BCS-BASED STUDY SUMMARY AND FORMULATION TABLES

Table 1. Method Validation for Solubility Testing

Information Requested	Analyte 1
Bioanalytical Method Validation Report Location	
Study Report Number	
Analyte	
Internal Standard (IS) (if applicable)	
Method Description	
Limit of Quantitation	
% Recovery (and %CV) at Each Concentration Tested (if applicable)	
Average Recovery of IS (%) (if applicable)	
Standard Curve Concentrations (units/mL)	
QC Concentrations (units/mL)	
QC Precision Range (%)	
QC Accuracy Range (%)	
Stability (hrs/temperature) (if applicable)	
Dilution Integrity (if applicable)	
Selectivity	
Stability Indicating for the Testing Period? Y/N	

Table 2. Solubility Data for (Drug Name) in Different Buffered Media at (pH range)

Buffer	Volume	Mean Drug Solubility	Initial Drug Concentration Used for Solubility	pH After Addition of Drug Substance	pH at End of Study	Time of Sampling	Number of Replicates (n=)	%RSD

Table 3. Standard Operating Procedures*

SOP No.	Effective Date of SOP	SOP Title

*For all tests and their method validation studies conducted to support the current BCS-based waiver request (e.g., permeability, solubility, dissolution, gastric stability tests, etc.)

Table 4. Permeability Study Method Validation Information

Description	
Reagents & Materials	
Testing Site (Method Validation Facility)	
Analytical Site	
Cell Culture Plates Type, Filter Type, and Well Format	
Cell Culture (e.g. Cell source, Feeding Schedule, Monolayer Age)	
Permeability Assay Buffer (e.g. Composition, pH)	
Quality Control of Cell Monolayers (e.g. TEER, Zero Permeability Marker) and Acceptance Criteria	
Description of Permeability Assay	
Analytical Methods for Test Compounds	
Permeability and Recovery Calculation	

Table 5. Permeability Study Validation Summary Data: Permeability Coefficients, % Recovery for Model Compounds

Model Compound	Receiver Sampling Time Points (minutes)	Donor Sample Time Points (if different)	Conc (μM)	Papp (10^{-6} cm/s)	% RSD	% Recovery	R^2	Permeability Class	Reference For Human Fraction Absorbed

Include high ($f_a \geq 85\%$), moderate (f_a = 50-84%), and low (f_a <50%) permeability model compounds (a minimum of 5 for each), plus a zero permeability marker.

Table 6. Analytical Method Validation (For Pivotal Permeability Study)

	Test Compound	High Permeability Standard	Moderate Permeability Standard
Name of the Analyte/Internal Standard			
Analytical Method Description			
Analytical Method Validation Report Location			
Standard Curve Range			
Limit of quantitation			
Average Recovery of Drug from Top Chamber (%)			
Average Recovery of Drug from Bottom Chamber (%)			
Average Recovery of IS from Top Chamber (%)			
Average Recovery of IS from Bottom Chamber			
QC Concentrations (units/mL)			
QC Intraday Precision Range (%)			
QC Intraday Accuracy Range (%)			
QC Interday Precision Range (%)			
QC Interday Accuracy Range (%)			
Bench-top Stability (hrs)			
Stock (Refrigerator) stability (hrs)			
Processed (Autosampler) stability (hrs)			
***Freeze-thaw Stability (cycles)**			
***Long-term Storage Stability (days)**			
Dilution Integrity			
Specificity			
Method Validation SOP Location			

* If applicable

Table 7. Pivotal Permeability Study Information

Study Information	
Study Number	
Method (i.e. in vivo mass balance/absolute BA/Caco-2 permeability)	
Rationale for Method Selection	
Study Title	
Study Objective	
Testing Site (Permeability Facility)	
Analytical Site	
Study/Analysis Dates	
Storage Period (no. of days from the first day of sample collection to the last day of sample analysis)	
Testing Conditions	
Permeability Assay Description and Sampling Time Points	
Sample Analysis	
Internal Control Compounds	
Permeability Buffer (e.g. Composition, pH) of donor and receiver compartments	
Reagents & Materials	
Cell Culture Plates Type, Filter Type, Well Format	
Cell Culture (e.g. Cell Source, Feeding Schedule, Monolayer Age)	
Quality Control of Cell Monolayers (e.g. TEER, Zero Permeability Marker) and Acceptance Criteria	
Internal Standards and Model Efflux Drug Acceptance Criteria for Papp	
Dosing Solutions	
# of Replicates	
Permeability and Recovery Calculation	

Table 8. Pivotal Permeability Study: Apical-to-Basolateral (A-to-B) Permeability of Test Compound and Internal Standards

Drug	Parameter	Nominal Dosing Concentration (units)		
		Conc. 1	Conc. 2	Conc. 3
Test Compound	Papp (mean ± SD)			
	Recovery (%)			
High Internal Standard	Papp (mean ± SD)			
	Recovery (%)			
Moderate Internal Standard	Papp (mean ± SD)			
	Recovery (%)			

Units of Papp are 10^{-6} cm/s; e.g., "1.0" represents a value of 1.0×10^{-6} cm/s.

Table 9. Pivotal Permeability Study: Basolateral-to-Apical (B-to-A) Permeability of Test Compound and Internal Standards

Drug	Parameter	Nominal Dosing Concentration (units)		
		Conc. 1	Conc. 2	Conc. 3
Test Compound	Papp (mean ± SD)			
	Recovery (%)			
High Internal Standard	Papp (mean ± SD)			
	Recovery (%)			
Moderate Internal Standard	Papp (mean ± SD)			
	Recovery (%)			

Table 10. Pivotal Permeability Study: Ratio of B-to-A Papp vs. A-to-B Papp

Drug	Papp (mean ± SD)	Nominal Dosing Concentration (units)		
		Conc 1	Conc 2	Conc 3
Test Compound	A-to-B			
	B-to-A			
	Efflux Ratio (B-to-A)/(A-to-B)			
High Internal Standard	A-to-B			
	B-to-A			
	Efflux Ratio (B-to-A)/(A-to-B)			
Moderate Internal Standard	A-to-B			
	B-to-A			
	Efflux Ratio (B-to-A)/(A-to-B)			

Table 11. Drug Substance Stability in the Gastrointestinal Tract (if applicable)

File Location:					
Medium	Time of Incubation	Incubation Temperature	Concentration		% Degradation
			Before Incubation	After Incubation	
Gastric Fluid or Simulated Gastric Fluid					
Intestinal Fluid/ Simulated Intestinal Fluid					
File Location of SOP					

Table 12. Dissolution Method Information (For BCS Classification)

Lot Nos. of Test Product & Manufacture Date (each strength)	
Lot Nos. of Reference Product & Expiration Date (each strength)	
Medium 1	
Medium 2	
Medium 3	
Volume (mL) (≤900 mL, 37°C)	
USP Apparatus Type	
Rotation (rpm)	

Table 13. Information of Analytical Method Used to Analyze Dissolution Samples

HPLC Parameters (if applicable)	
Mobile Phase:	
Column:	
Flow Rate:	
Wavelength:	
Injection Volume:	
Column Temperature	
Run Time:	

UV Parameters (if applicable)	
Wavelength:	
Cell Path Length	

Analytical Method Validation Report # and Date	
Submission of SOP for Method Validation (Yes/No, Effective Date)	
Address of Method Validation Site	
Address of Dissolution Testing Site	
Submission of Dissolution Method Transfer Report (if the dissolution testing site is different from the method validation site) (Yes/No, Location of the Report)	
Sample Processing	
Analyte	
Method Description	
Specificity/Placebo Interference	
Linearity and Range (unit)	
Accuracy/Recovery	
Precision	
Repeatability (% RSD)	
Intermediate Precision (% RSD)	
Samples Filtered During Collection?	☐ Yes ☐ No
Filter Equivalency (% difference)	
Robustness	
Standard and Sample Solution Stability	

Table 14. Dissolution Data**

Dissolution Conditions	**Apparatus:**	
	Sinker:	☐ Yes ☐ No
	Speed of Rotation:	
	Medium:	
	Volume:	
	Temperature:	
Applicant'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**					**Study Report Location**
						min	**min**	**min**	**min**	**min**	
Study Report #:		Test Product	mg Tablet Capsule	12 (individual units tested only)	Mean						
					Range						
					%CV						
Study Report #:		Reference Product	mg Tablet Capsule	12	Mean						
					Range						
					%CV						

*Testing using pooled samples is not accepted.

**Comparative dissolution data should be provided for the regulatory dissolution method as well as for multi-pH dissolution testing.

Table 15. Formulation

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

Table 16. Core Excipient Data (for BCS Class III biowaiver, if applicable)

Core Ingredient	Function	Amount (mg)/Tablet		Proportion Relative to Core Weight (% w/w)	
		Strength 1	Strength 2	Strength 1	Strength 2
Total Core Weight					