitation** | LOQ, units |
| **Average recovery of drug (%)** | % |
| **Average recovery of IS (%)** | % |
| **Standard curve concentrations (units/mL)** | Standard curve range and appropriate concentration units |
| **QC concentrations (units/mL)** | List all the concentrations used |
| **QC Intraday precision range (%)** | Range or per QC |
| **QC Intraday accuracy range (%)** | Range or per QC |
| **QC Interday precision range (%)** | Range or per QC |
| **QC Interday accuracy range (%)** | Range or per QC |
| **Bench-top stability (hrs)** | hours @ room temperature |
| **Stock stability (days)** | days @ 4°C |
| **Processed stability (hrs)** | hours @ room temperature; hours @ 4°C |
| **Freeze-thaw stability (cycles)** | # cycles |
| **Long-term storage stability (days)** | 17 days @ -20°C (or other) |
| **Dilution integrity** | Concentration diluted X-fold |
| **Selectivity** | No interfering peaks noted in blank plasma samples |

Please include table for each analyte.
Please submit all Method Validation SOPs.

## Table 5 Summary of In Vitro Dissolution Studies

| | | |
|---|---|---|
| **Dissolution Conditions** | **Apparatus:** | |
| | **Speed of Rotation:** | |
| | **Medium:** | |
| | **Volume:** | |
| | **Temperature:** | |
| **Firm's Proposed Specifications** | | |
| **Dissolution Testing Site (Name, Address)** | | |

| **Study Ref No.** | **Testing Date** | **Product ID \ Batch No. (Test - Manufacture Date) (Reference – Expiration Date)** | **Dosage Strength & Form** | **No. of Dosage Units** | | **Collection Times (minutes or hours)** | | | | | **Study Report Location** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | |
| Study Report #: | | Test Product | mg Tablet Capsule | 12 | Mean | | | | | | |
| | | | | | Range | | | | | | |
| | | | | | % CV | | | | | | |
| Study Report #: | | Reference Product | mg Tablet Capsule | 12 | Mean | | | | | | |
| | | | | | Range | | | | | | |
| | | | | | % CV | | | | | | |

Provide dissolution data for all strengths (test and reference).

**Table 6 Formulation Data**

| Ingredient | Amount (mg) / Tablet | | Amount (%) / Tablet | |
|---|---|---|---|---|
| | Strength 1 | Strength 2 | Strength 1 | Strength 2 |
| **Cores** | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| **Coating** | | | | |
| | | | | |
| | | | | |
| **Total** | | | **100.00** | **100.0** |

Please include the formulation of all strengths.

**Table 7 Demographic Profile of Subjects Completing the Bioequivalence Study**

| Study No. | | | |
|---|---|---|---|
| | | Treatment Groups | |
| | | Test Product N= | Reference Product N = |
| Age (years) | Mean ± SD | 50 ± 15 | |
| | Range | 21 - 64 | |
| Age Groups | < 18 | N (%) | N (%) |
| | 18 – 40 | N (%) | N (%) |
| | 41 – 64 | N (%) | N (%) |
| | 65 – 75 | N (%) | N (%) |
| | > 75 | N (%) | N (%) |
| Sex | Male | N (%) | N (%) |
| | Female | N (%) | N (%) |
| Race | Asian | N (%) | N (%) |
| | Black | N (%) | N (%) |
| | Caucasian | N (%) | N (%) |
| | Hispanic | N (%) | N (%) |
| | Other | N (%) | N (%) |
| BMI | Mean ± SD | | |
| | Range | | |
| Other Factors | | | |

Please provide a separate table for each Bioequivalence Study

## Table 8 Incidence of Adverse Events in Individual Studies

| Body System / Adverse Event | Reported Incidence by Treatment Groups | |
|---|---|---|
| | Fasted/Fed Bioequivalence Study Study No. | |
| | Test | Reference |
| Body as a whole | | |
| Dizziness | N (%) | N (%) |
| Etc. | N (%) | N (%) |
| Cardiovascular | | |
| Hypotension | | |
| Etc. | | |
| Gastrointestinal | | |
| Constipation | | |
| Etc. | | |
| Other organ sys. | | |
| | | |
| | | |
| Total | N (%) | N (%) |

Provide separate table for each Bioequivalence Study

## Table 9 Reanalysis of Study Samples

| Study No.<br>Additional information in Volume(s), Page(s) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Reason why assay was repeated** | **Number of samples reanalyzed** | | | | **Number of recalculated values used after reanalysis** | | | |
| | **Actual number** | | **% of total assays** | | **Actual number** | | **% of total assays** | |
| | **T** | **R** | **T** | **R** | **T** | **R** | **T** | **R** |
| Pharmacokinetic[1] | | | | | | | | |
| Reason A (e.g. below LOQ) | | | | | | | | |
| Reason B | | | | | | | | |
| Reason C | | | | | | | | |
| Etc. | | | | | | | | |
| Total | | | | | | | | |

1 - If no repeats were performed for pharmacokinetic reasons, insert "0.0."
Please provide a separate table for each analyte measured for each in-vivo study.

## Table 10 Study Information

| | | | | |
|---|---|---|---|---|
| **Study Number** | | | | |
| **Study Title** | | | | |
| **Study Type** | ☐ In Vivo BE | ☐ In Vitro BE | ☐ Permeability | ☐ Other |
| **Submission Location:** **Study Report** | location, ex: 5.3.1.2 | | | |
| **Validation Report** | location, ex: 5.3.1.2 | | | |
| **Bioanalytical Report** | location, ex: 5.3.1.4 | | | |
| **Clinical Site (Name, Address, Phone #, Fax #)** | | | | |
| **Principal Clinical Investigator (Name, Email)** | | | | |
| **Dosing Dates** | | | | |
| **Analytical Site (Name, Address, Phone #, Fax #)** | | | | |
| **Analysis Dates** | | | | |
| **Principal Analytical Investigator (Name, Email)** | | | | |
| **Sample Storage :** **(a) Duration (no. of days from the first day of sample collection to the last day of sample analysis)** **(b) Temperature Range (e.g., -20° C to -80° C)** | | | | |
| **Long-Term Storage Stability (LTSS) Coverage (no. days @ temp °C)** | Analyte 1:<br>Analyte 2: (If applicable)<br>**Note: The LTSS should be conducted @ the upper limit of the storage temperature range** | | | |
| **LTSS Data Location** | **Specify the exact location of the LTSS study reports and data, including Module, Section, Subsection, and page(s). Provide hyperlink(s) to the locations as appropriate.** | | | |

Please provide separate table for each Bioequivalence Study

**Table 11 Product Information**

| Product | Test | Reference |
|---|---|---|
| **Treatment ID** | | |
| **Product Name** | | |
| **Manufacturer** | | |
| **Batch/Lot No.** | | |
| **Manufacture Date** | | N/A |
| **Expiration Date** | N/A | |
| **Strength** | | |
| **Dosage Form** | | |
| **Bio-batch Size** | | N/A |
| **Production Batch Size** | | N/A |
| **Potency** | | |
| **Content Uniformity (mean, %CV)** | | N/A |
| **Dose Administered** | | |
| **Route of Administration** | | |

## Table 12 Dropout Information

| Study No. | | | | |
|---|---|---|---|---|
| **Subject No** | **Reason for dropout/replacement*** | **Period** | **Replaced?** | **Replaced with** |
| | | | | |
| | | | | |
| | | | | |

Please provide separate table for each Bioequivalence Study

* Please provide time, treatment (test or reference), and cause of dropout, if reason of dropout is other than "personal reasons".

## Table 13 Protocol Deviations

| Study No. 073-11 | | |
|---|---|---|
| **Type** | **Subject #s (Test)** | **Subject #s (Ref.)** |
| | | |
| | | |
| | | |

Please provide a separate table for each Bioequivalence Study

**Table 14 Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses***

| Bioequivalence Study No.<br>Analyte Name | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **Standard Curve Samples** | | | | | | |
| Concentration (ng, mcg/mL) | | | | | | | |
| Inter day Precision (%CV) | | | | | | | |
| Inter day Accuracy (%Actual) | | | | | | | |
| Linearity | (Range of $R^2$ values) | | | | | | |
| Linearity Range (ng, mcg/mL) | | | | | | | |
| Sensitivity/LOQ (ng, mcg/mL) | | | | | | | |

| Bioequivalence Study No.<br>Analyte Name | | | | |
|---|---|---|---|---|
| **Parameter** | **Quality Control Samples** | | | |
| Concentration (ng, mcg/mL) | | | | |
| Inter day Precision (%CV) | | | | |
| Inter day Accuracy (%Actual) | | | | |

* If applicable, please provide separate tables for the parent drug and metabolite(s)

## Table 15 SOP's Dealing with Bioanalytical Repeats of Study Samples*

| SOP No. | Effective Date of SOP | SOP Title |
|---|---|---|
| | | |

* Please include the SOP for Bioanalytical Repeats in your submission.

**Table 16 Composition of Non-Standard Breakfast Meal Used in Fed Bioequivalence Study**

| **Standard FDA Meal* Used?** | ☐ **Yes** ☐ **No** | | | | |
|---|---|---|---|---|---|
| **If No, then meal components and composition is listed in the tables below** | | | | | |
| **Composition of Non-standard FDA Meal Used in Fed Bioequivalence Study** | | | | | |
| **Ingredients** | **Amount (g)** | **Energy (kcal)** | **Protein (kcal)** | **Fat (kcal)** | **Carbohydrate (kcal)** |
| | | | | | |
| | | | | | |
| | | | | | |
| **TOTAL** | | | | | |
| **PERCENTAGE** | | | | | |

* If the standard meal referenced in the CDER Guidance for Industry Food-Effect Bioavailability and Fed Bioequivalence Studies is used, then it is not necessary to complete the table. In that case, please add a statement in the fed bioequivalence study report indicated that the "FDA standard meal" was used. If an alternative meal is used, then please complete the above summary table.

## Table 17 Comparative Physicochemical Data of Ophthalmic Solution Drug Products

| **Is the Product an Ophthalmic Solution** | ☐ **Yes** ☐ **No** | | | | | |
|---|---|---|---|---|---|---|
| **If Yes, then complete the table below** | | | | | | |
| **Physico Chemical Properties** | **Results** | | | | | |
| | **Test** | | | **Reference** | | |
| | **(Exhibit) Lot #** | **Lot #** | **Lot #** | **Lot #** | **Lot #** | **Lot #** |
| pH | | | | | | |
| Viscosity | | | | | | |
| Specific Gravity | | | | | | |
| Osmolality | | | | | | |
| Buffer Capacity | | | | | | |
| Other Properties as Appropriate | | | | | | |

- Measurements should be made in triplicate.
- Lots other than exhibit test lot should be provided ***only if available***
- The above listed properties are not meant to be inclusive. Depending on the drug products under review, comparative physicochemical data for additional properties may be requested at the time of review. However, each ANDA should include ***at least*** the data for ***5 properties listed*** above.

**SAS Transport Formatted Tables for Submission of Data from In-Vivo Pharmacokinetic (PK) Bioequivalence Studies**

**Plasma Concentration Data** (Please see the definitions of variables on the next pages)

| SUB | SEQ | PER | GRP | TRT | C1 | C2 … | Cn | T1 | T2… | Tn | KE_FIRST | KE_LAST |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | |
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**PK Parameter Data** (Please see the definitions of the variables on the next pages)

| SUB | SEQ | PER | GRP | TRT | Tmax | Cmax | AUCt | AUCi | Ke | Thalf |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | |
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**Definition Table for SAS Transport Dataset of Individual Plasma Concentration Data**

| Variable Name | Variable Label | Type | Notes |
|---|---|---|---|
| SUB | Subject Identification Number | Char/Num | Unique subject identifier |
| PER | Period | Numeric | Period identifier |
| SEQ | Sequence | Numeric | Sequence identifier (1=RT; 2=TR) |
| TRT | Treatment | Numeric | Treatment group (1=Test; 2=Reference) |
| GRP | Group Identification Number | Numeric | Dosing group identifier if subjects are dosed in more than one group |
| C1 | Concentration Time 1 | Numeric | Concentration at the first time point |
| C2 | Concentration Time 2 | Numeric | Concentration at the second time point |
| Cn | Concentration Time n | Numeric | Concentration at the nth time point |
| T1 | Time Point 1 | Numeric | First Actual Sampling Time (e.g., 0 hour) |
| T2 | Time Point 2 | Numeric | Second Actual Sampling Time (e.g., 0.25 hour) |
| Tn | Nth Time Point | Numeric | Nth Actual Sampling Time (e.g., 120 hours) |
| KE_FIRST | First time point for KE calculation | Numeric | First time point of the elimination segment (of the concentration-time curve) selected for calculating KE* |
| KE_LAST | Last time point for KE calculation | Numeric | Last time point of the elimination segment (of the concentration-time curve selected for calculating KE* |

*NOTE: KE_FIRST and KE_LAST should be given as the sequential numbers of the time points, and NOT the time values themselves. For example:

KE_FIRST = 10 which means the $10^{th}$ time point, not "10 hours"

KE_LAST = 24 which means the $24^{th}$ time point, not "24 hours"

**Definition Table for SAS Transport Dataset of Individual PK Parameter Data**

| Variable Name | Variable Label | Type | Notes |
|---|---|---|---|
| SUB | Subject Identification Number | Char/Num | Unique subject identifier |
| PER | Period | Numeric | Period identifier |
| SEQ | Sequence | Numeric | Sequence identifier (1=RT; 2=TR) |
| TRT | Treatment | Numeric | Treatment group (1=Test; 2=Reference) |
| GRP | Group Identification Number | Numeric | Dosing group identifier if subjects are dosed in more than one group |
| AUCT | Area Under the Curve from zero hour (0) to the last sampling time (t) | Numeric | Area under the curve from time 0 to t |
| AUCI | Area Under the Curve from zero hour (0) to infinity | Numeric | Area under the curve from time 0 to infinity |
| CMAX | Cmax | Numeric | Maximum concentration |
| TMAX | Tmax | Numeric | Time at maximum concentration |
| THALF | Half-life | Numeric | Half-life calculated from the terminal phase of the elimination |
| KE | Ke | Numeric | Elimination rate constant |