BIOEQUIVALENCE SUMMARY TABLES FOR METERED DOSE INHALER PRODUCTS

Please note that the tables listed in this document only include the bioequivalence summary tables related to the **in vitro** and **in vivo PD** studies recommended for metered dose inhaler products.

For the bioequivalence summary tables related to the **in vivo PK** BE tests, the applicant should refer to the Bioequivalence Summary Tables published on the Office of Generic Drugs website at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM120957.pdf

For the bioequivalence summary tables related to the **in vivo Clinical Endpoint** BE tests, the applicant should refer to the Bioequivalence Summary Tables published on the Office of Generic Drugs website at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM400548.pdf

Table 1. Formulation Table

INGREDIENTS	TEST		
	Amount per Actuation	Amount per mL	% (w/w)
TOTALS			
NET FILL WEIGHT			

Table 2. Batch Information

TEST								
Study Type	**Lot No.**	**Potency*** **	**Lot Size (# of Canisters)****		**Manufacture Date for Test Expiration Date for Reference**	**API Lot(s)**	**Critical Excipient (e.g. surfactant, co-solvent, etc) Lot (s)**	**Container Closure System (e.g. Valve, Actuator, Canister) lot(s)**
			Theoretical	**Actual**				
Bioequivalence study (PK study) *								
Bioequivalence study (PD study) *								
In-Vitro* equivalence studies *								
REFERENCE								
Bioequivalence study (PK study) *								
Bioequivalence study (PD study) *								
In-Vitro* equivalence studies *								

* If recommended
** Include lot numbers from each *in vitro* test
*** Data obtained from Certificate of Analysis
**** The size of exhibited batches should be at least one-third of the to-be-marketed production batch size

Table 3. Device Comparability

	TEST	REFERENCE
Canister		
Canister Supplier		
Material		
Canister Volume		
Valve		
Valve Supplier		
Metering Volume		
Gasket and Seat Elastomers (material)		
Metering Chamber and Body (material)		
Core and Core Extension/Base		
Actuator		
Actuator Supplier		
Actuator Orifice Diameter (μm)		
Material		
Protection Cap Description		
Dose Counter/Indicator	☐ Yes ☐ No	☐ Yes ☐ No
Number of Doses		
Cleaning instructions (similar cleaning instruction and frequency? *)		

*With alternate device design, the applicant should provide justification and evidence to support that there will be no confusion with respect to cleaning.

Table 4. Actuation Methods

Which tests (if any) used MANUAL actuation?				
If some tests used manual actuation(s), describe methods used to avoid Test to RLD bias in dose release.				
Which tests (if any) used AUTOMATED actuation?				
What were the parameters of automated actuation? (units)*			Test	RLD
	Force Driven System [e.g., MDI AS, Hand Actuation Monitor (HAM), etc.]	**Force (kg or N)**		
		Force Rise Time (msec)		
		Force Fall time (msec)		
		Hold Time (msec)		
		Agitation Shaking (msec)		
	Velocity Driven Actuator [e.g., Vereo Actuator SFMDx, SPRAYTEC with SPRAYER module, etc.]	**Velocity (mm/s)**		
		Acceleration (mm/s^2)		
		Initial Hold Time (msec)		
		Hold Time (msec)		
		Final Delay (msec)		
		Pre-Stage Position		
Are the actuation parameters the same for the test and reference products? If No, please comment	☐ Yes ☐ No			

*Parameters may vary depending on the instrument

The Table 5 Series is for Single Actuation Content through Container Life Test

Table 5. 1. Study Information

Study No.	
Study Site Name and address	
Principal Investigator	
Study Dates	
SOP No.	
SOP Effective Date	
SOP Title	
Test Method Description	
Testing Equipment Used (e.g., name, model, etc.)	
Operating Conditions for Testing Equipment Used (e.g., temperature, humidity, etc.)	
Analytical Method Description	
Analytical Equipment Used (e.g., name, model, etc.)	

Table 5. 2. Analytical Method Validation for HPLC

Information Requested	
Analytical method validation report location	Provide the volume(s) and page(s)
Analyte	Provide the name(s) of the analyte(s)
Internal Standard (IS)	Only if applicable
Method description	Brief descriptions of extraction method; analytical
Selectivity or Specificity	Brief comments
Limit of quantitation	LOQ, unit
Detection Limit	LOD, unit
Linearity Range (ng, mcg/mL)	Range, unit
Linearity (R^2) (e.g., 0.99**)**	
Accuracy (% recovery)	Avg.: HQC: MQC: LQC:
Precision – Repeatability (CV%)	QC
Precision -- Intermediate Precision	By Date: By Analyst:
Bench-top stability (hrs (CV%)) (working std solution) (e.g. 2 days @ room temperature**)**	
Stock solution stability (days (CV %))	Only if applicable
Robustness	Brief comments

Calibration of Manual and/or Automated MDI Actuation (For Single Actuation Content)

Table 5.3. Precision and Ruggedness

	Precision	Ruggedness	
Content assay (µg) (Mean and CV%)		Day 1*:	Day 2*:
		Analyst 1:	Analyst 2:
		Unit 1**:	Unit 2**
Shot weight (mg) (Mean and CV%)		Day 1*:	Day 2*:
		Analyst 1:	Analyst 2:
		Unit 1**:	Unit 2**:
% Difference in Content assay means		Between Day 1 and 2:	
		Between Analyst 1 and 2:	
		Between Unit 1 and 2:	
Content assay (% CV)		Inter day:	
		Inter analyst	
% Difference in shot weight means		Inter unit	
		Between Day 1 and 2:	
		Between Analyst 1 and 2:	
		Between Unit 1 and 2:	
Shot weight (% CV)		Inter day:	
		Inter analyst:	
		Inter unit:	
Acceptance criteria defined by SOP	*Example* Precision: Intermediate Precision by Date: Intermediate Precision by Analyst: Intermediate Precision by Unit: % Difference Day-to-Day: % Difference Analyst-to-Analyst: % Difference Unit-to-Unit:		
Reference Product lot numbers, expiration dates			
Number of units			
Number of sprays/unit			
Automated or manual actuation used	Automated / Manual		

* Ruggedness by day: By same analyst

** Ruggedness by units: If more than 1 unit used in the validation

Table 5. 4. Results Summary – Single Actuation Content

SINGLE ACTUATION CONTENT THROUGH CONTAINER LIFE														
		Spray #	Mean				Variability (%CV)					Mean Ratio (T/R)	
			Drug Mass (mg)		% label claim		Within Lot (n=10)			Between Lot (n=3)	Total (n=30)		
			Arith	Geo	Arith	Geo	Lot 1	Lot 2	Lot 3			Arith (n=30)	Geo (n=30)
BEG	**Test**												
	Ref												
MID	**Test**												
	Ref												
END	**Test**												
	Ref												

Table 5.4.1. Summary of Population Bioequivalence Results

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

The Single Actuation Content comparison of the T and R products is based on the population bioequivalence (PBE). Refer to draft budesonide inhalation suspension BE guidance for additional information regarding PBE analysis procedures.
(http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM319977.pdf).

The Table 6 Series is for Priming & Re-priming Test

Table 6.1. Study Information

Study No.	
Study Site Name and Address	
Principal Investigator	
Study dates	
SOP No.	
SOP Effective Date	
SOP Title	
Test Method Description	
Testing Equipment Used (e.g., name, model, etc)	
Operating Conditions for Testing Equipment Used (e.g., temperature, humidity, etc..)	
Analytical Method Description	
Analytical Equipment Used (e.g., name, model, etc)	

Note: The repriming test should be performed following storage for the specified period of non-use after initial use and/or other conditions (e.g., dropping), if the reference product labeling provides such repriming information.

Table 6. 2. Analytical Method Validation for HPLC

To be completed only if different from Table 5.2

Information Requested	
Analytical method validation report location	Provide the volume(s) and page(s)
Analyte	Provide the name(s) of the analyte(s)
Internal Standard (IS)	Only if applicable
Method description	Brief descriptions of extraction method; analytical
Selectivity or Specificity	Brief comments
Limit of quantitation	LOQ, unit
Detection Limit	LOD, unit
Linearity Range (ng, mcg/mL)	Range, unit
Linearity (R^2) (e.g., 0.99**)**	
Accuracy (% recovery at the high and low concentrations)	Avg.: HQC: MQC: LQC:
Precision – Repeatability (CV%)	QC
Precision -- Intermediate Precision	By Date: By Analyst:
Bench-top stability (hrs (CV%)) (working std solution) (e.g. 2 days @ room temperature**)**	
Stock solution stability (days (CV %))	Only if applicable
Robustness	Brief comments

Table 6.3. Precision and Ruggedness

To be completed only if different from Table 5.3

	Precision	Ruggedness	
Content assay (µg) (Mean and CV%)		Day 1*:	Day 2*:
		Analyst 1:	Analyst 2:
		Unit 1**:	Unit 2**
Shot weight (mg) (Mean and CV%)		Day 1*:	Day 2*:
		Analyst 1:	Analyst 2:
		Unit 1**:	Unit 2**:
%Difference in content assay means		Between Day 1 and 2:	Inter day %CV
		Between Analyst 1 and 2:	Inter analyst %CV
		Between Unit 1 and 2:	Inter unit %CV
%Difference in shot weight means		Between Day 1 and 2:	Inter day %CV
		Between Analyst 1 and 2:	Inter analyst %CV
		Between Unit 1 and 2:	Inter unit %CV
Acceptance criteria defined by SOP	*Example* Precision: Intermediate Precision by Date: Intermediate Precision by Analyst: Intermediate Precision by Unit: % Difference Day-to-Day: % Difference Analyst-to-Analyst: % Difference Unit-to-Unit:		
RLD lot numbers, expiration dates			
Number of units			
Number of sprays/unit			
Automated or manual actuation used	Automated / Manual		

* Ruggedness by day: By same analyst

** Ruggedness by units: If more than 1 unit used in the validation

Table 6. 4. Results Summary – Priming & Re-Priming

PRIMING												
Number of actuations used to **prime** each product =												
Actuation number used for testing each product =												
	Spray #	**Mean**				**Variability (%CV)**					**Mean Ratio (T/R)**	
		Drug Mass (mg)		**% label claim**		Within Lot (n=10)			Between Lot (n=3)	Total (n=30)		
		Arith	Geo	Arith	Geo	Lot 1	Lot 2	Lot 3			Arith (n=30)	Geo (n=30)
Test												
Ref												

RE-PRIMING												
Period of time each product was stored per RLD label following priming =												
Number of actuations used to **re-prime** each product =												
Actuation number used for testing each product =												
	Spray #	**Mean**				**Variability (%CV)**					**Mean Ratio (T/R)**	
		Drug Mass (mg)		**% label claim**		Within Lot (n=10)			Between Lot (n=3)	Total (n=30)		
		Arith	Geo	Arith	Geo	Lot 1	Lot 2	Lot 3			Arith (n=30)	Geo (n=30)
Test												
Ref												

Table 6. 4. 1. Summary of Population Bioequivalence Results

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
Priming						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
Repriming						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

The Table 7 Series is for Aerodynamic Particle Size Distribution (APSD) by Cascade Impaction

Table 7. 1. Study Information

Study No.	
Study Site Name and address	
Principal Investigator	
Study dates	
SOP No.	
SOP Effective Date	
SOP Title	
Testing Method Description [Eg. Test batches, B and E Lifestages, Number of canisters/batch, CI set up, flow rate determination, plate/cup coating, priming regimen, actuation method, filter, extraction diluent]	
Testing Equipment Used [e.g., name, model, etc, equipment includes but not limited to USP Apparatus (ACI or NGI), Flow Controller, Flow meter, Pump]	
Operating Conditions for Testing Equipment Used (e.g., temperature, humidity, etc..)	
Analytical Method Description	
Analytical Equipment Used (e.g., name, model, etc)	

Validation Summary Tables for Aerodynamic Particle Size Distribution (APSD) by Cascade Impaction

Table 7.2. Analytical Method Validation for HPLC

Information Requested	
Analytical method validation report location	Provide the volume(s) and page(s)
Analyte	Provide the name(s) of the analyte(s)
Internal Standard (IS) (If applicable)	
Method description	Brief descriptions of extraction method; analytical
Selectivity or Specificity	
Limit of quantitation (unit)	LOQ, unit
Detection Limit (unit)	LOD, unit
Linearity Range (ng, mcg/mL)	Range, unit
Linearity (R^2) (e.g., 0.99**)**	
Accuracy (% recovery)	Avg.: HQC: MQC: LQC:
Precision – Repeatability, (%CV)	QC
Intermediate Precision	By Date: By Analyst:
Bench-top stability (hrs (CV%)) (working std solution) (e.g. 2 days @ room temperature**)**	
Stock solution stability (days (CV %) (If applicable)	
Robustness	

Table 7.3 Method Validation for Cascade Impaction

	Precision (n = #)	Robustness (By Analyst/Day)	
Impactor-Sized Mass, (μg, mg/actuation) (mean and CV%)		Analyst 1	Analyst 2
		Day 1	Day 2
Fine Particle Mass (μg, mg/actuation) (mean and CV%)		Analyst 1	Analyst 2
		Day 1	Day 2
Mass Median Aerodynamic Diameter (μm) (mean and %CV)		Analyst 1	Analyst 2
		Day 1	Day 2
Geometric Standard Deviation (mean and %CV, if applicable)		Analyst 1	Analyst 2
		Day 1	Day 2
Delivered Dose (μg, mg) (mean and CV%)		Analyst 1:	Analyst 2:
		Day 1	Day 2
Mass Balance (mg) (mean and CV%)		Analyst 1:	Analyst 2:
		Day 1	Day 2
% Difference in Impactor-Sized Mass		Between Analyst 1 and 2:	
		Between Day 1 and 2:	
Impactor-Sized mass (% CV)		Inter analyst:	
		Inter day:	
% Difference in Fine Particle Mass		Between Analyst 1 and 2:	
		Between Day 1 and 2:	
Fine Particle Mass (% CV)		Inter analyst:	
		Inter day:	
% Difference in Delivered Dose		Between Analyst 1 and 2:	
		Between Day 1 and 2:	
Delivered Dose (% CV)		Inter analyst:	
		Inter day:	
%Difference in Mass Balance		Between Analyst 1 and 2:	
		Between Day 1 and 2:	
Mass Balance (% CV)		Inter analyst:	
		Inter day:	
Acceptance criteria defined by SOP	*Example* Precision: Intermediate Precision by Analyst: Intermediate Precision by Day: % Difference Analyst-to-Analyst: % Difference Day-to-Day:		
Reference Product lot numbers			
Number of units			

Number of actuation/unit	
Automated or manual actuation used	Automated / Manual

Table 7.4 Results Summary – Aerodynamic Particle Size Distribution by Cascade Impaction

Aerodynamic Particle Size Distribution										
		Mean Drug Deposition (μg)		**Variability (%CV)**					**Mean Ratio (T/R)**	
				Within Lot (n=20)			Between Lot (n=3)	Total (n=60)		
		Arith	Geo	Lot 1	Lot 2	Lot 3			Arith (n=60)	Geo (n=60)
Delivered Dose (μg)	**Test**									
	Ref									
Fine Particle Mass (μg)	**Test**									
	Ref									
Impactor-Sized Mass (μg)	**Test**									
	Ref									

Test Lot #1 – xxxxx, Lot #2 – xxxxx, Lot #3 – xxxxx; Reference Lot #1 – xxxxx, Lot #2 – xxxxx, Lot #3 – xxxxx

MASS BALANCE* (% of label claim)		
		Arithmetic Mean and Range (Min – Max) (n=30)
Mass Balance (%)	**Test**	
	Ref	

* Determined from mouthpiece adapter, the induction port, each stage of the cascade impactor (CI) and the filter, and any other accessories.

Table 7.5 Summary of Population Bioequivalence Results

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T/Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
ISM						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

The Table 8 Series is for Spray Pattern Test

Table 8.1 Study Information

Study No.	
Study Site Name and Address	
Principal Investigator	
Study dates	
SOP No.	
SOP Effective Date	
SOP Title	
Testing Method Description	
Testing Equipment Used (e.g., name, model, etc)	
Image Analysis Apparatus Used (i.e., automated = Laser Imaging; or manual = TLC)	
Operating Conditions for Testing Equipment Used (e.g., temperature, humidity, etc..)	

Validation Summary Table for Spray Pattern

Table 8.2 Precision and Ruggedness

	Distance (e.g., 3 cm and 6 cm)	Precision	Ruggedness	
Area[1] (mean and CV%)	Distance 1		Day 1*:	Day 2*:
			Analyst 1:	Analyst 2:
	Distance 2		Day 1*:	Day 2*:
			Analyst 1:	Analyst 2:
Ovality Ratio (mean and CV%)	Distance 1		Day 1*:	Day 2*:
			Analyst 1:	Analyst 2:
	Distance 2		Day 1*:	Day 2*:
			Analyst 1:	Analyst 2:
Difference in Area[1] (%)	Distance 1		Between Day 1 and 2:	
			Between Analyst 1 and 2:	
	Distance 2		Between Day 1 and 2:	
			Between Analyst 1 and 2:	
Area (% CV)	Distance 1		Inter day:	
			Inter analyst:	
	Distance 2		Inter day:	
			Inter analyst:	
Difference in Ovality Ratio (%)	Distance 1		Between Day 1 and 2:	
			Between Analyst 1 and 2:	
	Distance 2		Between Day 1 and 2:	
			Between Analyst 1 and 2:	
Ovality Ratio (% CV)	Distance 1		Inter day:	
			Inter analyst:	
	Distance 2		Inter day:	
			Inter analyst:	
Acceptance criteria defined by SOP		*Example* Precision: Intermediate Precision by Date: Intermediate Precision by Analyst: % Difference Day-to-Day: % Difference Analyst-to-Analyst:		
Reference Product lot numbers				
Number of units				
Number of sprays/unit				
Automated or manual actuation used				

* Ruggedness by day: By same analyst

1. This parameter varies with the type of spray pattern analysis. If it is an automated analysis, e.g., Laser imaging, "area" should be used. If it is a manual analysis, e.g., TLC, "Dmax" should be used.

Table 8.3 Results Summary – Spray Pattern

AREA* – SPRAY PATTERN SUMMARY										
	Dist (cm)	**Mean (mm^2)**		**Variability (%CV)**					**Mean Ratio (T/R)**	
				Within Lot (n=10)			Between Lot (n=3)	Total (n=30)		
		Arith	Geo	Lot 1	Lot 2	Lot 3			Arith (n=30)	Geo (n=30)
Test										
Ref										

*This parameter varies with the type of spray pattern analysis. If it is an automated analysis, e.g., Laser imaging, "area" should be used. If it is a manual analysis, e.g., TLC, "Dmax" should be used.

OVALITY RATIO – SPRAY PATTERN SUMMARY										
	Dist (cm)	**Mean**		**Variability (%CV)**					**Mean Ratio (T/R)**	
				Within Lot (n=10)			Between Lot (n=3)	Total (n=30)		
		Arith	Geo	Lot 1	Lot 2	Lot 3			Arith (n=30)	Geo (n=30)
Test										
Ref										

Table 8.3.1. Summary of Population Bioequivalence Results

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
Area at X cm						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
Area at Y cm						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
Ovality Ratio at X cm						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

Variable	Mean (log Scale)		Mean Difference (log Scale)	Standard Deviation		Sigma T /Sigma R Ratio
	Test	Reference		Sigma T	Sigma R	
Ovality Ratio at Y cm						

Scaled	Linearized Point Estimate	95% Upper Confidence Bound	Pass or Fail PBE
Reference-scaled			
Constant-scaled			

The Table 9 Series is for Plume Geometry Test

Table 9.1. Study Information

Study No.	
Study Site Name and Address	
Principal Investigator	
Study dates	
SOP No.	
SOP Effective Date	
SOP Title	
Testing Method Description (e.g., Actuation distance; criteria for defining the plume angle and width, etc.**)**	
Criteria for defining plume angle and width borders	
Testing Equipment Used (e.g., name, model, etc)	
Image Analysis Apparatus Used	
Operating Conditions for Testing Equipment Used (e.g., temperature, humidity, etc..)	

The applicant needs to submit representative photographs (manual) or digital images (automated) and spray intensity (actuation) profiles as supportive data.

Validation Summary Table for Plume Geometry

Table 9.2 Precision and Ruggedness

	Precision	Ruggedness	
Plume Width (mean and CV%)		Day 1*:	Day 2*:
		Analyst 1:	Analyst 2:
Plume Angle (mean and CV%)		Day 1*:	Day 2*:
		Analyst 1:	Analyst 2:
Difference in Plume Width (%)		Between Day 1 and 2:	
		Between Analyst 1 and 2:	
Plume Width (% CV)		Inter day:	
		Inter analyst:	
Difference in Plume Angle (%)		Between Day 1 and 2:	
		Between Analyst 1 and 2:	
Plume Angle (% CV)		Inter day:	
		Inter analyst:	
Acceptance criteria defined by SOP	*Example* Precision: Intermediate Precision by Date: Intermediate Precision by Analyst: % Difference Day-to-Day: % Difference Analyst-to-Analyst:		
Reference Product lot numbers			
Number of units			
Number of sprays/unit			
Automated or manual actuation used			

*Ruggedness by day: By same analyst

Table 9.3 Robustness for various parameters (the selection of parameters is optional)

	Plume Width				Plume Angle			
Parameter*	**camera distance** 1*	**camera distance** 2*	**camera distance** 3*	**camera distance** 4*	**camera distance** 1*	**camera distance** 2*	**camera distance** 3*	**camera distance** 4*
Mean								
%CV (Precision/ Repeatability)								

*The selection of parameters is optional. Examples of parameters of robustness study include camera distance, delay time, velocity, acceleration, etc.

Table 9.4 Results – Plume Geometry

	Mean Width (mm) or Mean Angle (°)		Variability (%CV)					Mean Ratio (T/R)	
			Within Lot (n=10)			Between Lot (n=3)	Total (n=30)		
	Arith	Geo	Lot 1	Lot 2	Lot 3			Arith	Geo
Plume Angle (°)									
Test									
Ref									
Plume Width (mm)									
Test									
Ref									

For SAS Data Tables for MDI product In Vitro Bioequivalence Study Data Submission, Please Refer to the related section in "Bioequivalence Summary Tables for Aqueous Nasal Spray Products" published on the Office of Generic Drugs at https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/UCM209446.pdf

The Table 10 Series is for the Pharmacodynamic (PD) Bioequivalence (BE) Bronchoprovocation Study

Table 10.1. Study Information

Study Number	
Study Title	
Clinical Site(s) (Name & Address)	
Principal Clinical Investigator(s)	
Clinical Study Date Range	

Table 10.2. Product Information

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

Table 10.3. Demographic Profile of Subjects Completing the BE Study

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

Table 10.4. Dropout Information

Subject No.	Reason for dropout/replacement	Period	Replaced?	Replaced With

Table 10.5. Incidence of Adverse Events in the PD BE Study

Body System / Adverse Event	Reported Incidence by Treatment Groups		
	PD Study No.		
	Test	Reference*	Placebo
Body as a whole			
Dizziness	N (%)	N (%)	N (%)
Etc.	N (%)	N (%)	N (%)
Cardiovascular			
Hypotension	N (%)	N (%)	N (%)
Etc.	N (%)	N (%)	
Gastrointestinal			
Emesis*	N (%)	N (%)	N (%)
Constipation	N (%)	N (%)	N (%)
Etc.	N (%)	N (%)	N (%)
Other organ sys.			
	N (%)	N (%)	N (%)
	N (%)	N (%)	N (%)
Total	N (%)	N (%)	N (%)

*Please separate the R treatments by dose

Table 10.6. Protocol Deviations

Type	Subjects with deviation				
	Test	Reference Dose 1	Reference Dose 2	Placebo	Total

Table 10.7. Statistical Summary for the PD BE Study
Table 10.7a. Point Estimates and 90% Confidence Intervals, Raw Data

Drug name Dose Pharmacodynamic Study No. (study number), N=N1 Point Estimates and 90% Confidence Intervals			
Parameter	**Point Estimate**	**90% C.I.**	
F			

Note: Please submit the estimated value for E0, ED50R, and EmaxR. ED50R and EmaxR refer to the modeled ED50 and Emax for the reference product only.

Table 10.7b. Point Estimates and 90% Confidence Intervals, Bootstrapping Procedure

Drug name Dose Pharmacodynamic Study No. (study number), N=N1 Point Estimates and 90% Confidence Intervals			
Parameter	**Point Estimate**	**90% C.I.**	
F			

Note: Please submit the estimated value for E0, ED50R, and EmaxR. ED50R and EmaxR refer to the modeled ED50 and Emax for the reference product only.

Table 10.8. PD BE Study, Additional Information

Subjects excluded in statistical analysis for each period and reason for exclusion [include Subject #, Product (T, R, or placebo), and Dose]	
Subjects that failed to reduce the FEV1 by 20% following the highest dose of methacholine [include Subject #, Product (T, R, or placebo), and Dose]	
Stepwise method of PC20 estimation	

Table 10.9. SAS Data Table for MDI product In Vivo PD BE Study Data Submission

Data in this table should be arranged in columns as shown in examples. Data sets should be submitted as SAS Transport files.

Variable Name	Variable Type	Content	Notes
Subject ID	Numeric	Numeric values	Identifier for subject
Treatment	Numeric	Numeric values	Identifier for treatment (product and dose)
Period	Numeric	Numeric values	Identifier for period
Dose	Numeric	Numeric values	Identifier for dose
PC20	Numeric	Numeric values	The provocative concentration or dose, respectively, of the methacholine challenge agent required to reduce the forced expiratory volume in one second (FEV1) by 20% following administration of differing doses of study drug (or placebo) by inhalation.

Subject ID	Treatment	Period	Dose	PC20	lnPC20