SUMMARY TABLES FOR SUBMISSIONS CONTAINING IRRITATION/SENSITIZATION/ADHESION (I/S/A) STUDIES
[Specifically for Transdermal and Topical Delivery Systems (TDS)]

Table 1: Submission Summary

Drug Product Name	
Strength(s)	
Drug Class	
Reference Listed Drug (RLD) or Reference Standard (RS)	
RLD Applicant	
New Drug Application (NDA) #	
Date of RLD Approval	
Approved Indication(s)	

Table 2: Source of Irritation/Sensitization/Adhesion (I/S/A) Study Data

Protocol Number	
Study Title	
Study Design	
Objectives	
Study Period	
Enrollment	# Subjects
National Clinical Trial (NCT) Identifier	
CRO	Name and Contact Information

Table 3: Protocol Review

Protocol Version	Protocol Date(s)	IRB Approval Date(s)	Changes from Previous Version
Original			
Additional versions or amendments			

Table 4: FDA Product-Specific Guidance Deviations (if applicable)

FDA Product-Specific Guidance (PSG) referenced for current study (link):			
Date of Recommendation:			
Last Revised:			
Element of PSG	**Section of PSG**	**Deviation**	**Justification**

Table 5a: Summary of Skin Irritation/Sensitization/Adhesion (I/S/A) Study(ies)

Study type #1:	**Skin Irritation/Sensitization Study**
Study Number:	
Study Title:	
Study Treatment:	Test (mg/hr) Reference (mg/hr) Vehicle/placebo Positive control Negative control
During Induction	
TDS application frequency:	e.g., 3 times a week, every day
TDS size (XX cm^2)	e.g., ½ cut, whole TDS
Application location	e.g., upper shoulder, hip
Simultaneous application on the same subject or parallel?	
Application duration	e.g., 48-72 hours for 21 days
Use of overlay or reinforcement tape	e.g., overlay, reinforcement tape, none
Irritation score evaluation time points	e.g., on days 3, 8, 10, 12, 15, 17, 19, 21
Rest period (days)	e.g., 14 days
Meet FDA non-inferiority limit?	Yes/No
During Challenge	
TDS application location	e.g., upper shoulder, hip
Application duration	e.g., 48 hours
Sensitization score evaluation time points	e.g., 0, 24, 48, 72 hours after removal
Re-challenge initiation (if any)	e.g., 4 to 8 weeks after the conclusion of the challenge phase
Meet FDA non-inferiority limit?	Yes/No
Adhesion evaluation*	
Application duration	e.g., 48-72 hours
Use of overlay or reinforcement tape	Yes/no

Adhesion evaluation time points	e.g., 12, 24, 36, 48, 60, 72 hours after TDS application

*Adhesion is assessed during the irritation/sensitization study to provide assurance that TDS contact with the skin is continuous during the given TDS application. If adhesion is assessed for a PK BE & adhesion study, please use Table 5b below. If adhesion is assessed for an adhesion study, please use Table 5c below.

Table 5b: Adhesion Data from a Two-Way Crossover PK BE & Adhesion Study

Study Type #2:	Adhesion Data from a PK BE & Adhesion Study
Study Number:	
Study Title:	
Study Treatment:	Test (mg/hr) Reference (mg/hr)
TDS size (XX cm^2)	e.g., ½ cut, whole TDS
Application location	e.g., upper shoulder, hip
Application duration	e.g., 48 hours
Adhesion evaluation time points	e.g., 12, 24, 36, 48, 60, 72 hours after TDS application
Use of overlay or reinforcement tape	e.g., overlay, reinforcement tape, none
Meet FDA non-inferiority limit?	Yes/no

Table 5c: Two-Way Crossover or Parallel Design Adhesion Study

Study Type #3:	Adhesion Study
Study Number:	
Study Title:	
Study Treatment:	Test Reference
TDS application frequency:	e.g., 3 times a week, every day
TDS size (XX cm^2)	e.g., ½ cut, whole TDS
Application location	e.g., upper shoulder, hip
Simultaneous application on the same subject or parallel or crossover?	
Application duration	e.g., 48-72 hours for 21 days
Use of overlay or reinforcement tape	Yes/No
Adhesion score evaluation time points	e.g., 12, 24, 36, 48, 60, 72 hours after TDS
Meet FDA non-inferiority limit?	Yes/no

Table 6: Study Center Information

Site Number	Principal Investigator and Location	Subjects Enrolled (n)	Included in Safety Population (n)	Included in PP Population (n)
01				
02				
03				

Table 7: Study Inclusion/Exclusion Criteria

	Inclusion Criteria
1	
2	
3	

	Exclusion Criteria
1	
2	
3	

Table 8: Prohibited Concomitant Medication List

Drug Class, Type or Name	Examples (NOT comprehensive)	Washout Period (minimum)	Notes

Table 9: Product Information

Product	Test	Reference	Placebo/Vehicle
Treatment ID (if applicable)			
Product Name			
Manufacturer			
Batch/Lot #.			
Manufacture Date			
Expiration Date			
Strength			
Dosage Form			
Route of administration			
Dose administered			
Dosing regimen (e.g., BID, QD)			
Dosing duration			
Dosing timing			
Assignment Ratio			
TDS size			
Application site			
Adhesion assessment times			

Table 10: Study Schedule (for example)

Visit Number	**Visit 1**	**Visit 2**	**Visit 3**	
Visit Type	**Baseline**		**End of Study/ Early Termination**	**Unscheduled Visit**
Visit Day	**Day 1**	**Day 4 (± 4 days)**	**Day 14 (± 4 days)**	
Screening/Consent	X			
Demographics	X			
Medical History	X			
Physical Examination	X			
Urine Pregnancy Test	X			
Inclusion/Exclusion Criteria Review	X			
[Applicant to add additional items]				

Table 11: Subject Populations

	Test	Reference	Placebo	Total
Enrolled				
Total Safety Population				
Total PP population for Irritation (PPPI)				
Total exclusion from PPPI				
Reason for exclusion from PPPI				
Adverse events				
Non-compliance				
Voluntary withdrawal				
TDS-free for >24 hr				
Other				
[Applicant to add additional items]				
Total PP Population for Sensitization (PPPS)				
Total exclusion from PPPS				
Reason for exclusion from PPPS				
Adverse events				
Non-compliance				
TDS-free for >24 hr				
Other				
[Applicant to add additional items]				
Total PP Population for Adhesion (PPPA)				
Total exclusion from PPPA				
Reason for exclusion from PPPA				
Adverse events				
Non-compliance				
Other				
[Applicant to add additional items]				

Table 12: Summary of Protocol Deviations

Protocol Deviation Type	Test	Reference	Placebo/Vehicle	Total
Randomized in error	N, subject no.			
Non-Compliance				
Lost To Follow Up				
Outside Visit Window				
Restricted Medication				
[Applicant to add additional items]				

Table 13: Summary of Subject Discontinuation/Early Termination From the Study

Reason for Discontinuation	Test	Reference	Placebo/Vehicle	Total
Adverse Events	N, subject no.			
Insufficient Therapeutic Response/Treatment Failure				
Lost to follow-up				
Restricted Medication				
Withdrew Consent				
Non-Compliance				
Protocol violation				
Investigator decision				
[Applicant to add additional items]				

Table 14: Demographic Characteristics at Baseline for the Safety Population and Per Protocol Population

Demographic		Test (N)	Reference (N)	Placebo/ Vehicle (N)	p value
Age (years)	Mean ± SD				
	Min-Max				
Sex (N and %)	Female				
	Male				
Ethnicity (N and %)	Hispanic/Latino				
	Not Hispanic/Latino				
Race (N and %)	White				
	Black/African American				
	Native Hawaiian/Other Pacific Islander				
	Asian				
	American Indian/Alaska Native				
	Other				

* Please see FDA Guidance for Industry, *Collection of Race and Ethnicity Data in Clinical Trials*, for clarification of demographic data collection.

Table 15a: Summary Statistics for the Mean Irritation and Mean Adhesion Scores (Per Protocol Population)

Mean Irritation	Test (N)	Reference (N)
MEAN ± SD		
MIN-MAX		
MEDIAN		
Mean Adhesion	**Test (N)**	**Reference (N)**
MEAN ± SD		
MIN-MAX		
MEDIAN		

Table 15b: Non-inferiority Analysis Results for a Skin Irritation Study – Mean Irritation Score (Per Protocol Population)

	Mean Irritation Score			
	Test LS Mean (±STD. ERROR)	**Reference LS Mean (±STD. ERROR)**	**95% Upper Bound of μ_T- 1.25 x μ_R**	**Pass The Non-Inferiority Test?**
Dichotomized Irritation Analyses	**Test (N)**	**Reference (N)**		
Proportion of TDSs with Total Irritation score at Day 22=0 (no evidence of irritation)	X% (X/XXX)	X% (X/XXX)		
Proportion of TDSs with Total Irritation score at Day 22 = 1 (minimal erythema, barely perceptible)	X% (X/XXX)	X% (X/XXX)		
Proportion of TDSs with Total Irritation Score at Day 22 = 2 (definite erythema)				
Proportion of TDSs with Total Irritation Score at Day 22 ≥3 (erythema and papules to strong reaction spreading beyond the application site)				

Table 15c: Non-inferiority Analysis Results for a Skin Adhesion Study – Mean Adhesion Score (Per Protocol Population)

	Mean Adhesion Score			
	Test LS Mean (±STD. ERROR)	**Reference LS Mean (±STD. ERROR)**	**95% Upper Bound of μ_T-μ_R**	**Pass The Non-Inferiority Test?**
Dichotomized Adhesion Analyses	**Test (N)**	**Reference (N)**		
Proportion of TDSs with Adhesion Score at X Hours = 0 (≥ 90% adhered)	X% (X/XXX)	X% (X/XXX)		
Proportion of TDSs with Adhesion Score at X Hours = 1 (≥ 75% to <90% adhered)	X% (X/XXX)	X% (X/XXX)		
Proportion of TDSs with Adhesion Score at X Hours = 2 (≥50% to <75% adhered)				
Proportion of TDSs with Adhesion Score at X Hours = 3 (>0% to <50% adhered)				
Proportion of TDSs with Adhesion Score at X Hours = 4 (0% adhered, TDS detached)				

Table 15d: Number (N) and Frequency (%) of Sensitization Reactions During the Challenge Phase (Per Protocol Population)

Product	No Sensitization Response N (%)	Potential Sensitization Response N (%)
Test (N)		
Reference (N)		

Table 16a: Frequency Tables - Induction Phase Irritation Scores (Combined Dermal Response and Other Effect Scores) for Per Protocol Population

		Irritation Score					
Evaluation Day	Product	0	1	2	3	4	5
For Example: Day 3	Test (n) Reference (n)	XX (%) XX (%)					
e.g., Day 5							
e.g., Day 8							
e.g., Day 10							

Table 16b: Frequency Tables - Induction Phase Irritation Scores (Dermal Response) for Per Protocol Population

		Irritation Score					
Evaluation Day	Product	0	1	2	3	4	5
For Example: Day 3	Test (n) Reference (n)	XX (%) XX (%)					
e.g., Day 5							
e.g., Day 8							
e.g., Day 10							

Table 16c: Frequency Tables - Induction Phase Irritation Scores (Other Effects) for Per Protocol Population

		Irritation Score					
Evaluation Day	Product	0	1	2	3	4	5
For Example: Day 3	Test (n) Reference (n)	XX (%) XX (%)					
e.g., Day 5							
e.g., Day 8							
e.g., Day 10							

Table 16d: Frequency Tables - Irritation Scores (Combined Dermal Response and Other Effects Scores) for Per Protocol Population During Challenge Phase/Re-Challenge Phase

Score During Challenge/Re-Challenge Phase	Product	30 Minutes Post Removal	24 Hours Post Removal	48 Hours Post Removal	72 Hours Post Removal
0	Test (n) Reference (n)	XX (%) XX (%)			
1	Test (n) Reference (n)				
2	Test (n) Reference (n)				
3	Test (n) Reference (n)				

Table 16e: Frequency Tables - Irritation Scores (Dermal Response) for Per Protocol Population During Challenge Phase/Re-Challenge Phase

Score During Challenge/Re-Challenge Phase	Product	30 Minutes Post Removal	24 Hours Post Removal	48 Hours Post Removal	72 Hours Post Removal
0	Test (n) Reference (n)	XX (%) XX (%)			
1	Test (n) Reference (n)				
2	Test (n) Reference (n)				
3	Test (n) Reference (n)				

Table 16f: Frequency Tables - Irritation Scores (Other Effects) for Per Protocol Population During Challenge Phase/Re-Challenge Phase

Score During Challenge/Re-Challenge Phase	Product	30 Minutes Post Removal	24 Hours Post Removal	48 Hours Post Removal	72 Hours Post Removal
0	Test (n) Reference (n)	XX (%) XX (%)			
1	Test (n) Reference (n)				
2	Test (n) Reference (n)				
3	Test (n) Reference (n)				

Table 16g: Frequency Tables - Adhesion Scores for Per Protocol Population

Time Point	T Score (N=) n (%)						R Score (N=) n (%)					
	0	1	2	3	4	Mean	0	1	2	3	4	Mean
1												
2												
3												
4												
5												
All												

Table 17: TDS Removal or Move Due to Skin Irritation Score ≥ 3

	Irritation Score		
Product	Total Irritation Score (Dermal Response + Other Effects) ≥ 3 N (%)	TDS Moved or Removed Due to Significant Skin Irritation N (%)	Mean Days Until Repeat Applications to Same Site Discontinued Due to Irritation
Test			
Reference			

Table 18: Proportion of Subjects with Adhesion Score of 2 or More and 3 or More per Treatment

Adhesion Score	N	Test N (%)	Reference N (%)
<2			
≥2			
<3			
≥3			

Table 19: Duration of TDS Wear Prior to Adhesion Score >2 in the Per Protocol Population (Specific for Skin Adhesion Studies)

Product	Number of subjects with TDSs that have adhesion score > 2 (N)	Mean time from application to adhesion score > 2 M± SD
Test	XX	XX
Reference	XX	XX

Table 20: Summary of Adverse Events in Safety Population

Description	Test N(%)	Reference N(%)	Placebo N(%)	Total N(%)
Subjects in Safety Population				
Total number of AEs reported				
Number of subjects with at least one AE				
Number of subjects discontinued study drug due to above AE				
AEs reported				
Mild				
Moderate				
Severe				
Serious AEs (SAEs)				
Pregnancies				
Deaths				
[Applicant to add additional items]				

Table 21: Formulation

Ingredients	Function	Test Amount (mg, %) (e.g., % w/v, %w/w, mg/1 spray)			RLD/RS*	Placebo/Vehicle	IID limit
		%w/w	%w/v	%v/v			

*for RLD used in study; Add additional column if formulation is different than marketed product.

21a. For a waiver of bioequivalence study requirements or for a test product that requires qualitative and quantitative sameness to the RLD/RS (Reference Standard), if applicable

		Test			RLD/RS*	IID limit
Ingredient	**Function**	**%w/w**	**%w/v**	**%v/v**		

*for RLD used in study; Add additional column if formulation is different than marketed product.

Any differences in formulation (e.g. including overages, etc.) between test product used in I/S/A study and proposed commercial/to-be-marketed product?	☐ Yes (please explain) ☐ No
Any differences in any aspects of manufacturing (e.g. processes) of test product used in I/S/A study and proposed commercial/to-be-marketed product?	☐ Yes, Please explain ☐ No
Any differences in any aspects of device (including any components) used with test product used in I/S/A study and proposed commercial/to-be-marketed device product?	☐ Yes, Please explain ☐ No ☐ Not applicable

*If answered "yes" to any of the above questions, provide list and description of information to justify any differences between drug-device product used in I/S/A study and proposed commercial/to-be-marketed drug-device product.