Technical Specifications—Comparative Clinical Endpoint Bioequivalence Study Analysis Datasets for Abbreviated New Drug Applications

Guidance for Industry

For questions regarding this guidance document, contact CDER at cder-edata@fda.hhs.gov

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September 2018	1.0	Initial Version

Contains Nonbinding Recommendations

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Comparative Clinical Endpoint Bioequivalence Study Analysis Datasets for Abbreviated New Drug Applications

Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

1.0 Introduction

1.1 Background

This guidance provides recommended technical specifications and general considerations on how certain comparative clinical endpoint bioequivalence study data and skin adhesion and irritation/sensitization study data for Abbreviated New Drug Applications (ANDAs) should be submitted using FDA-supported[1] data standards located in the FDA Data Standards Catalog (Catalog). This guidance provides additional information related to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Standardized Study Data* (eStudy Data). The eStudy Data binding guidance implements the electronic submission requirements of section 745A(a) of the Food Drug & Cosmetic (FD&C) Act with respect to standardized study data contained in certain investigational new drug applications (INDs); new drug applications (NDAs); abbreviated new drug applications (ANDAs); and certain biologics license applications (BLAs) that are submitted to the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER).

The document provides the sample data tables for the Clinical Data Interchange Standards Consortium (CDISC) analysis data model (ADaM) following the Analysis Data Model Implementation Guide Version 1.1 (ADaMIG)[2]. This specification is not intended to cover the Study Data Tabulation Model (SDTM) study datasets. All study-specific data for evaluating the

[1] This guidance has been prepared by the Office of Translational Sciences in the Center for Drug Evaluation and Research at the Food and Drug Administration. You may submit comments on this guidance at any time. Submit comments to Docket No. FDA-2018-D-1216 (available at https://www.regulations.gov/docket?D=FDA-2018-D-1216) (see the instructions for submitting comments in the docket).

[2] http://www.cdisc.org/adam

generic products should be submitted using the recommended data standards currently supported by FDA and listed in the Catalog.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency's guidances means that something is suggested or recommended, but not required.

1.2 Purpose

This guidance document is intended to complement interactions between applicants and FDA review divisions. It is not intended to replace the need for applicants to communicate directly with review divisions regarding approaches or issues relating to data standards. If there is a question regarding a specific submission or a particular data standard, the applicant should contact the review division for specific submission questions or the appropriate contact for data standards issues at cder-edata@fda.hhs.gov. For more general recommendations on the use and submission of standardized study data, the applicant should refer to the Study Data Technical Conformance Guide[3].

Recommended specifications for analysis datasets for human drug product comparative clinical and analytical studies are provided by the ADaM standard. While ADaM provides a valuable representation that may facilitate review, it does not always provide data structured in a way that supports all analyses used for review. This guidance is designed to provide recommendations for detailed data specifications for the data elements used to analyse certain comparative clinical endpoint bioequivalence studies submitted in the ANDA.

This document provides detailed data specification for the following clinical studies:

- The adhesion study for transdermal delivery systems (TDS) and topical patches
- The irritation/sensitization study for transdermal delivery systems (TDS) and topical patches
- The comparative clinical endpoint bioequivalence study using the following primary endpoints: lesion count, 100% clearance of all actinic keratosis (AK) lesions, total nasal symptom score, treatment success based on Physician's Global Assessment (PGA) and Psoriasis Area Severity Index (PASI), Intraocular pressure (IOP) and therapeutic cure based on clinical and mycological cures

For the comparative clinical endpoints that are not covered in this document, please refer to the Office of Generic Drugs product specific guidance and the standards currently supported by FDA and listed in the Catalog.

[3] https://www.fda.gov/downloads/forindustry/datastandards/studydatastandards/ucm384744.pdf

2.0 Dataset Specifications for Comparative Clinical Study Endpoints

This section provides examples for the ADaM Subject Level Analysis Datasets (ADSL) and the ADaM Basic Data Structure (BDS) for each of the comparative clinical studies described in Section 1.0. For the comparative clinical endpoint bioequivalence studies, we consider the modified intent-to-treat (mITT) population, including those subjects who are randomized and take at least one dose of study medication. The exception is for the endpoint of therapeutic cure which is a composite endpoint of both mycological and clinical cure. For more details, please refer to Section 2.8. The mITT population includes those subjects who are randomized, apply at least one dose of study medication and have a positive baseline skin fungal culture. In general, ADSL contains one record per subject. However, for certain types of studies, e.g., adhesion study and irritation/sensitization study, the structure of ADSL is different. Please refer to Sections 2.1 and 2.2 for details. A BDS dataset contains one or more records per subject, per analysis parameter, and per analysis time point if applicable.

The data tables that facilitate the regulatory review contain both standard ADaM variables and variables not referenced in a CDISC therapeutic area user guide or the ADaM IG. The non-referenced ADaM variables are created to accommodate the analysis needs for specific endpoints and/or the design of the study, e.g., the criteria for analysis populations, specific inclusion/exclusion criteria, etc. We use italics to identify these non-referenced ADaM variables. These data tables may contain additional information and/or may not contain all information applicable to the proposed study.

The data should be defined consistently for the same type of variables. For example, for the variables indicating reasons for exclusion from a certain population in the ADSL, the same reasons should be written consistently using the same character string.

The format for date and date time variables should follow ISO8601. The imputation rules for date and date time variables should be specified in the define file if applicable.

2.1 Adhesion

This section provides the examples of data tables for the transdermal patch studies using the primary endpoint of adhesion score. The tables below specify the recommended data elements and format to be included in the analysis datasets.

2.1.1 ADSL Table

The following example of ADSL table is for 2 by 2 cross-over design. For other cases, you should use the appropriate variables for the specific design that is used for the adhesion study.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID

USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID
SITEID	Study Site Identifier	Char		DM.SITEID
AGE	Age	Num		DM.AGE
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX
RACE	Race	Char	(RACE)	DM.RACE
SAFFL	Safety Population Flag	Char	Y, N	
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPREAS	*Reason for Exclusion from Per-Protocol Population*	*Char*		
RANDFL	Randomized Population Flag	Char	Y, N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRTxxP	Planned Treatment for Period xx	Char	A, B	A=Test, B=Reference
TRTxxPN	Planned Treatment for Period xx (N)	Num	1, 2	1=Test, 2=Reference
TRTxxA	Actual Treatment for Period xx	Char		User should complete if actual treatment does not match Planned Treatment for Period xx listed in TRTxxP.
TRTxxAN	Actual Treatment for Period xx (N)	Num		
TRTSEQP	Planned Sequence of Treatments	Char	AB, BA	
TRTSEQPN	Planned Sequence of Treatments (N)	Num	1, 2	1=AB, 2=BA
TRTSEQA	Actual Sequence of Treatments	Char		User should complete if a subject received a sequence of treatments other than what was planned.
TRTSEQAN	Actual Sequence of Treatments (N)	Num		
TRxxSDTM	Datetime of First Exposure in Period xx	Num		
TRxxSDTF	Date 1st Exposure Period xx Imput. Flag	Char	(DATEFL)	If the date part of TRxxSDTM was imputed, TRxxSDTF should be populated.
TRxxSTMF	Time 1st Exposure Period xx Imput. Flag	Char	(TIMEFL)	If the time part of TRxxSDTM was imputed, TRxxSTMF should be populated.
TRxxEDTM	Datetime of Last Exposure in Period xx	Num		
TRxxEDTF	Date Last Exposure Period xx Imput. Flag	Char	(DATEFL)	If the date part of TRxxEDTM was imputed, TRxxEDTF should be populated. .
TRxxETMF	Time Last Exposure Period xx Imput. Flag	Char	(TIMEFL)	If the time part of TRxxEDTM was imputed, TRxxETMF should be populated .

TRxxDURH	Treatment Duration in Period xx (Hours)	Num		Time from individual test article application to removal or complete detachment.
APxxSDTM	Period xx Start Datetime	Num		
APxxEDTM	Period xx End Datetime	Num		
EOTxxSTT	End of Treatment Status in Period xx	Char		
DCTxxRS	Reason for Discont of Treatment in Period xx	Char		Reason for discontinuing treatment in period xx.
DCTxxRSP	Reason Spec for Disc of Trt in Period xx	Char		If applicable, additional detail regarding subject's discontinuation of treatment in period xx (e.g., description of "other").
EOPxxSTT	End of Period xx Status	Char		
DCPxxRS	Reason for Discont from Period xx	Char		Reason for discontinuing analysis period xx.
DCPxxRSP	Reason Spec for Discont from Period xx	Char		If applicable, additional detail regarding subject's discontinuation from period xx (e.g., description of "other").
ENRLDT	Date of Enrollment	Num		
RANDDT	Date of Randomization	Num		
DTHDT	Date of Death	Num		
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*INEXFL = Y if the subject met all inclusion and exclusion criteria.*
RMFL	*Patch Remove Flag*	*Char*	*Y, N*	*RMFL = Y if the patch is removed due to irritation.*
AEFL	Adverse Event Flag	Char	Y, N	
CMFL	Concomitant Medication Flag	Char	Y, N	

2.1.2 Analysis Dataset for Adhesion (ADAD)

The ADAD should contain a separate line for each individual patch per subject per evaluation time.

For the definition of primary endpoint – mean adhesion score, please refer to the draft guidance "Assessing Adhesion with Transdermal Delivery Systems and Topical Patches for ANDA". Please use the DTYPE variable to indicate the method to compute the mean adhesion score, e.g., average or weighted average, and provide the detailed algorithm or formula in define.xml. To enable the analysis with or without imputed scores, ANL01FL (with imputed scores) and ANL02FL (without imputed scores) should be populated.

For a TDS that completely detaches, a score of 4 should be assigned for all remaining assessments scheduled for that TDS across the study duration.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID
SITEID	Study Site Identifier	Char		DM.SITEID
SAFRFL	Safety Analysis Record-Level Flag	Char	Y, N	
PPROTRFL	Per-Protocol Record-Level Flag	Char	Y, N	
TRTP	Planned Treatment	Char	A, B	A=Test, B=Reference
TRTPN	Planned Treatment (N)	Num	1, 2	1=Test, 2= Reference
TRTA	Actual Treatment	Char	A, B	User should populate when actual treatment does not match planned. A=Test, B=Reference
TRTAN	Actual Treatment (N)	Num	1, 2	1=Test, 2= Reference
ADTM	Analysis Datetime	Num		Adhesion assessment/scoring datetime recorded in the CRF
ADTF	Analysis Date Imputation Flag	Char	(DATEFL)	If the date part of ADTM was imputed, ADTF should be populated.
ATMF	Analysis Time Imputation Flag	Char	(TIMEFL)	If the time part of ADTM was imputed, ATMF should be populated.
ATPT	Analysis Timepoint	Char		ATPT represents the analysis timepoint recorded in the CRF (e.g., 12 hr, 24 hr, 36 hr, etc.).
ATPTN	Analysis Timepoint (N)	Num		
AVISIT	Analysis Visit	Char		
AVISITN	Analysis Visit (N)	Num		
APERIOD	Period	Num		For example, APERIOD =1 and 2 for 2x2 cross-over design.
APERIODC	Period (C)	Char		For example, APERIODC = Period 1 and Period 2 for 2x2 cross-over design.
PARAM	Parameter	Char		Adhesion Score
PARAMCD	Parameter Code	Char		ADHESION = Adhesion Score
AVAL	Analysis Value	Num		Guidance-recommended 5-point numerical scale: 0 = ≥ 90% adhered 1 = ≥ 75% to < 90% adhered 2 = ≥ 50% to < 75% adhered 3 = > 0% to < 50% adhered but not detached 4 = 0% adhered (completely detached)
DTYPE	Derivation Type	Char	(DTYPE)	Examples of DTYPE values: LOCF = last observation carried forward AVERAGE = average of values IMPUTED = higher adhesion score imputed

ANLzzFL	Analysis Flag zz	Char	Y, N	ANL01FL = analysis with imputed scores ANL02FL = analysis without imputed scores
ACONy	Analysis Condition y	Char		For secondary endpoint analysis, define ACON1 = Adhesion Score > 2 at any time point, ACON2 = T mean adhesion score greater than the corresponding R mean adhesion score by 1 or more, ACON3 = R mean adhesion score greater than the corresponding T mean adhesion score by 1 or more.
ACONyFL	Analysis Condition y Evaluation Result	Char	Y, N	
DTFL	*Patch Detachment Flag Variable*	*Char*	*Y, N*	*DTFL = Y if the patch is completely detached.*
DTDTM	*Date and Time of Detachment*	*Num*		*User should complete if the patch is detached.*
RMRFL	*Patch Remove Record-Level Flag*	*Char*	*Y, N*	*RMRFL = Y if the patch is removed due to irritation during this visit.*
AERFL	Adverse Event Record-Level Flag	Char	Y, N	AERFL = Y if adverse event reported during this visit.
CMRFL	Concomitant Medication Record-Level Flag	Char	Y, N	CMRFL = Y if concomitant medication reported during this visit.
EVAL	*Evaluator Initials*	*Char*		

2.2 Irritation/Sensitization

This section provides the examples of data tables for the transdermal patch studies using the primary endpoint of irritation score and potential sensitization. The skin irritation and sensitization study includes induction phase and challenge phase or induction phase, challenge phase, and re-challenge phase if re-challenge phase is conducted. Analysis data should be prepared and submitted in one dataset from all phases. The tables below specify the recommended data elements and format to be included in the analysis datasets.

2.2.1 ADSL Table

The ADSL dataset for Irritation/Sensitization study should contain a separate line for each patch type per subject.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID
SITEID	Study Site Identifier	Char		DM.SITEID
AGE	Age	Num		DM.AGE
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX

RACE	Race	Char	(RACE)	DM.RACE
SAFFL	Safety Population Flag	Char	Y, N	
IPPFL	*Irritation Per-Protocol Population Flag*	*Char*	*Y, N*	
IPPREAS	*Reason for Exclusion from Irritation Per-Protocol Population*	*Char*		
SPPFL	*Sensitization Per-Protocol Population Flag*	*Char*	*Y, N*	
SPPREAS	*Reason for Exclusion from Sensitization Per-Protocol Population*	*Char*		
COMPLwFL	Completers of Phase w Flag	Char	Y, N	COMPLwFL = Y if the subject completed Phase w, where w=1 if induction phase, w=2 if challenge phase, w=3 if re-challenge phase.
RANDFL	Randomized Population Flag	Char	Y, N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment	Char	A, B, C, D	A=Test, B= Reference, C=Vehicle, D=Positive control (if applicable).
TRT01PN	Planned Treatment (N)	Num	1, 2, 3, 4	1=Test, 2= Reference, 3=Vehicle, 4=Positive control (if applicable).
TRT01A	Actual Treatment	Char	A, B, C, D	User should populate when actual treatment does not match planned. A=Test, B= Reference, C=Vehicle, D=Positive control (if applicable).
TRT01AN	Actual Treatment (N)	Num	1, 2, 3, 4	1=Test, 2= Reference, 3=Vehicle, 4=Positive control (if applicable).
TRwSDTM	Datetime of First Exposure in Phase w	Num		Datetime of first exposure to treatment in phase w, where w=1 if induction phase, w=2 if challenge phase, w=3 if re-challenge phase.
TRwSDTF	Date 1st Exposure Phase w Imput. Flag	Char	(DATEFL)	User should populate if the date part of TRwSDTM is imputed.
TRwSTMF	Time 1st Exposure Phase w Imput. Flag	Char	(TIMEFL)	User should populate if the time part of TRwSDTM is imputed.
TRwEDTM	Datetime of Last Exposure in Phase w	Num		The datetime of last exposure to treatment in phase w.
TRwEDTF	++++++++++++++++Date Last Exposure Phase w Imput. Flag	Char	(DATEFL)	User should populateif the date part of TRwEDTF is imputed.
TRwETMF	Time Last Exposure Phase w Imput. Flag	Char	(TIMEFL)	User should populate if the time part of TRwEDTF is imputed.
PHwSDTM	Phase w Start Datetime	Num		
PHwEDTM	Phase w End Datetime	Num		

EOTwSTT	End of Treatment Status in Phase w	Char		
DCTwRS	Reason for Discontinuation of Treatment in Phase w	Char		Reason for discontinuing treatment in phase w.
DCTwRSP	Reason Specify for Discont of Treatment in Phase w	Char		If applicable, additional detail regarding subject's discontinuation of treatment in phase w (e.g., description of "other").
ENRLDT	Date of Enrollment	Num		
RANDDT	Date of Randomization	Num		User should populate if randomized trial.
TRwDURD	Treatment Duration in Phase w (Days)	Num		Treatment duration for phase w, as measured in days.
DTHDT	Date of Death	Num		
LOCw	*Location of Patch Application in Phase w*	*Char*		*Specific anatomical site of the original patch application where w=1 if induction phase, w=2 if challenge phase, w=3 if re-challenge phase*
MOVFL	*Patch Move Flag*	*Char*	*Y, N*	*MOVFL = Y if the patch was moved at least once during the induction phase.*
NMOV	*Number of Patch Moves*	*Num*		*Total number of times that the patch was moved during the induction phase.*
MOViDTM	*Datetime of ith Patch Move*	*Num*		*Applicable only if a patch is moved during the induction phase. Datetime of the ith time that the patch was moved during the induction phase, where i=1 if 1st move, i=2 if 2nd move, etc.*
MOViDTFL	*Date of ith Patch Move Flag*	*Char*	*(DATEFL)*	User should populate*if the date part of MOViDTM was imputed.*
MOViTMFL	*Time of ith Patch Move Flag*	*Char*	*(TIMEFL)*	User should populate *if the time part of MOViDTM was imputed.*
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*INEXFL = Y if the subject met all inclusion and exclusion criteria.*
AEFL	Adverse Event Flag	Char	Y, N	
CMFL	Concomitant Medication Flag	Char	Y, N	

2.2.2 Analysis Dataset for Irritation/Sensitization (ADIS)

The ADIS should contain a separate line for each individual patch per subject per evaluation time.

For the subjects who experience excessive irritation, the patch may be moved to a new site in order to complete the Induction Phase and continue with the sensitization part of the study. In this case, the last score observed prior to the discontinuation of the original patch application site should be carried forward for all remaining observations of the induction phase. The

imputed score should be indicated using the DTYPE variable, e.g., LOCF. The irritation scores recorded in each site should still be submitted using the variable "$score_i$" where the sub-script i refers to the i^{th} site, if applicable.

The criterion variable "ACONy" and the flag variable "PSFL" reflect the FDA's practice for the definition of potential sensitization. PSFL is Y if a subject satisfies ACON1 and ACON2 in absence of a re-challenge phase or ACON1 – ACON4 if the subject completed both the challenge and re-challenge phases. You should provide the details in define.xml if a different definition is applied to the study.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID
SITEID	Study Site Identifier	Char		DM.SITEID
TRTP	Planned Treatment	Char	A, B, C, D	A=Test, B=Reference, C=Vehicle, D=Positive control (if applicable).
TRTPN	Planned Treatment (N)	Num	1, 2, 3, 4	1=Test, 2= Reference, 3=Vehicle, 4=Positive control (if applicable).
TRTA	Actual Treatment	Char	A, B, C, D	User should populate when actual treatment does not match planned. A=Test, B= Reference, C=Vehicle, D=Positive control (if applicable).
TRTAN	Actual Treatment (N)	Num	1, 2, 3, 4	1=Test, 2= Reference, 3=Vehicle, 4=Positive control (if applicable).
ADT	Analysis Date	Num		The date recorded in the CRF
ADTM	Analysis Datetime	Num		Irritation Assessment/Scoring Date and Time recorded in the CRF
ADY	Analysis Relative Day	Num		The number of days from the baseline visit to ADT.
ADTF	Analysis Date Imputation Flag	Char	(DATEFL)	User should populate if ADT (or the date part of ADTM) was imputed.
ATMF	Analysis Time Imputation Flag	Char	(TIMEFL)	User should populate if the time part of ADTM was imputed.
ASTDTM	Analysis Start Datetime	Num		Patch Application Datetime.
ASTDTF	Analysis Start Date Imputation Flag	Char	(DATEFL)	User should populate if the date part of ASTDTM was imputed.
ASTTMF	Analysis Start Time Imputation Flag	Char	(TIMEFL)	User should populate if the time part of ASTDTM was imputed.
AENDTM	Analysis End Datetime	Num		Patch Removal Datetime.
AENDTF	Analysis End Date Imputation Flag	Char	(DATEFL)	User should populate if the date part of AENDTM was imputed.
AENTMF	Analysis End Time Imputation Flag	Char	(TIMEFL)	User should populate if the time part of AENDTM was imputed.
AVISIT	Analysis Visit	Char		

AVISITN	Analysis Visit (N)	Num		
APHASE	Phase	Char		Induction = Induction Phase, Challenge = Challenge Phase, Rechallenge = Rechallenge Phase (if applicable)
APHASEN	Phase (N)	Num		1=Induction Phase, 2=Challenge Phase, 3 = Rechallenge Phase (if applicable)
PARAM	Parameter	Char		Dermal Response Other Effects Combined Score
PARAMCD	Parameter Code	Char		DERMAL = Dermal Response OTHER = Other Effects COMBINED = Combined Score
AVAL	Analysis Value	Num		Numerical scores from the original application site. If a patch is moved, its numerical scores from the moved application sites should be recorded in 'SCOREi' variable below. Dermal Response = {0, 1, 2, 3, 4, 5, 6, 7} Other Effects = {0, 1, 2, 3} Combined Score = {0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10}
DTYPE	Derivation Type	Char	(DTYPE)	Examples of DTYPE values: LOCF = last observation carried forward MAXIMUM = maximum of values AVERAGE = average of values
SCOREi	*Irritation Scores After ith Move*	*Num*		*Applicable only if a patch is moved during the induction phase. SCOREi records the numerical scores of Dermal Response and Other Effects observed from the moved application site after the ith move during the induction phase.*
OTHERi	*Other Effect Character Score After ith Move*	*Char*		*Applicable only if a patch is moved during the induction phase. OTHERi records the character scores (A, B, C, F, G, or H) of Other Effects that are observed from the moved application site after the ith move during the induction phase.*
ACONy	Analysis Condition y	Char		For sensitization analysis, define the following variables: ACON1 = combined irritation score ≥ 2 at the last evaluation after 24 hours during the Challenge Phase; and ACON2 = maximum of combined irritation score during the Challenge Phase > maximum of combined irritation score during the Induction Phase. If a subject completed a Rechallenge Phase, in addition to ACON1 and ACON2 define the following variables: ACON3 = combined irritation score ≥ 2 at the last evaluation after 24 hours during the Rechallenge Phase; and ACON4 = maximum of combined irritation score during the Rechallenge Phase > maximum of combined irritation score during the Induction Phase
ACONyFL	Analysis Condition y Evaluation Result	Char	Y, N	
SAFRFL	Safety Analysis Record-Level Flag	Char	Y, N	
IPPRFL	*Irritation Per-Protocol Record-Level Flag*	*Char*	*Y, N*	
SPPRFL	*Sensitization Per-Protocol Record-Level Flag*	*Char*	*Y, N*	

ADH	*Adhesion Scores*	*Num*		*0 = ≥ 90% adhered* *1 = ≥ 75% to < 90% adhered* *2 = ≥ 50% to < 75% adhered* *3 = > 0% to < 50% adhered but not detached* *4 = 0% adhered (completely detached)*
DTFL	*Patch Detachment Flag*	*Char*	*Y, N*	*DTFL = Y if the patch is completely detached.*
DT24FL	*Patch Detachment Over 24 Hrs. Flag*	*Char*	*Y, N*	*DT24FL = Y if the patch is completely detached more than 24 hours.*
DTDTM	*Patch Detachment Datetime*	*Num*		*Date and time of detachment.* User should populate *if a patch is completely detached.*
DTDTF	*Patch Detachment Date Imputation Flag*	*Char*	*(DATEFL)*	User should populate *if the date part of DTDTM was imputed.*
DTTMF	*Patch Detachment Time Imputation Flag*	*Char*	*(TIMEFL)*	User should populate *if the time part of DTDTM was imputed.*
RADTM	*Patch Reapplication Datetime*	*Num*		*Date and time of reapplication if a patch is reapplied after detachment.*
RADTF	*Patch Reapplication Date Imputation Flag*	*Char*	*(DATEFL)*	User should populate *if the date part of RADTM was imputed.*
RATMF	*Patch Reapplication Time Imputation Flag*	*Char*	*(TIMEFL)*	User should populate *if the time part of RADTM was imputed.*
TRDURH	Treatment Duration (Hours)	Num		Hours from individual patch application to removal or complete detachment (AENDTM – ASTDTM or DTDTM – ASTDTM).
MOVRFL	*Patch Move Record-Level Flag*	*Char*	*Y, N*	*MOVRFL = Y if the patch is moved during this visit.*
PSFL	*Potential Sensitization Flag*	*Char*	*Y, N*	*PSFL=Y if the subject is potentially sensitized.*
RIFL	*Reinforcement Flag*	*Char*	*Y, N*	*RIFL = Y if the patch is reinforced with tape or overlay.*
AERFL	Adverse Event Record-Level Flag	Char	Y, N	AERFL = Y if adverse event reported during this visit.
CMRFL	Concomitant Medication Record-Level Flag	Char	Y, N	CMRFL = Y if concomitant medication reported during this visit.
EVAL	*Evaluator Initials*	*Char*		

2.3 Lesion Count

This section provides the examples of data tables for the comparative clinical studies using the primary endpoint of inflammatory and/or non-inflammatory lesion counts. The tables below specify the recommended data elements and format to be included in the analysis datasets.

2.3.1 ADSL Table

Applicant should calculate the study drug compliance rate based on the scheduled doses for the specified duration of the study for the particular product. Applicant should provide the formula or algorithm in the submission.

The variable "MISDOSFL" is used to capture the information if a subject misses the pre-specified number of scheduled doses for more than pre-specified number of consecutive days for the particular product (e.g., 1 consecutive day).

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SITEGRy	Pooled Site Group y	Char		User should populate if the sites are pooled.
AGE	Age	Num		DM.AGE.
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX.
RACE	Race	Char	(RACE)	DM.RACE.
SAFFL	Safety Population Flag	Char	Y, N	These flags identify whether or not the subject is included in the specified population. A minimum of one subject-level population flag variable should be included in ADSL.
SAFEREAS	*Reason for exclusion from safety population*	*Char*		
ITTFL	Intent-To-Treat Population Flag	Char	Y, N	
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	
MITTREAS	*Reason for exclusion from mITT population*	*Char*		
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPREAS	*Reason for exclusion from PP population*	*Char*		
RANDFL	Randomized Population Flag	Char	Y,N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment	Char	A, B, C	TRTP would be the treatment to which the subject was randomized. TRTP might be derived from the SDTM DM variable ARM. e.g. A=Test, B= Reference, C=Placebo

TRT01PN	Planned Treatment	Num	1, 2, 3	1 = Test, 2 = Reference, 3 = Placebo
TRT01A	Name of Actual Treatment	Char	A, B, C	e.g. A=Test, B= Reference, C=Placebo
TRT01AN	Name of Actual Treatment	Num	1, 2, 3	1 = Test, 2 = Reference, 3 = Placebo
EXLOC	*Location of Treatment Area*	*Char*		*e.g., F=face, etc.*
ENRLDT	Date of Enrollment	Num		
TRTSDTM	Datetime of First Exposure to Treatment	Num		Datetime of first exposure to treatment for a subject in a study.
TRTSDTF	Date of First Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of first exposure to treatment. If the date part of TRTSDTM was imputed, TRTSDTF should be populated.
TRTSTMF	Time of First Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of first exposure to treatment. If the time part of TRTSDTM was imputed, TRTSTMF should be populated.
TRTEDTM	Datetime of Last Exposure to Treatment	Num		Datetime of last exposure to treatment for a subject in a study.
TRTEDTF	Date of Last Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of last exposure to treatment. If the date part of TRTEDTM was imputed, TRTEDTF should be populated.
TRTETMF	Time of Last Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of last exposure to treatment. If the time part of TRTEDTM was imputed, TRTETMF should be populated.
EOSSTT	End of Study Status	Char		The subject's status as of the end of study or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
EOSDT	End of Study Date	Num		Date subject ended the study – either date of completion or date of discontinuation or data cutoff date for interim analyses.
DCSREAS	Reason for Discontinuation from Study	Char		Reason for subject's discontinuation from study. Null for subjects who completed the study.
DCSREASP	Reason Spec for Discont from Study	Char		Additional detail regarding subject's discontinuation from study (e.g., description of "other").
ADDTRTFL	*Subject required additional treatment due to unsatisfactory treatment response*	*Char*	*Y, N*	*Y=Yes, N=No*
EOTSTT	End of Treatment Status	Char		The subject's status as of the end of treatment or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.

DCTREAS	Reason for Discontinuation of Treatment	Char		If a subject discontinued treatment in the study, then this variable indicates the reason for discontinuation. This is for discontinuation of treatment in the overall study and should not be used for discontinuation reason within individual treatment periods.
DCTREASP	Reason Spec for Discontinuation of Treatment	Char		Additional detail regarding subject's discontinuation from treatment (e.g., description of "other").
RANDDT	Date of Randomization	Num		User should populate if randomized trial
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*Y if the subject met all inclusion and exclusion criteria.*
TRCMP	Treatment Compliance (%)	Num		Overall percent compliance with treatment in the trial.
MISDOSFL	*Missed the scheduled applications for more than x consecutive days*	*Char*	*Y, N*	*Y=Yes, N=No*
TRTDURD	Total Treatment Duration (Days)	Num		Total treatment duration, as measured in days.
NUMINFBL	*Total number of inflammatory lesions on face at baseline*	*Num*		
NUMNONBL	*Total number of noninflammatory lesions on face at baseline*	*Num*		
NUMNODBL	*Total number of nodular/cystic lesions on face at baseline*	*Num*		
IGABL	*IGA score at baseline*	*Num*		
AEFL	Adverse Event reported	Char	Y, N	Y=Yes, N=No
CMFL	Concomitant Medication	Char	Y, N	Y=Yes, N=No
EVAL	*Evaluator initial*	*Char*		

2.3.2 Analysis Dataset for Lesion Count (ADLC)

For the secondary endpoint of clinical success based on the Investigator's Global Assessment (IGA) severity score, applicant should provide the definition if it is different from the recommendation in the product-specific guidance.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.

SAFFL	Safety Population Flag	Char	Y, N	These indicators identify whether or not the subject is included in the analysis population for the specific parameter.
MITTFL	Modified Intent-To-Treat Flag	Char	Y, N	
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
TRTP	Planned Treatment	Char	A, B, C	A=Test, B= Reference, C=Placebo
TRTPN	Planned Treatment	Num	1, 2, 3	1=Test, 2= Reference, 3=Placebo
TRTA	Actual Treatment	Char	A, B, C	A=Test, B= Reference, C=Placebo
TRTAN	Actual Treatment	Num	1, 2, 3	1=Test, 2= Reference, 3=Placebo
ADT	Analysis Date	Num		The date associated with AVAL and /or AVALC in numeric format recorded in the CRF
ADY	Analysis Relative Day	Num		The relative day of AVAL and/or AVALC. The number of days from the baseline date (not necessarily DM.RFSTDTC) to ADT.
AVISIT	Analysis Visit	Char		The analysis visit description
AVISITN	Analysis Visit	Num		A numeric representation of analysis visit description
AWFL	*Visit window Flag*	*Char*	*Y, N*	*Y, if the visit is within the visit window.*
AWDAYS	*Visit Window Days*	*Num*		*AWDAYS=actual visit date minus the scheduled visit date, e.g, actual visit happened on Day 5 but the scheduled visit should be on Day 8. Then, AWDAYS = -3. Or actual visit happened on Day 10 but the scheduled visit should be on Day 8. Then, AWDAYS = 2.*
PARAM	Parameter	Char		Total number of inflammatory lesion, Total number of non-inflammatory lesions, IGA score, Skin reaction erythema score, burning/stinging score, erosion score, edema score, pain score, itching score, Clinical success or not
PARAMCD	Parameter Code	Char		NUMINF= Total number of inflammatory lesion on face, NUMNON= Total number of non-inflammatory lesions on face, IGA= IGA score, ERY=Skin reaction erythema score, BURSTI=Skin reaction burning/stinging score EROSION =Skin reaction erosion score EDEMA=Skin reaction edema score PAIN=Skin reaction pain score ITCH=Skin reaction itching score SUCC= Clinical success or not
AVAL	Analysis Value	Num		IGA=0,1,2,3, or 4 Skin reaction score, e.g., 0=absent, 1=mild, (slight, barely perceptible), 2=moderate (distinct presence), 3=severe (marked, intense) SUCC=0,1
BASE	Baseline Value	Num		For inflammatory lesion and non-inflammatory lesion
CHG	Change from Baseline	Num		For inflammatory lesion and non-inflammatory lesion

DTYPE	Derivation Type	Char		e.g., LOCF=last observation carried forward
ADDTRTFL	*Additional Treatment required during this visit*	*Char*	*Y, N*	*Y=Yes, N=No*
ADDTRT	*Additional Treatment Drug Name*	*Char*		*The drug name of the additional treatment due to unsatisfactory treatment response*
AERFL	Adverse Event reported during this visit	Char	Y, N	Y=Yes, N=No
CMRFL	Concomitant Medication reported during this visit	Char	Y, N	Y=Yes, N=No
LBRFL	Laboratory testing performed during this visit	Char	Y, N	Y=Yes, N=No

2.4 100% Clearance of Actinic Keratosis (AK) Lesions

This section provides the examples of data tables for the comparative clinical studies using the primary endpoint of 100% clearance of all AK lesions. The tables below provide the recommended data elements and format to be included in the analysis datasets.

2.4.1 ADSL Table

Applicant should calculate the study drug compliance rate based on the scheduled doses for the specified duration of the study for the particular product. Applicant should provide the formula or algorithm in the submission.

The variable "MISDOSFL" is designed to capture the information if a subject misses the pre-specified number of scheduled doses for more than pre-specified number of consecutive days for the particular product (e.g., 1 consecutive day).

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SITEGRy	Pooled Site Group y	Char		If applicable. Only when study sites are pooled
AGE	Age	Num		DM.AGE.
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX.
RACE	Race	Char	(RACE)	DM.RACE.
SAFFL	Safety Population Flag	Char	Y, N	These flags identify whether or not the subject is included in the specified population. A minimum of one subject-level population flag variable should be included in ADSL.

SAFEREAS	*Reason for exclusion from safety population*	*Char*		
ITTFL	Intent-To-Treat Population Flag	Char	Y, N	
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	MITT population includes subjects who were randomized and applied study product.
MITTREAS	*Reason for exclusion from mITT population*	*Char*		
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPREAS	*Reason for exclusion from PP population*	*Char*		
ARM	Description of Planned Arm	Char		DM.ARM
RANDFL	Randomized Population Flag	Char	Y,N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment	Char	A, B, C	TRTP would be the treatment to which the subject was randomized. TRTP might be derived from the SDTM DM variable ARM. e.g. A=Test, B= Reference, C=Placebo
TRT01PN	Planned Treatment	Num	1, 2, 3	1 = Test, 2 = Reference, 3 = Placebo
TRT01A	Name of Actual Treatment	Char	A, B, C	e.g. A=Test, B= Reference, C=Placebo
TRT01AN	Name of Actual Treatment	Num	1, 2, 3	1 = Test, 2 = Reference, 3 = Placebo
EXLOC	*Location of Treatment Area*	*Char*		*e.g. RC=right cheek, RF=right forehead, F=right and left forehead, S=bald scalp, etc.*
ENRLDT	Date of Enrollment	Num		
TRTSDTM	Datetime of First Exposure to Treatment	Num		Datetime of first exposure to treatment for a subject in a study.
TRTSDTF	Date of First Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of first exposure to treatment. If the date part of TRTSDTM was imputed, TRTSDTF should be populated .
TRTSTMF	Time of First Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of first exposure to treatment. If the time part of TRTSDTM was imputed, TRTSTMF should be populated .
TRTEDTM	Datetime of Last Exposure to Treatment	Num		Datetime of last exposure to treatment for a subject in a study.

TRTEDTF	Date of Last Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of last exposure to treatment. If the date part of TRTEDTM was imputed, TRTEDTF should be populated .
TRTETMF	Time of Last Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of last exposure to treatment. If the time part of TRTEDTM was imputed, TRTETMF should be populated .
EOSSTT	End of Study Status	Char		The subject's status as of the end of study or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
EOSDT	End of Study Date	Num		Date subject ended the study – either date of completion or date of discontinuation or data cutoff date for interim analyses.
DCSREAS	Reason for Discontinuation from Study	Char		Reason for subject's discontinuation from study. Null for subjects who completed the study.
DCSREASP	Reason Spec for Discont from Study	Char		Additional detail regarding subject's discontinuation from study (e.g., description of "other").
ADDTRTFL	*Subject required additional treatment due to unsatisfactory treatment response*	*Char*	*Y, N*	*Y=Yes, N=No*
EOTSTT	End of Treatment Status	Char		The subject's status as of the end of treatment or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
DCTREAS	Reason for Discontinuation of Treatment	Char		If a subject discontinued treatment in the study, then this variable indicates the reason for discontinuation. This is for discontinuation of treatment in the overall study and should not be used for discontinuation reason within individual treatment periods.
DCTREASP	Reason Spec for Discontinuation of Treatment	Char		Additional detail regarding subject's discontinuation from treatment (e.g., description of "other").
RANDDT	Date of Randomization	Num		User should populate if randomized trial
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*Y if the subject met all inclusion and exclusion criteria.*
TRCMP	Treatment Compliance (%)	Num		Overall percent compliance with treatment in the trial.
MISDOSFL	*Missed the scheduled applications for more than pre-specified number of consecutive days*	*Char*	*Y, N*	*Y=Yes, N=No*
TRTDURD	Total Treatment Duration (Days)	Num		Total treatment duration, as measured in days.

AKNUMBL	*Total number of AK lesion in the treatment area at baseline*	*Num*		
AKNUM4BL	*Total number of AK lesion in the treatment area at baseline with at least 4mm in diameter*	*Num*		
SUCCFL	*Final designation as treatment success or failure*	*Char*	*Y, N*	*Y=Success, N=Failure* *Treatment success is defined as 100% clearance of all AK lesions within the treatment area*
AEFL	Adverse Event reported	Char	Y, N	Y=Yes, N=No
CMFL	Concomitant Medication	Char	Y, N	Y=Yes, N=No
EVAL	*Evaluator Initial*	*Char*		

2.4.2 Analysis Dataset for AK Lesion (ADAK)

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SAFFL	Safety Population Flag	Char	Y, N	These indicators identify whether or not the subject is included in the analysis population for the specific parameter.
MITTFL	Modified Intent-To-Treat Flag	Char	Y, N	
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
TRTP	Planned Treatment	Char	A, B, C	A=Test, B= Reference , C=Placebo
TRTPN	Planned Treatment	Num	1, 2, 3	1=Test, 2= Reference , 3=Placebo
TRTA	Actual Treatment	Char	A, B, C	A=Test, B= Reference , C=Placebo
TRTAN	Actual Treatment	Num	1, 2, 3	1=Test, 2= Reference , 3=Placebo

ADT	Analysis Date	Num		The date associated with AVAL and /or AVALC in numeric format recorded in the CRF
ADY	Analysis Relative Day	Num		The relative day of AVAL and/or AVALC. The number of days from the baseline date (not necessarily DM.RFSTDTC) to ADT.
AVISIT	Analysis Visit	Char		The analysis visit description
AVISITN	Analysis Visit	Num		A numeric representation of analysis visit description
AWFL	*Visit window*	*Char*	*Y, N*	*Y, if the visit is within the visit window.*
AWDAYS	*Visit Window Days*	*Num*		*AWDAYS=actual visit date minus the scheduled visit date, e.g, actual visit happened on Day 5 but the scheduled visit should be on Day 8. Then, AWDAYS = -3. Or actual visit happened on Day 10 but the scheduled visit should be on*
PARAM	Parameter	Char		Total number of AK lesion, erythema score, burning/stinging score, erosion score, edema score, pain score, itching score, treatment success or failure
PARAMCD	Parameter Code	Char		AK= Total number of AK lesion ERY=Skin reaction erythema score, BURSTI=Skin reaction burning/stinging score EROSION =Skin reaction erosion score
AVAL	Analysis Value	Num		Skin reaction score, e.g., 0=absent, 1=mild, (slight, barely perceptible), 2=moderate (distinct presence), 3=severe (marked, intense)
DTYPE	Derivation Type	Char		e.g. LOCF=last observation carried forward
ADDTRTFL	*Additional Treatment required during this visit*	*Char*	*Y, N*	*Y=Yes, N=No*
ADDTRT	*Additional Treatment Drug Name*	*Char*		*The drug name of the additional treatment due to unsatisfactory treatment response*
NEWAKFL	*New AK Lesion appears*	*Char*	*Y, N*	*Y=Yes, N=No*
NEWAK	*Number of New AK Lesion*	*Num*		*Number of new AK lesion developed*
AERFL	Adverse event reported during this visit	Char	Y, N	Y=Yes, N=No

CMRFL	Concomitant medication reported during this visit	Char	Y, N	Y=Yes, N=No
LBRFL	Laboratory testing performed during this visit	Char	Y, N	Y=Yes, N=No

2.5 Treatment Success Based on Physician's Global Assessment (PGA) and Psoriasis Area Severity Index (PASI)

The applicant should define the treatment success on PGA and clinical success on PASI and any other derived variable such as treatment compliance in define.xml and/or define.pdf files based on the study design. If the applicant uses a different formula to calculate such variables, justification should be provided in the submission. The tables below specify the recommended data elements and format that should be included in the analysis datasets.

2.5.1 ADSL Table

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SITEGRy	Pooled Site Group y	Char		User should populate if the sites are pooled.
AGE	Age	Num		DM.AGE.
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX.
RACE	Race	Char	(RACE)	DM.RACE.
SAFFL	Safety Population Flag	Char	Y, N	These flags identify whether or not the subject is included in the specified population. A minimum of one subject-level population flag variable should be included in ADSL.
SAFRS	*Reason for Excl from Safety Population*	*Char*		Reason for Exclusion from Safety Population.
ITTFL	Intent-To-Treat Population Flag	Char	Y, N	
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	

MITTRS	*Reason for Excl from mITT Population*	*Char*		Reason for Exclusion from mITT Population.
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPROTRS	*Reason for Excl from PP Population*	*Char*		Reason for Exclusion from PP Population.
RANDFL	Randomized Population Flag	Char	Y, N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment	Char		
TRT01PN	Planned Treatment (N)	Num		
TRT01A	Actual Treatment	Char		
TRT01AN	Actual Treatment (N)	Num		
TRTSDTM	Datetime of First Exposure to Treatment	Num		Datetime of first exposure to treatment for a subject in a study.
TRTSDTF	Date of First Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of first exposure to treatment. If the date part of TRTSDTM was imputed, TRTSDTF should be populated
TRTSTMF	Time of First Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of first exposure to treatment. If the time part of TRTSDTM was imputed, TRTSTMF should be populated
TRTEDTM	Datetime of Last Exposure to Treatment	Num		Datetime of last exposure to treatment for a subject in a study.
TRTEDTF	Date of Last Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of last exposure to treatment. If the date part of TRTEDTM was imputed, TRTEDTF should be populated
TRTETMF	Time of Last Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of last exposure to treatment. If the time part of TRTEDTM was imputed, TRTETMF should be populated
EOSSTT	End of Study Status	Char		The subject's status as of the end of study or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
EOSDT	End of Study Date	Num		Date subject ended the study – either date of completion or date of discontinuation.
EOSDTF	End of Study Date Imput. Flag	Char	(DATEFL)	The level of imputation of the end of study date. If EOSDT was imputed, EOSDTF should be populated.
DCSREAS	Reason for Discontinuation from Study	Char		Reason for subject's discontinuation from study. Null for subjects who completed the study. The reasons should be consistently written, i.e., the same reason should be written identically using the same character string.
DCSREASP	Reason Spec for Discont from Study	Char		Additional detail regarding subject's discontinuation from study (e.g., description of "other").

EOTSTT	End of Treatment Status	Char		The subject's status as of the end of treatment or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
DCTREAS	Reason for Discontinuation of Treatment	Char		If a subject discontinued treatment in the study, then this variable should indicate the reason for discontinuation. The reasons should be consistently written, i.e., the same reason should be written identically using the same character string.
DCTREASP	Reason Spec for Discont of Treatment	Char		Additional detail regarding subject's discontinuation from treatment (e.g., description of "other").
ENRLDT	Date of Enrollment	Num		Date of subject's enrollment into trial.
RANDDT	Date of Randomization	Num		User should populate if randomized trial.
TRCMP	Treatment Compliance (%)	Num		
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*Y if the subject met all inclusion and exclusion criteria*
PGAFL	*PGA Treatment Success Flag*	*Char*	*Y,N*	*Whether the subject has treatment success on PGA based on CRIT1FL in the analysis dataset*
PASIFL	*PASI Clinical Success Flag*	*Char*	*Y,N*	*Whether the subject has clinical success on PASI based on CRIT2FL in the analysis dataset*
TDOSE	*Total Dose (Weight)*	*Num*		*Total weight of doses during the treatment, if applicable*
TDOSEU	*Total Dose (Weight) Units*	*Char*		*Unit of total dose*
PKTRGH	*PK Trough Level*	*Num*		*PK trough level for the subject during the treatment*
PKTRGHU	*PK Trough Level Units*	*Char*		*Unit of PK trough level*
BSABL	*Percent of BSA Involvement at Baseline*	*Num*		*Percent of Body Surface Area Involvement at Baseline*
EXLOC	*Location of Treatment Area*	*Char*		*Location of treatment area, e.g., Arm, Leg, Face, etc.*
SIZETRT	*Size of Treatment Area*	*Num*		
SIZETRTU	*Units of the Size of Treatment Area*	*Char*		*For example, cm^2.*
AEFL	Adverse Event reported	Char	Y, N	Y=Yes, N=No
CMFL	Concomitant Medication	Char	Y, N	Y=Yes, N=No
EVAL	*Evaluator initial*	*Char*		

2.5.2 Analysis Dataset for Treatment Success based on PGA and PASI (ADGS)

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes

STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SAFFL	Safety Population Flag	Char	Y, N	These flags identify whether or not the subject is included in the specified population. A minimum of one subject-level population flag variable should be included in ADSL.
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRTP	Planned Treatment	Char		
TRTPN	Planned Treatment (N)	Num		
TRTA	Actual Treatment	Char		
TRTAN	Actual Treatment (N)	Num		
AVISIT	Analysis Visit	Char		
AVISITN	Analysis Visit (N)	Num		
ADY	Analysis Relative Day	Num		The relative day of AVAL and AVALC. The number of days from randomization.
ADT	Analysis Date	Num		The date recorded in the CRF
ADM	Analysis Time	Num		
ADTM	Analysis Datetime	Num		The datetime recorded in the CRF
ADTF	Analysis Date Imputation Flag	Char	(DATEFL)	The level of imputation of analysis date. If ADT (or date part of ADTM) was imputed, ADTF should be populated.
ATMF	Analysis Time Imputation Flag	Char	(TIMEFL)	The level of imputation of analysis time. If ATM (or time part of ADTM) was imputed, ATMF should be populated.

PARAM	Parameter	Char		Physician's Global Assessment (PGA) score (0-5) Psoriasis Area Severity Index (PASI) score (0-5) - Total Score* PASI Erythema score (0-5) PASI Scaling score (0-5) PASI Plaque elevation score (0-5) PGA treatment success (Y, N) PASI clinical success (Y, N) Skin reaction erythema score (0-3) Skin reaction dryness score (0-3) Skin reaction burning score (0-3) Skin reaction erosion score (0-3) Skin reaction edema score (0-3) Skin reaction pain score (0-3) Skin reaction itching score (0-3)
PARAMCD	Parameter Code	Char		PGA=Physician's Global Assessment (PGA) score (0-5) PASI_TOT=Psoriasis Area Severity Index (PASI) score (0-5) Total Score* PASI_E=PASI Erythema score (0-5) PASI_S=PASI Scaling score (0-5) PASI_P=PASI Plaque elevation score (0-5) PGA_TS=PGA treatment success (Y, N) PASI_CS=PASI clinical success (Y, N) SR_ERTH=Skin reaction erythema score (0-3) SR_DRNS=Skin reaction dryness score (0-3) SR_BRNG=Skin reaction burning score (0-3) SR_ERSN=Skin reaction erosion score (0-3) SR_EDMA=Skin reaction edema score (0-3) SR_PAIN=Skin reaction pain score (0-3) SR_ITCH=Skin reaction itching score (0-3) CLINICAL_SUCCESS= PASI_E⩽1 and PASI_S⩽1 and PASI_P⩽1 (YN)
PARCAT1	Parameter Category 1	Char		PGA, PASI
AVAL	Analysis Value	Num		Numeric analysis value described by PARAM. If AVAL represents categories for a parameter, all possible values of that parameter should be listed and the mapping between AVAL and AVALC should be stated in define.xml.
AVALC	Analysis Value (C)	Char		Character analysis value described by PARAM. All possible character values of the parameter should be listed and the mapping between AVAL and AVALC should be stated in define.xml.
CRIT1	Analysis Criterion 1	Char		PGA≤1 (treatment success)
CRIT1FL	Criterion 1 Evaluation Result	Char	Y	
CRIT2	Analysis Criterion 2	Char		PASI_E≤1 and PASI_S≤1 and PASI_P≤1 (clinical success)
CRIT2FL	Criterion 2 Evaluation Result	Char	Y	
ABLFL	Baseline Record Flag	Char	Y	Character indicator to identify the baseline record for each subject and parameter
BASE	Baseline Value	Num		
CHG	Change from Baseline	Num		AVAL-BASE

DTYPE	Derivation Type	Char	(DTYPE)	For example, LOCF
CA	*Serum Calcium Level*	*Num*		
CAU	*Units of Serum Calcium Level*	*Char*		
ALB	*Serum Albumin Level*	*Num*		
ALBU	*Units of Serum Albumin Level*	*Char*		
CACR	*Albumin-Corrected Serum Calcium Level*	*Num*		
CACRU	*Units of Albumin-Corrected Serum*	*Char*		
ANPTRT	*Previous Use of Antineoplastic Treatment*	*Char*	*Y, N*	
ADDTRTFL	*Additional Trt required during this visit*	*Char*		*Additional Treatment required during this visit. Y=Yes, N=No*
ADDTRT	*Additional Treatment Drug Name*	*Char*		*The drug name of the additional treatment due to unsatisfactory treatment response*
AERFL	Adverse Event Flag	Char	Y, N	The variable indicates if the subject had any adverse events during the visit.
CMRFL	Concomitant Medication Flag	Char	Y, N	The variable indicates if the subject had taken any concomitant medications during the visit.
LBRFL	Laboratory Test Flag	Char	Y, N	The variable indicates if laboratory testing was performed during the visit.
EVAL	*Evaluator initial*	*Char*		

2.6 Total Nasal Symptom Score

This section provides examples of data tables for nasal spray studies. The data tables provide some specific examples of treatment (dosing) compliance, rating compliance, criteria for placebo responder, which ratings are used to calculate the baseline total nasal symptom scores and the treatment period average of the total nasal symptom scores, etc. The applicant should define such variables or any other derived variables in define.xml based on the study design. If the applicant uses a different formula to calculate such variables, justification should be provided in the submission. The tables below specify the recommended data elements and format that should be included in the analysis datasets.

2.6.1 ADSL Table

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID

SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SITEGRy	Pooled Site Group y	Char		User should complete if the sites are pooled.
AGE	Age	Num		DM.AGE.
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX.
RACE	Race	Char	(RACE)	DM.RACE.
SAFFL	Safety Population Flag	Char	Y, N	These flags identify whether or not the subject is included in the specified population. A minimum of one subject-level population flag variable should be completed in ADSL
SAFEREAS	*Reason for Exclfrom Safety Population*	*Char*		Reason for Exclusion from Safety Population
ITTFL	Intent-To-Treat Population Flag	Char	Y, N	
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	
MITTREAS	*Reason for Excl from mITT Population*	*Char*		Reason for Exclusion from mITT Population
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPREAS	*Reason for Excl from PP Population*	*Char*		Reason for Exclusion from PP Population
RANDFL	Randomized Population Flag	Char	Y, N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment for Period 1	Char		Period 1= Placebo run-in period
TRT01PN	Planned Treatment for Period 1 (N)	Num		Period 1= Placebo run-in period
TRT01A	Actual Treatment for Period 1	Char		Period 1= Placebo run-in period
TRT01AN	Actual Treatment for Period 1 (N)	Num		Period 1= Placebo run-in period
TRT02P	Planned Treatment for Period 2	Char		Period 2= Active treatment period
TRT02PN	Planned Treatment for Period 2 (N)	Num		Period 2= Active treatment period
TRT02A	Actual Treatment for Period 2	Char		Period 2= Active treatment period
TRT02AN	Actual Treatment for Period 2 (N)	Num		Period 2= Active treatment period
TR01SDTM	Datetime First Exposure in Period 1	Num		Datetime of first exposure to treatment for a subject in Period 1.
TR01SDTF	Date 1st Exposure Period 1 Imput. Flag	Char	(DATEFL)	The level of imputation of date of first exposure to treatment in Period 1. If the date part of TR01SDTM was imputed, TR01SDTF should be populated.

TR01STMF	Time 1st Exposure Period 1 Imput. Flag	Char	(TIMEFL)	The level of imputation of time of first exposure to treatment in Period 1. If the time part of TR01SDTM was imputed, TR01STMF should be populated.
TR01EDTM	Datetime Last Exposure in Period 1	Num		The datetime of last exposure to treatment for a subject in Period 1
TR01EDTF	Date Last Exposure Period 1 Imput. Flag	Char	(DATEFL)	The level of imputation of date of last exposure to treatment in Period 1. If the date part of TR01EDTM was imputed, TR01EDTF should be populated.
TR01ETMF	Time Last Exposure Period 1 Imput. Flag	Char	(TIMEFL)	The level of imputation of time of last exposure to treatment in Period 1. If the time part of TR01EDTM was imputed, TR01ETMF should be populated.
TR02SDTM	Datetime First Exposure in Period 2	Num		Datetime of first exposure to treatment for a subject in Period 2.
TR02SDTF	Date First Exposure Period 2 Imput. Flag	Char	(DATEFL)	The level of imputation of date of first exposure to treatment in Period 2. If the date part of TR02SDTM was imputed, TR02SDTF should be populated.
TR02STMF	Time 1st Exposure Period 2 Imput. Flag	Char	(TIMEFL)	The level of imputation of time of first exposure to treatment in Period 2. If the time part of TR02SDTM was imputed, TR02STMF should be populated.
TR02EDTM	Datetime Last Exposure in Period 2	Num		The datetime of last exposure to treatment for a subject in Period 2
TR02EDTF	Date Last Exposure Period 2 Imput. Flag	Char	(DATEFL)	The level of imputation of date of last exposure to treatment in Period 2. If the date part of TR02EDTM was imputed, TR02EDTF should be populated.
TR02ETMF	Time Last Exposure Period 2 Imput. Flag	Char	(TIMEFL)	The level of imputation of time of last exposure to treatment in Period 2. If the time part of TR02EDTM was imputed, TR02ETMF should be populated.
EOSSTT	End of Study Status	Char		The subject's status as of the end of study or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
EOSDT	End of Study Date	Num		Date subject ended the study – either date of completion or date of discontinuation.
EOSDTF	End of Study Date Imput. Flag	Char	(DATEFL)	The level of imputation of the end of study date. If EOSDT was imputed, EOSDTF should be populated.
DCSREAS	Reason for Discontinuation from Study	Char		Reason for subject's discontinuation from study. Null for subjects who completed the study.
DCSREASP	Reason Spec for Discont from Study	Char		Additional detail regarding subject's discontinuation from study (e.g., description of "other").
EOTSTT	End of Treatment Status	Char		The subject's status as of the end of treatment or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.

DCTREAS	Reason for Discontinuation of Treatment	Char		If a subject discontinued treatment in the study, then this variable indicates the reason for discontinuation. This is for discontinuation of treatment in the overall study and should not be used for discontinuation reason within individual treatment periods. The reasons should be consistently written, i.e., the same reason should be written identically using the same character string.
DCTREASP	Reason Spec for Discont of Treatment	Char		Additional detail regarding subject's discontinuation from treatment (e.g., description of "other").
EOT01STT	End of Treatment Status in Period 1	Char		The subject's treatment status as of the end of period 1, or data cutoff if within period 1. Examples: COMPLETED, DISCONTINUED, ONGOING.
DCT01RS	Reason for Discont of Trt in Period 1	Char		Reason for discontinuing treatment in period 1. The reasons should be consistently written, i.e., the same reason should be written identically using the same character string.
DCT01RSP	Reason Spec Discont of Trt in Period 1	Char		Additional detail regarding subject's discontinuation from treatment in period 1 (e.g., description of "other").
EOT02STT	End of Treatment Status in Period 2	Char		The subject's treatment status as of the end of period 2, or data cutoff if within period 2. Examples: COMPLETED, DISCONTINUED, ONGOING.
DCT02RS	Reason for Discont of Trt in Period 2	Char		Reason for discontinuing treatment in period 2. The reasons should be consistently written, i.e., the same reason should be written identically using the same character string.
DCT02RSP	Reason Spec Discont of Trt in Period 2	Char		Additional detail regarding subject's discontinuation from treatment in period 2 (e.g., description of "other").
ENRLDT	Date of Enrollment	Num		Date of subject's enrollment into trial.
RANDDT	Date of Randomization	Num		User should populate if randomized trial
TRCMP01	Treatment Compliance (%) in Period 1	Num		For example, 100% x (Number of daily doses taken in the last 7 days of Period 1)/7
TRCMP02	Treatment Compliance (%) in Period 2	Num		For example, 100% x (Number of daily doses taken in the first 14 days of Period 2)/14
NDOSE01	*Num of Doses in Last X Days of Period 1*	*Num*		*For example, Number of Doses in Last 7 Days of Period 1*
NDOSE02	*Num of Doses in the First X Days of Period 2*	*Num*		*For example, Number of Doses in the First 14 Days of Period 2*
RRT01	*Non-missing Refl Ratings in Last X in P1*	*Num*		*Number of Non-missing Reflective Ratings Among the Last X Scheduled Ratings in Period 1. For example, number of non-missing reflective ratings among the last 7 scheduled ratings in Period 1. For a scheduled reflective rating to be non-missing, all reflective symptom scores should be non-missing for that rating.*
RRT02	*Non-missing Refl Ratings in 1st X in P2*	*Num*		*Number of Non-missing Reflective Ratings Among the First X Scheduled Ratings in Period 2. For example, number of non-missing reflective ratings among the first 27 scheduled ratings in Period 2. For a scheduled reflective rating to be non-missing, all reflective symptom scores should be non-missing for that rating.*

IRT01	*Non-missing Inst Ratings in Last X in P1*	*Num*		*Number of Non-missing Instantaneous Ratings Among the Last XScheduled Ratings in Period 1. For example, number of non-missing instantaneous ratings among the last 7 scheduled ratings in Period 1. For a scheduled instantaneous rating to be non-missing, all instantaneous symptom scores should be non-missing for that rating.*
IRT02	*Non-missing Inst Ratings in 1st X in P2*	*Num*		*Number of Non-missing Instantaneous Ratings Among the First X Scheduled Ratings in Period 2. For example, number of non-missing instantaneous ratings among the first 27 scheduled ratings in Period 2. For a scheduled instantaneous rating to be non-missing, all instantaneous symptom scores should be non-missing for that rating.*
RRTCMP01	*Rating Compliance for Refl Symptoms in P1*	*Num*		*Rating Compliance (%) for Reflective Symptoms in Period 1. For example, 100% x(Number of non-missing reflective ratings among the last 7 scheduled ratings in Period 1)/7*
RRTCMP02	*Rating Compliance for Refl Symptoms in P2*	*Num*		*Rating Compliance (%) for Reflective Symptoms in Period 2. For example, 100% x(Number of non-missing reflective ratings among the first 27 scheduled ratings in Period 2)/27*
IRTCMP01	*Rating Compliance for Inst Symptoms in P1*	*Num*		*Rating Compliance (%) for Instantaneous Symptoms in Period 1. For example, 100% x(Number of non-missing instantaneous ratings among the last 7 scheduled ratings in Period 1)/7*
IRTCMP02	*Rating Compliance for Inst Symptoms in P2*	*Num*		*Rating Compliance (%) for Instantaneous Symptoms in Period 2. For example, 100% x(Number of non-missing instantaneous ratings among the first 27 scheduled ratings in Period 2)/27*
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*Y if the subject met all inclusion and exclusion criteria*
PLRESPFL	*Placebo Responder Flag*	*Char*	*Y,N*	*Whether the subject is a placebo responder based on CRIT1FL in the analysis dataset*
ITNSSBL	*Baseline ITNSS*	*Num*		*Baseline Instantaneous Total Nasal Symptom Score. Should be same as the value of AVAL for the parameter BITNSS in the analysis dataset*
TITNSS	*Avg ITNSS in Active Treatment Period*	*Num*		*Average Instantaneous Total Nasal Symptom Score During the Active Treatment Period. Should be same as the value of AVAL for the parameter TITNSS in the analysis dataset*
RTNSSBL	*Baseline RTNSS*	*Num*		*Baseline Reflective Total Nasal Symptom Score. Should be same as the value of AVAL for the parameter BRTNSS in the analysis dataset*
TRTNSS	*Avg RTNSS in Active Treatment Period*	*Num*		*Average Reflective Total Nasal Symptom Score During the Active Treatment Period. Should be same as the value of AVAL for the parameter TRTNSS in the analysis dataset*
AEFL	Adverse Event Flag	Char	Y, N	Y=Yes, N=No The variable indicates if the subject had any adverse events during the study.
CMFL	Concomitant Medication Flag	Char	Y, N	Y=Yes, N=No The variable indicates if the subject had taken any concomitant medications during the study.
EVAL	*Evaluator initial*	*Char*		

2.6.2 Analysis Dataset for Total Nasal Symptom Score (ADNS)

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SAFFL	Safety Population Flag	Char	Y, N	These indicators identify whether or not the subject is included in the analysis population for the specific parameter.
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
TRT01P	Planned Treatment for Period 1	Char		Period 1= Placebo run-in period
TRT01PN	Planned Treatment for Period 1 (N)	Num		Period 1= Placebo run-in period
TRT01A	Actual Treatment for Period 1	Char		Period 1= Placebo run-in period
TRT01AN	Actual Treatment for Period 1 (N)	Num		Period 1= Placebo run-in period
TRT02P	Planned Treatment for Period 2	Char		Period 2 = Active treatment period
TRT02PN	Planned Treatment for Period 2 (N)	Num		Period 2= Active treatment period
TRT02A	Actual Treatment for Period 2	Char		Period 2 = Active treatment period
TRT02AN	Actual Treatment for Period 2 (N)	Num		Period 2= Active treatment period
APERIOD	Period	Num	1, 2	Period: Period 1= Placebo run-in period, Period 2 = Active treatment period
ADY	Analysis Relative Day	Num		The relative day of AVAL and AVALC. The number of days from randomization date. For example, placebo lead-in period days are -7, -6,…,-1 and active treatment period days are 1, 2, …, 14.
ATPT	Analysis Timepoint	Char		Analysis timepoint within ADY. 0H=0 hour, 12H=12 hours, etc recorded in the CRF.
ATPTN	Analysis Timepoint (N)	Num		Numeric value for analysis timepoint within ADY. 0=0 hour, 12=12 hours, etc.
ATPTREF	Analysis Timepoint Reference	Char		
ADTM	Analysis Datetime	Num		The datetime recorded in the CRF.
ADTF	Analysis Date Imputation Flag	Char	(DATEFL)	The level of imputation of analysis date. If ADT (or date part of ADTM) was imputed, ADTF should be populated.
ATMF	Analysis Time Imputation Flag	Char	(TIMEFL)	The level of imputation of analysis time. If ATM (or time part of ADTM) was imputed, ATMF should be populated.

PARAM	Parameter	Char		Instantaneous nasal congestion rating Instantaneous runny nose rating Instantaneous sneezing rating Instantaneous itchy nose rating Instantaneous total nasal symptom score* Reflective nasal congestion rating Reflective runny nose rating Reflective sneezing rating Reflective itchy nose rating Reflective total nasal symptom score** Average baseline instantaneous total nasal symptom score Average treatment period instantaneous total nasal symptom score Average baseline reflective total nasal symptom score Average treatment period reflective total nasal symptom score
PARAMCD	Parameter Code	Char		INC = Instantaneous nasal congestion rating IRN = Instantaneous runny nose rating ISN = Instantaneous sneezing rating IIN = Instantaneous itchy nose rating ITNSS = Instantaneous total nasal symptom score RNC = Reflective nasal congestion rating RRN = Reflective runny nose rating RSN = Reflective sneezing rating RIN = Reflective itchy nose rating RTNSS = Reflective total nasal symptom score BITNSS = Average baseline instantaneous total nasal symptom score TITNSS = Average treatment period instantaneous total nasal symptom score BRTNSS = Average baseline reflective total nasal symptom score TRTNSS = Average treatment period reflective total nasal symptom score
PARCAT1	Parameter Category 1	Char		Instantaneous (if PARAMCD is one of INC, IRN, ISN, IIN, ITNSS, BITNSS, TITNSS), Reflective (if PARAMCD is one of RNC, RRN, RSN, RIN, RTNSS, BRTNSS, TRTNSS)
AVAL	Analysis Value	Num		Numeric analysis value described by PARAM
ABLFL	Baseline Record Flag	Char	Y	Character indicator to identify the baseline record for each subject and parameter
BASE	Baseline Value	Num		The value of BITTNS for ITNSS and TITNSS and the value of BRTTNS for RTNSS and TRTNSS
CHG	Change from Baseline	Num		AVAL - BASE
ANL01FL	Analysis Flag 01 for Baseline Calc	Char	Y	This flag indicated the records used for calculation of the baseline of a parameter, for example, the final 7 records of ITNSS or RTNSS to calculate the corresponding baseline value
ANL02FL	Analysis Flag 02 for Endpoint Calc	Char	Y	This flag indicated the records used for calculation of the baseline of a parameter, for example, the first 27 values of ITNSS or RTNSS to calculate the average of the corresponding parameter during the active treatment period.
CRIT1	Analysis Criterion 1	Char		A text string identifying placebo responders, for example, BRTNSS of at least 6. It should be populated for every row of the relevant parameter, for example BRTNSS.

CRIT1FL	Criterion 1 Evaluation Result Flag	Char	Y	Character flag variable indicating whether the criterion defined in CRIT1 was met by the data on the record.
DTYPE	Derivation Type	Char	(DTYPE)	For example, AVERAGE for BITNSS, TITTNS, BRTTNS or TRTNSS
AERFL	Adverse Event reported during this visit	Char		Y=Yes, N=No
CMRFL	Concomitant Med reported at this visit	Char		Y=Yes, N=No

*Instantaneous total nasal symptom score (ITNSS) for a subject for a time point is the sum of INC, IRN, ISN, IIN for the same subject for the same time point.
**Reflective total nasal symptom score (RTNSS) for a subject for a time point is the sum of RNC, RRN, RSN, RIN for the same subject for the same time point.

2.7 Intraocular Pressure

This section provides the examples of data tables for the comparative clinical endpoint studies using the primary endpoint of intraocular pressure for both eyes. The tables below provide the recommended data elements and format that should be included in the analysis datasets.

2.7.1 ADSL Table

Applicant should calculate the study drug compliance rate based on the scheduled doses for the specified duration of the study for the particular product. Applicant should provide the formula or algorithm in the submission.

The variable "MISDOSFL" is used to capture the information if a subject misses the pre-specified number of scheduled doses for more than pre-specified number of consecutive days for the particular product (e.g., 1 consecutive day).

Applicant should provide the population flag variable for the modified ITT population if it is pre-specified in the protocol.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SITEGRy	Pooled Site Group y	Char		User should complete if the sites are pooled.
AGE	Age	Num		DM.AGE.
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX.
RACE	Race	Char	(RACE)	DM.RACE.

IRISCOL	*Iris Color*	*Char*		
SAFFL	Safety Population Flag	Char	Y, N	These flags identify whether or not the subject is included in the specified population. A minimum of one subject-level population flag variable should be included in ADSL.
SAFEREAS	*Reason for exclusion from safety population*	*Char*		
ITTFL	Intent-To-Treat Population Flag	Char	Y, N	
MITTFL	Modified Intent-To-Treat Population Flag (if applicable)	Char	Y, N	
MITTREAS	*Reason for exclusion from mITT population (if applicable)*	*Char*		
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPREAS	*Reason for exclusion from PP population*	*Char*		
RANDFL	Randomized Population Flag	Char	Y,N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment	Char	A, B	TRTP should be the treatment to which the subject was randomized. TRTP might be derived from the SDTM DM variable ARM. e.g., A=Test, B= Reference
TRT01PN	Planned Treatment	Num	1, 2	1 = Test, 2 = Reference
TRT01A	Name of Actual Treatment	Char	A, B	e.g., A=Test, B= Reference
TRT01AN	Name of Actual Treatment	Num	1, 2	1 = Test, 2 = Reference
ENRLDT	Date of Enrollment	Num		
TRTSDTM	Datetime of First Exposure to Treatment	Num		Datetime of first exposure to treatment for a subject in a study.
TRTSDTF	Date of First Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of first exposure to treatment. If the date part of TRTSDTM) was imputed, TRTSDTF should be populated .
TRTSTMF	Time of First Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of first exposure to treatment. If the time part of TRTSDTM) was imputed, TRTSTMF should be populated .
TRTEDTM	Datetime of Last Exposure to Treatment	Num		Datetime of last exposure to treatment for a subject in a study.
TRTEDTF	Date of Last Exposure Imput. Flag	Char	(DATEFL)	The level of imputation of date of last exposure to treatment. If the date part of TRTEDTM) was imputed, TRTEDTF should be populated .
TRTETMF	Time of Last Exposure Imput. Flag	Char	(TIMEFL)	The level of imputation of time of last exposure to treatment. If the time part of TRTEDTM) was imputed, TRTETMF should be populated .

EOSSTT	End of Study Status	Char		The subject's status as of the end of study or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
EOSDT	End of Study Date	Num		Date subject ended the study – either date of completion or date of discontinuation or data cutoff date for interim analyses.
DCSREAS	Reason for Discontinuation from Study	Char		Reason for subject's discontinuation from study. Null for subjects who completed the study.
DCSREASP	Reason Spec for Discont from Study	Char		Additional detail regarding subject's discontinuation from study (e.g., description of "other").
ADDTRTFL	*Subject required additional treatment due to unsatisfactory treatment response*	*Char*	*Y, N*	*Y=Yes, N=No*
EOTSTT	End of Treatment Status	Char		The subject's status as of the end of treatment or data cutoff. Examples: COMPLETED, DISCONTINUED, ONGOING.
DCTREAS	Reason for Discontinuation of Treatment	Char		If a subject discontinued treatment in the study, then this variable should indicate the reason for discontinuation. This is for discontinuation of treatment in the overall study and should not be used for discontinuation reason within individual treatment periods.
DCTREASP	Reason Spec for Discontinuation of Treatment	Char		Additional detail regarding subject's discontinuation from treatment (e.g., description of "other").
RANDDT	Date of Randomization	Num		User should populate if randomized trial
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*Y if the subject met all inclusion and exclusion criteria.*
TRCMP	Treatment Compliance (%)	Num		Overall percent compliance with treatment in the trial.
MISDOSFL	*Missed the scheduled applications for more than pre-specified number of consecutive days*	*Char*	*Y, N*	*Y=Yes, N=No*
TRTDURD	Total Treatment Duration (Days)	Num		Total treatment duration, as measured in days.
IOPLBL	*IOP of left eye at baseline (Day0/hour0)*	*Num*		
IOPRBL	*IOP of right eye at baseline (Day0/hour0)*	*Num*		
VisLBL	*Best corrected visual acuity of left eye at baseline*	*Char*	*Y, N*	*Yes if 20/200 or better*
VisRBL	*Best corrected visual acuity of right eye at baseline*	*Char*	*Y, N*	*Yes if 20/200 or better*
AEFL	Adverse Event reported	Char	Y, N	Y=Yes, N=No
CMFL	Concomitant Medication	Char	Y, N	Y=Yes, N=No
EVAL	*Evaluator initial*	*Char*		

2.7.2 Analysis Dataset for Introcular Pressure (ADIP)

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID.
SITEID	Study Site Identifier	Char		DM.SITEID.
SAFFL	Safety Population Flag	Char	Y, N	These indicators identify whether or not the subject is included in the analysis population.
MITTFL (if applicable)	Modified Intent-To-Treat Flag	Char	Y, N	
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
TRTP	Planned Treatment	Char	A, B	A=Test, B= Reference
TRTPN	Planned Treatment	Num	1, 2	1=Test, 2= Reference
TRTA	Actual Treatment	Char	A, B	A=Test, B= Reference
TRTAN	Actual Treatment	Num	1, 2	1=Test, 2= Reference
ADT	Analysis Date	Num		The date associated with AVAL and /or AVALC in numeric format recorded in the CRF.
ADY	Analysis Relative Day	Num		The relative day of AVAL and/or AVALC. The number of days from the baseline date (not necessarily DM.RFSTDTC) to ADT.
AVISIT	Analysis Visit	Char		The analysis visit description.
AVISITN	Analysis Visit	Num		A numeric representation of analysis visit description.
AWFL	*Visit Window Flag*	*Char*	*Y, N*	*Y, if the visit is within the visit window.*
AWTIME	*Visit Window Time*	*Num*		*AWTIME=actual visit datetime minus the scheduled visit datetime in minutes*
ATPT	Analysis Timepoint	Char		e.g., Hour 0, hour 2
ATPTN	Analysis Timepoint	Num		e.g., 0, 2
PARAM	Parameter	Char		Intraocular pressure (IOP) Left Intraocular pressure (IOP) Right Mean IOP of both eyes
PARAMCD	Parameter Code	Char		IOPL= Intraocular pressure of left eye IOPR= Intraocular pressure of right eye MEANIOP=mean IOP of both eyes
AVAL	Analysis Value	Num		

ADDTRTFL	*Additional Treatment required due to unsatisfactory treatment response during this visit*	*Char*	*Y, N*	*Y=Yes, N=No*
ADDTRT	*Additional treatment drug name*	*Char*		*The drug name of the additional treatment due to unsatisfactory treatment response.*
AERFL	Adverse Event reported during this visit	Char	Y, N	Y=Yes, N=No
CMRFL	Concomitant Medication reported during this visit	Char	Y, N	Y=Yes, N=No

2.8 Therapeutic Cure

This section provides the examples of data tables for the comparative clinical endpoint bioequivalence studies using the primary endpoint of therapeutic cure, defined as both mycological cure and clinical cure. The tables below specify the recommended data elements and format that should be included in the analysis datasets.

2.8.1 ADSL Table

Applicant should calculate the study drug compliance rate based on the scheduled doses for the specified duration of the study for the particular product. Applicant should provide the formula or algorithm in define.xml in the submission.

For the variable “SSINCFL”, please refer to the product specific guidance for the inclusion criteria based on sign and symptom.

The mITT population should include all randomized subjects who applied at least one dose of study medication and had a positive baseline skin fungal culture. For more information regarding specific fungus or fungi, please refer to the product specific guidance.

For the variable “BCULTUR” (Skin Fungal Culture Test at Baseline), please refer to the product specific guidance for the list of fungi to be considered eligible for the per-protocol and modified ITT populations.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID
SITEID	Study Site Identifier	Char		DM.SITEID
SITEGRy	Pooled Site Group y	Char		Should be populated if study sites are pooled.
AGE	Age	Num		DM.AGE
AGEU	Age Units	Char	(AGEU)	DM.AGEU
SEX	Sex	Char	(SEX)	DM.SEX
RACE	Race	Char	(RACE)	DM.RACE

SAFFL	Safety Population Flag	Char	Y, N	
SAFEREAS	*Reason for exclusion from safety population*	*Char*		
ITTFL	Intent-To-Treat Population Flag	Char	Y, N	
MITTFL	Modified Intent-To-Treat Population Flag	Char	Y, N	
MITTREAS	*Reason for exclusion from mITT population*	*Char*		
PPROTFL	Per-Protocol Population Flag	Char	Y, N	
PPREAS	*Reason for exclusion from PP population*	*Char*		
RANDFL	Randomized Population Flag	Char	Y, N	
ARM	Description of Planned Arm	Char		DM.ARM
ACTARM	Description of Actual Arm	Char		DM.ACTARM
TRT01P	Planned Treatment	Char	A, B, C	A=Test, B= Reference, C=Placebo
TRT01PN	Planned Treatment(N)	Num	1, 2, 3	1=Test, 2= Reference, 3=Placebo
TRT01A	Actual Treatment	Char	A, B, C	Should be populated when actual treatment does not match planned. A=Test, B= Reference, C=Placebo
TRT01AN	Actual Treatment (N)	Num	1, 2, 3	1=Test, 2= Reference, 3=Placebo
TRTSDTM	Datetime of First Exposure to Treatment	Num		
TRTSDTF	Date of First Exposure Imput. Flag	Char	(DATEFL)	If the date part of TRTSDTM was imputed, TRTSDTF should be populated.
TRTSTMF	Time of First Exposure Imput. Flag	Char	(TIMEFL)	If the time part of TRTSDTM was imputed, TRTSTMF should be populated.
TRTEDTM	Datetime of Last Exposure to Treatment	Num		
TRTEDTF	Date of Last Exposure Imput. Flag	Char	(DATEFL)	If the date part of TRTEDTM was imputed, TRTEDTF should be populated.
TRTETMF	Time of Last Exposure Imput. Flag	Char	(TIMEFL)	If the time part of TRTEDTM was imputed, TRTETMF should be populated.
EOSSTT	End of Study Status	Char		Examples: COMPLETED, DISCONTINUED, ONGOING.
DCSREAS	Reason for Discontinuation from Study	Char		
DCSREASP	Reason Spec for Discont from Study	Char		If applicable, additional detail regarding subject's discontinuation of study (e.g., description of "other").
EOTSTT	End of Treatment Status	Char		Examples: COMPLETED, DISCONTINUED, ONGOING.
DCTREAS	Reason for Discontinuation of Treatment	Char		

DCTREASP	Reason Specify for Discont of Treatment	Char		If applicable, additional detail regarding subject's discontinuation of treatment (e.g., description of "other").
ENRLDT	Date of Enrollment	Num		
RANDDT	Date of Randomization	Num		User should populate if randomized trial
TRCMP	Treatment Compliance (%)	Num		
TRTDURD	Total Treatment Duration (Days)	Num		Total treatment duration, as measured in days.
DTHDT	Date of Death	Num		
CLICURFL	*Clinical Cure Flag*	*Char*	*Y, N*	*CLICURFL = Y if the subject achieved clinical cure.*
MYCCURFL	*Mycological Cure Flag*	*Char*	*Y, N*	*MYCCURFL = Y if the subject achieved mycological cure.*
THECURFL	*Therapeutic Cure Flag*	*Char*	*Y, N*	*THECURFL = Y if the subject achieved therapeutic cure, defined as both mycological cure and clinical cure.*
CULTURBL	*Skin Fungal Culture Test at Baseline*	*Char*	*Positive, Negative*	*Refer drug specific guidance for the specific fungus/fungi for which the baseline skin fungal culture test is positive.*
TPFLBL	*Clinical Diagnosis of Tinea Pedis at Baseline Flag*	*Char*	*Y, N*	*BTPFL = Y if Clinical Diagnosis of Tinea Pedis at baseline*
KOHBL	*KOH prep result at Baseline*	*Char*	*Positive, Negative*	
FISCRABL	*Fissuring/Cracking Score at Baseline*	*Num*		*Sign and Symptom Scores:* *0 = none (complete absence of any signs for symptoms)* *1 = mild (slight)* *2 = moderate (definitely present)* *3 = severe (marked, intense)*
ERYBL	*Erythema Score at Baseline*	*Num*		
MACBL	*Maceration Score at Baseline*	*Num*		
SCABL	*Scaling Score at Baseline*	*Num*		
PRUBL	*Pruritus Score at Baseline*	*Num*		
BURSTIBL	*Burning/Stinging Score at Baseline*	*Num*		
SSINCFL	*Sign and Symptom Inclusion Criteria Flag*	*Char*	*Y, N*	*SSINCFL = Y if the subject met sign and symptom inclusion criteria defined in the drug specific guidance.*
INEXFL	*Inclusion Exclusion Criteria Flag*	*Char*	*Y, N*	*INEXFL = Y if the subject met all inclusion and exclusion criteria.*
ONYFL	*Medical History of Onychomycosis Flag*	*Char*	*Y, N*	*If applicable.*
AEFL	Adverse Event Flag	Char	Y, N	
CMFL	Concomitant Medication Flag	Char	Y, N	

2.8.2 Analysis Dataset for Therapeutic Cure (ADTC)

Applicant should submit all data to define the clinical cure (based on the sign and symptom) and mycological cure (based on the test results). Please refer to the product specific guidance for the details.

The variable FUNGCDy should be included if the fungal culture test result is positive. Applicant should use multiple variables, e.g., $FUNGCD_1$, $FUNGCD_2$…. if the test result shows multiple fungi present.

The variable "CRITy" is used to define the mycological cure, clinical cure and therapeutic cure. Please refer to the product specific guidance for the definitions.

Variable Name	Variable Label	Type	Codelist/ Controlled Terms	Notes
STUDYID	Study Identifier	Char		DM.STUDYID
USUBJID	Unique Subject Identifier	Char		DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		DM.SUBJID
SITEID	Study Site Identifier	Char		DM.SITEID
SITEGRy	Pooled Site Group y	Char		Should be populated if study sites are pooled.
ITTRFL	Intent-To-Treat Record-Level Flag	Char	Y, N	
MITTRFL	Modified Intent-To-Treat Record-Level Flag	Char	Y, N	
SAFRFL	Safety Analysis Record-Level Flag	Char	Y, N	
PPROTRFL	Per-Protocol Record-Level Flag	Char	Y, N	
TRTP	Planned Treatment	Char	A, B, C	A=Test, B= Reference, C=Placebo
TRTPN	Planned Treatment (N)	Num	1, 2, 3	1=Test, 2= Reference, 3=Placebo
TRTA	Actual Treatment	Char	A, B, C	Should be populated when actual treatment does not match planned. A=Test, B= Reference, C=Placebo
TRTAN	Actual Treatment (N)	Num	1, 2, 3	1=Test, 2= Reference, 3=Placebo
DOSEP	Planned Treatment Dose	Num		
DOSCUMP	Cumulative Planned Treatment Dose	Num		
DOSEA	Actual Treatment Dose	Num		Should be populated when actual treatment does not match planned.
DOSCUMA	Cumulative Actual Treatment Dose	Num		
DOSEU	Treatment Dose Unit	Char		
ADT	Analysis Date	Num		The date recorded in the CRF.

ADY	Analysis Relative Day	Num		The number of days from baseline to ADT (e.g., Day 0, Day 14, Day 42, etc.).
ADTF	Analysis Date Imputation Flag	Char	(DATEFL)	If ADT was imputed, ADTF should be populated.
AVISIT	Analysis Visit	Char		
AVISITN	Analysis Visit (N)	Num		
AWFL	*Visit Window Flag*	*Char*	*Y, N*	*AWFL = Y if the visit is within the visit window.*
AWDAYS	*Visit Window Days*	*Num*		*AWDAYS = actual visit date minus the scheduled visit date, e.g, actual visit happened on Day 5 but the scheduled visit should be on Day 8. Then, AWDAYS = -3. Or actual visit happened on Day 10 but the scheduled visit should be on Day 8. Then, AWDAYS = 2.*
PARAM	Parameter	Char		PARAM should include all signs and symptoms used for clinical cure definition and fungal tests used for mycological cure definition. For example, for Naftifine Hydrochloride, PARAM should include the following analysis parameters: Signs: Fissuring/Cracking, Erythema, Maceration, Scaling Symptoms: Pruritus, Burning/Stinging Total Severity Score: sum of sign and symptom scores Fungal Tests: KOH test, Fungal Culture test
PARAMCD	Parameter Code	Char		The short name of the analysis parameter in PARAM. For example, for Naftifine Hydrochloride, FISCRA = Fissuring/Cracking ERY = Erythema MAC = Maceration SCA = Scaling PRU = PRURITUS BURSTI = Burning/Stinging TOTAL = Total Severity Score KOH = KOH test CULTUR = Fungal Culture test
AVAL	Analysis Value	Num		For example, for Naftifine Hydrochloride, each individual sign and symptom score ranges from 0 to 3, where 0 = none, 1 = mild, 2 = moderate, and 3 = severe; and KOH and fungal culture test results are either 0 (=negative) or 1 (=positive).
DTYPE	Derivation Type	Char	(DTYPE)	Examples of DTYPE are: LOCF = last observation carried forward SUM = sum of values (for Total Severity Score)
FUNGUSy	*Fungus Name*	*Char*		*Should be populated if the fungal culture test results is positive.*
FUNGCDy	*Fungus Code*	*Char*		*FUNGCDy is the short name of the fungus names in FUNGUSy and should have an one-to-one mapping to FUNGUSy.*
ACONy	Analysis Condition y	Char		ACON1 = Mycological Cure ACON2 = Clinical Cure ACON3 = Therapeutic Cure
ACONyFL	Analysis Condition y Evaluation Result Flag	Char	Y, N	ACON1FL = Y if Mycological Cure ACON2FL = Y if Clinical Cure ACON3FL = Y if Therapeutic Cure

AERFL	Adverse Event Record-Level Flag	Char	Y, N	Y if adverse event reported during this visit.
CMRFL	Concomitant Medication Record-Level Flag	Char	Y, N	Y if concomitant medication reported during this visit.
LBRFL	Laboratory Testing Flag	Char	Y, N	Y if laboratory testing during this visit.
EVAL	*Evaluator initials*	*Char*		