Model Bioequivalence Data

Summary Tables

Technical Specifications Document

For questions regarding this technical specifications document,

contact the Office of Generic Drugs at genericdrugs@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Generic Drugs

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Revision History

Date	Version	Summary of Revisions
2007	1.0	Initial Version
2011	2.0	Minor revisions
2014	3.0	Minor revisions
2017	4.0	Minor revisions to accommodate compliance with the requirement to submit standardized study data including deletion of definition tables (see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292334.pdf)

These summary tables provide a standard format for data to be submitted to the Office of Generic Drugs in accordance with current recommendations. Please note that the tables listed in this document only include the bioequivalence summary tables related to the in vivo bioequivalence (BE) tests. Please provide the following tables if they are applicable to the in vivo BE tests for your drug product.

Table 1- Submission Summary[1]

Drug Product Name	
Strength(s)	
Applicant Name	
Address	
Point of Contact **Name** **Address** **Telephone Number** **Fax Number**	

[1] In lieu of completing Table 1, applicants may provide an electronic copy of Form FDA 356h. The information identified in this table 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 Office of Generic Drugs prefers that this information be submitted as an electronic Form FDA 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 #] Ref. product strength Tab./Cap./Susp p.o. [Batch #]	# completing (#M/#F) Healthy subjects or patients mean age (range)	M (%CV) M (%CV)	Median (Range) Median (Range)	M (%CV) M (%CV)	M (%CV) M (%CV)	M (%CV) M (%CV)	M (%CV) M (%CV)	Vol.# p.#
Study #	Fed study title	Randomized single-dose crossover	Test product strength Tab./Cap./Susp p.o. [Batch #] Ref. product strength Tab./Cap./Susp p.o. [Batch #]	# completing (#M/#F) Healthy subjects or patients mean age (range)	M (%CV) M (%CV)	Median (Range) Median (Range)	M (%CV) M (%CV)	M (%CV) M (%CV)	M (%CV) M (%CV)	M (%CV) 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=) Dose (# x mg) 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=) Dose (# x mg) 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[2]

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

[2] Include a table for each analyte and submit all method validation standard operating procedures (SOPs).

Table 5 Summary of In Vitro Dissolution Studies[3]

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						

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

Table 6 Formulation Data[4]

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

[4] Include the formulation of all strengths.

Table 7 Demographic Profile of Subjects Completing the Bioequivalence Study[5]

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			

[5] Provide a separate table for each bioequivalence study.

Table 8 Incidence of Adverse Events in Individual Studies[6]

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 (%)

[6] Provide a separate table for each bioequivalence study.

Table 9 Reanalysis of Study Samples[7]

Study No. 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[8]								
Reason A (e.g. below LOQ)								
Reason B								
Reason C								
Etc.								
Total								

[7] Provide a separate table for each analyte measured for each in vivo study.
[8] If no repeats were performed for pharmacokinetic reasons, insert "0.0."

Table 10 Study Information[9]

Study Number				
Study Title				
Study Type	☐ In Vivo BE	☐ In Vitro BE	☐ Permeability	☐ Other
Submission Location: **Study Report** **Validation Report** **Bioanalytical Report**	location, ex: 5.3.1.2 location, ex: 5.3.1.2 location, ex: 5.3.1.4			
Clinical Site **(Name, Address, Phone #, Fax#)**				
Principal Clinical Investigator **(Name, Email)**				
Analytical Site **(Name, Address, Phone #, Fax#)**				
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: Analyte 2: (if applicable) Note: The LTSS should be conducted at 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.			

[9] Provide a 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[10]

Study No.				
Subject No	**Reason for dropout/replacement[11]**	**Period**	**Replaced?**	**Replaced with**

[10] Provide separate tables for each bioequivalence study

[11] Provide time, treatment (test or reference), and cause of dropout, if reason is other than "personal reasons."

Table 13 Protocol Deviations[12]

Study No.		
Type	**Subject #s (Test)**	**Subject #s (Ref.)**

[12] Provide a separate table for each bioequivalence study.

Table 14 Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses[13]

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

[13] If applicable, provide separate tables for the parent drug and metabolite.

Table 15 SOPs dealing with Bioanalytical Repeats of Study Samples[14]

SOP No.	Effective Date of SOP	SOP Title

[14] 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?[15]	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					

[15] If the standard meal referenced in the 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 state in the fed bioequivalence study report that the FDA standard meal was used. If an alternative meal is used, please complete the summary table.

Table 17 Comparative Physiochemical Data of Ophthalmic Solution Drug Products[16]

Is the Product an Ophthalmic	**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						

[16] Please note the following when completing this table: 1) measurements should be made in triplicate; 2) lots other than exhibit test lot should be provided only if available; and 3) the properties listed in the table are not meant to be inclusive as comparative physiochemical data for additional properties may be requested at time of review. Each ANDA should include at least the data for 5 properties listed in this table.

Submission of Data from In-Vivo Pharmacokinetic (PK) Bioequivalence Studies

Please refer to Clinical Interchange Standards Consortium (CDISC) - Study Data Tabulation Model Implementation Guide (SDTMIG) located on CDISC website (https://www.cdisc.org/standards/foundational/sdtmig) for submitting electronic datasets including Plasma Concentration Data (Please see PC domain) and PK Parameter Data (Please see PP domain) and other applicable data domains for ANDA submissions.

For the most recent versions of FDA's study data guidance and technical specifications, check FDA's Study Data Standards Resources page at http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/default.htm. This page includes: FDA's December 2014 final guidance on study data standards, Providing Regulatory Submissions in Electronic Format—Standardized Study Data and relevant technical specifications: FDA Data Standards Catalog and the Study Data Technical Conformance Guide.