STATISTICAL ANALYSIS PLAN SIGNATURE FORM

Protocol Number:	N-AC302	CIL Code:	35220
Statistical Analysis Plan Version / Date:	Version 1.0 22Dec2016		

The **Lead Statistician** is signing below to confirm they have authored/reviewed and approved the Statistical Analysis Plan in accordance with the study protocol and CRF.

Signature:		Date: (dd mmm yyyy)	
Print Name:	Melissa Hays		

Melissa Hays
Manager, Biostatistics
I approved this document
27 Dec 2016 9:33 AM -05:00

The **Project Manager** is signing below to confirm they have reviewed and approved the Statistical Analysis Plan in accordance with the study protocol and CRF.

Signature:		Date: (dd mmm yyyy)	
Print Name:	Brandi Wade		

Brandi Wade

Brandi Wade
Project Director
I approved this document
28 Dec 2016 9:03 AM -05:00

The **Independent Statistician** is signing below to confirm they have reviewed and approved the Statistical Analysis Plan in accordance with the study protocol and CRF.

Signature:			
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The **Novan** representative is signing below to confirm they have reviewed and approved the Statistical Analysis Plan in accordance with the study protocol, CRF, and any other study requirements.

Signature:		Date: (dd mmm yyyy)	12/22/2016
Print Name:	M Joyce Rico, MD, MBA		
Title:	Chief Medical Officer		

Statistical Analysis Plan

A Phase 3 Multi-Center, Randomized, Double-Blinded, Vehicle-Controlled, Parallel Group Study Comparing the Efficacy, Tolerability and Safety of Once Daily SB204 and Vehicle Gel in the Treatment of Acne Vulgaris

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Document Status: Final

Version Date: Version 1.0 22Dec2016

Contents

Abbreviations

Abbreviation	Definition
AE	Adverse Event
BOCF	Baseline Observation Carried Forward
ET	Early Termination
IGA	Investigator's Global Assessment
ITT	Intent to Treat
IWRS	Interactive Web Response System
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities
MCMC	Markov chain Monte Carlo
MI	Multiple Imputation
NOVAN	Novan, Inc.
OCP	Oral Contraceptive Pill
PP	Per-Protocol
QD	Once a day
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SAS	Statistical Analysis Software
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Events
UPT	Urine Pregnancy Test
WHO	World Health Organization
WOCBP	Women of Child-Bearing Potential

1 Introduction

This document presents the statistical analysis plan (SAP) for Novan Inc., Protocol No. NI-AC302: A Phase 3 Multi-Center, Randomized, Double-Blinded, Vehicle-Controlled, Parallel Group Study Comparing the Efficacy, Tolerability and Safety of Once Daily SB204 and Vehicle Gel in the Treatment of Acne Vulgaris. It is based on Amendment 1 of the protocol dated 06Jan2016.

The SAP provides the detailed description of the planned statistical analysis of data from protocol NI-AC302.

2 Study Objectives

The primary objective of this study is to compare the efficacy, tolerability and safety of SB204 4% to Vehicle Gel once daily for 12 weeks in subjects with acne vulgaris.

2.1 Primary endpoints

Primary Efficacy Endpoints

The co-primary efficacy endpoints are:

- The absolute change in inflammatory lesion count from Baseline to Week 12/ET;
- The absolute change in non-inflammatory lesion count from Baseline to Week 12/ET;
- The proportion of success at Week 12/ET according to the dichotomized Investigator Global Assessment (IGA). A subject will be considered a success if the IGA is clear (0) or almost clear (1) and is at least two grades less than at Baseline.

2.2 Secondary endpoints

Secondary Efficacy Endpoints

The secondary efficacy endpoints include the following:

- The percent change in inflammatory lesion count from Baseline to Week 12/ET;
- The percent change in non-inflammatory lesion count from Baseline to Week 12/ET;
- The median time to a 35% reduction in inflammatory lesion counts;
- The median time to a two (2) or more grade improvement in IGA.

2.3 Tolerability endpoints

The cutaneous tolerability assessments include the evaluator's assessment of erythema, scaling, dryness at each visit, and the subject's report of pruritus and burning/stinging based on the preceding 24 hours.

2.4 Safety endpoints

Safety endpoints will include adverse events (AEs), and changes from Baseline in physical examination and vital sign measurements. Any clinically significant changes on physical exam or vital sign measurements will be recorded as AEs and included in the comparison.

3 Study Design

3.1 Study Design

This is a multi-center, double-blinded, randomized, vehicle-controlled, parallel group, study to be conducted in approximately 1300 subjects with acne vulgaris.

Subjects who satisfy the entry criteria will be randomized to SB204 4% QD or Vehicle Gel QD in a 1:1 ratio. Investigational drug will be delivered from a double barrel single pump dispenser. The pump dispenses product from two chambers (NVN1000 Gel and a hydrogel or Vehicle Gel and a hydrogel) which will be mixed together in the palm for approximately 5 seconds by the subject and applied to the entire face once daily after washing.

Subjects will return for post-baseline evaluation at Weeks 2, 4, 8, and 12/Early Termination (ET).

3.2 Study Treatment

Approximately 900 mg (1 ml) of SB204 4% or Vehicle Gel will be applied evenly over the entire face once a day for a period of up to 84 days. The product will be dispensed from a dual-chamber pump designed to deliver approximately equal amounts of NVN1000 Gel and hydrogel or Vehicle Gel and hydrogel.

3.3 Study Schedule

Study visits should occur at approximately the same time of day throughout the study.

PROCEDURES	Screening (Day -35 to Day 0)[1]	Baseline (Day 0)	Week 2[2] ±3 days (Day 14)	Week 4 ±5 days (Day 28)	Week 8 ±5 days (Day 56)	Week 12/ET[3] ±7 days (Day 84)
Informed Consent/Assent	X					
Demographics	X					
Medical History	X	X				
Medication History	X	X				
Inclusion/Exclusion Criteria	X	X				
Brief Physical Examination	X	X[4]				X
Urine Pregnancy Test (all WOCBP)	X	X[4]		X	X	X
Blood Pressure and Pulse	X	X	X	X	X	X
IGA	X	X	X	X	X	X
Lesion Counts	X	X	X	X	X	X
Cutaneous Tolerability Evaluation		X	X	X	X	X
Instruct on Study Drug Application and Provide Subject Instructions		X				
Study Drug and Diary Dispensed		X		X	X	
Study Drug and Diary Collected				X	X	X
Subject Compliance Reviewed			X	X	X	X
Photography[5]		X		X	X	X
Concomitant Medications		X	X	X	X	X
Adverse Events	X	X	X	X	X	X

[1]Subjects who meet all eligibility criteria at Screening and do not require a medication wash-out may complete all Baseline assessments and be randomized on the same day as the Screening visit.

[2]All visit dates are in reference to Baseline, e.g., Visit 2 occurs two weeks (14 days) after Baseline visit.

[3]All Week 12 procedures should be completed for subjects who prematurely discontinue.

[4]If the Baseline Visit is within 7 calendar days of the Screening visit, Physical Examination and UPT do not need to be repeated.

[5]Photography will be done at a subset of sites.

3.4 Concomitant Medication

Subjects will be permitted to apply non-comedogenic moisturizer or sunscreen on an as-needed basis. Moisturizer must not contain antibacterials and the subject must not change moisturizer and/or sunscreen used during the course of the study. If used, moisturizers and sunscreen must be applied at least 30 minutes after study drug application.

Subjects must not have used anti-acne treatments including topical agents to the face, systemic antibiotics or procedures that may impact acne (as described in Section 3.7.3 of the protocol) prior to Baseline. These medications and procedures are also prohibited during the trial. Topical anti-acne agents may be used to treat acne on the chest, back or upper shoulders in this study.

Subjects may not be concurrently on drugs associated with exacerbating acne vulgaris (see Appendix 1 of the protocol). Subjects who have used an investigational drug or device within 30 days of Baseline should not be enrolled. Subjects must not participate in a different interventional research study during the study period. Any subject who has participated in a previous study with SB204 or NVN1000 Gel must not participate.

Any medication/therapy used by the subject following first application of study product will be considered a concomitant medication/therapy (e.g., aspirin, acetaminophen, birth control pills, vitamins, etc.). Every attempt should be made to keep concomitant medication/therapy dosing constant during the study. Any change to concomitant medications/therapies should be noted on the subject's study record and in the study database. When applicable, an AE should be completed for any subject starting a concomitant medication/therapy after enrollment into the study.

3.5 Study Analysis Populations

Prior to breaking the blind, all study data will be reviewed in a blinded fashion to determine whether subjects should be excluded from any of the analysis populations defined below. For example, if a subject was randomized but did not receive study drug, the subject would be excluded from the Safety Population. Other additional criteria which may be population exclusion criteria may be considered to accommodate for unforeseen events that occurred during the conduct of the trial that result in noteworthy study protocol violations. This review will also assess dosing non-compliance criteria, which would be one of the criteria for exclusion from the Per Protocol Population.

3.5.1 Intent to Treat (ITT) Population

The intent to treat (ITT) population will include all study subjects who were randomized and dispensed study medication and grouped by the treatment to which they were assigned at randomization. All efficacy analyses will be performed on the ITT population.

3.5.2 Safety (SAF) Population

The safety (SAF) population will include all randomized subjects who received at least one dose (i.e. any application) of study medication and grouped by whether they ever received SB204 or not. All safety and tolerability analyses will be performed on the safety analysis population (SAF) population.

3.5.3 Per-Protocol (PP) Population

The per protocol (PP) population will include subjects in the SAF population who complete the Week 12 evaluation without noteworthy study protocol violations (i.e., any subject or investigator activity that could have possibly interfered with the therapeutic administration of the treatment or the precise evaluation of treatment efficacy). The PP population will include subjects who do not meet any of the following criteria:

- Violated the inclusion/exclusion criteria;
- Have taken any interfering concomitant medications;
- Did not attend the Week 12 visit;
- Have not been compliant with the dosing regimen;
- Out of visit window at the Week 12 visit by ±7 days;

Analyses of the co-primary efficacy outcomes will be performed on the Per Protocol (PP) population.

3.6 Randomization

Eligible subjects at the Baseline visit will be randomized 1:1 to SB204 4% QD or Vehicle Gel QD and treated for up to 12 weeks (84 days).

3.7 Blinding

Subjects will be randomized to SB204 4% or Vehicle Gel on a 1:1 basis through utilization of the interactive web response system (IWRS). The evaluator and subject will be blinded to the subject's treatment.

In the event that a subject should experience an AE for which it is medically necessary to break the blind in order to determine appropriate treatment, unblinding can be achieved by using the IWRS. A study subject for whom the blind is broken will be discontinued from the study.

3.8 Sample Size

Approximately 1300 subjects will be randomized into the study in a 1:1 ratio (650 in each arm) at approximately 50 sites in North America. In the previous phase 2 study, the pooled vehicle IGA 'success' rate was 7.1% and the pooled SB204 IGA success rate was 13.4%. Using NQuery Advisor v7 (Statistical Solutions, Ltd) to estimate sample size and statistical power, based on a vehicle IGA success rate of 7% and a 6% difference for the SB204 arm, a sample size of 1294 was estimated to have at least 95% power for a two-sided test at the alpha=0.05 level using the continuity corrected chi-square test.

The statistical power for detecting treatment differences in inflammatory or non-inflammatory lesions exceeds 99% once at least 256 subjects are treated in each group. This is based on the following assumptions:

- For inflammatory lesions: vehicle mean change = -7.6, SB204 mean change = -14.1, and a common standard deviation = 17.1
- For non-inflammatory lesions: vehicle mean change = -5.8, SB204 mean change = -11.3, and common standard deviation = 11.8

4 Statistical Methodology

4.1 Planned Analyses

All statistical processing will be performed using statistical analysis software (SAS®) version 9.3 or later unless otherwise stated. Statistical significance will be based on two-tailed tests of the null hypothesis resulting in p-values of ≤ 0.05 unless stated otherwise.

Continuous data will be summarized with sample size (N), mean, median, standard deviation, minimum and maximum. Categorical data will be summarized with N, frequency counts, and percentages, based on N. Data will be presented for the active treatment group and vehicle treatment group. Demographic and baseline data will also be presented over both treatment groups.

4.2 Imputation of Missing Data

Prior to analysis of the efficacy outcomes, missing post-baseline results at each visit will be imputed separately for each treatment group using a Markov chain Monte Carlo (MCMC) multiple imputation (MI) methodology. Separate multiple imputation procedures will be used for each outcome (i.e. lesion counts and IGA score), using SAS procedure MI (see Section 4.12 for sample code). Multiple imputation inference involves three distinct phases (Yuan, SAS270 Paper, 2014):

1) The missing data are filled in m times to generate m complete data sets.
2) The m complete data sets are analyzed by using standard procedures.
3) The results from the m complete data sets are combined for the inference using proc MIANALYZE.
4) The Type 3 estimates from the ANCOVA models will be combined using the approach detailed in Wand, Fang, and Jin (2014).

The analysis strategies described below are the standard procedures referenced in step 2. For all analyses using multiple imputation, step 3 will be completed and the results from that step are displayed in the summary tables. For the reduced model results, steps 2-4 will be repeated. When reducing models, only the following covariates will be considered for deletion: age group, pooled site, and gender. Treatment group and baseline will always remain in the model.

ITT subjects with only baseline assessments will have the baseline value carried forward across all visits. As PP subjects must have completed the Week 12 visit, only imputation of data from Weeks 2-8 will be done for the PP analyses. Imputation of missing IGA score will be done prior to determining whether IGA success has been achieved or not. No other imputation of missing data is planned.

4.3 Pooling of Study Sites

Sites with low subject enrollment will be pooled prior to including site as a covariate factor in testing for treatment differences. The algorithm for pooling sites will be as follows: If the site has enrolled greater than 48 subjects (2 times the average target enrollment), the site will not be considered a candidate for pooling. The remaining sites will be pooled until the count of total subjects within the pooled site is at least 48. The method will be similar to the one proposed by Shi and Chen, NESUG 2007. Centers eligible for pooling will be sorted randomly (using a fixed random seed) prior to entering into the pooling algorithm. The same pooled sites will be used for all analyses where site is included as a factor.

4.4 Disposition of Subjects

The number of subjects receiving study treatment, in each analysis population, who completed the study and the reasons for any premature discontinuation from the study, will be presented by treatment and overall for both treatments combined. Listings will indicate whether subjects met all inclusion and exclusion criteria, and, if not, which criteria were not met.

A summary and a listing of major and minor protocol deviations will be presented. Deviations not identified as major will be considered minor. Major protocol violations include:

- Deviation in data collection for IGA or lesion count assessments

- Deviations in reporting safety assessments including adverse events, changes in physical examination including vital signs
- Deviations in collecting local tolerability assessments on the face
- Informed consent not obtained at all, or not obtained prior to performing study procedures.
- Significant non-compliance with protocol schedules, assessments, study drug compliance
- Performing a study procedure that is not outlined in the IRB-approved protocol
- Protocol deviations pertaining to incorrect investigational product dispensing or application prescribed outside of the protocol

4.5 Baseline and Demographic Characteristics

Subject baseline and demographic characteristics will be summarized for the ITT population. Age will also be categorized and summarized as proportion of adults (age≥18 years) and juvenile (age<18 years).

For female subjects, child-bearing potential and contraceptive use at baseline will be summarized. Medical history will be summarized for each treatment group by SOC and PT and presented in listings.

4.6 Efficacy Analysis

4.6.1 Primary Efficacy Analysis

Efficacy of SB204 4% will be based on statistical superiority over vehicle for change from baseline in absolute lesion counts (inflammatory and non-inflammatory) and 'success' on the dichotomized IGA score at Week 12/ET.

There are 3 co-primary efficacy outcomes:

- Absolute change in inflammatory lesions counts at Week 12 /ET,
- Absolute change in non-inflammatory lesions counts at Week 12/ET and
- Success at Week 12/ET which is defined as an IGA score of clear (0) or almost clear (1) and ≥2 grades less than Baseline

All three co-primary outcomes must show superiority over vehicle ($p \leq 0.05$ for each) in order for efficacy to be demonstrated, therefore no adjustment for multiple testing is planned.

The primary analyses of the co-primary efficacy endpoints will be performed in the ITT population where missing data have been imputed as described above. To assess sensitivity to protocol violations analyses of the co-primary outcomes will be performed using the PP population. To assess sensitivity to imputation methods, analysis of the co-primary outcomes

will be performed on the ITT population using LOCF and BOCF imputed results (see Section 4.6.1.4).

4.6.1.1 Inflammatory Lesions

The analysis of treatment differences in the absolute change in inflammatory lesion counts at Week 12/ET will be conducted using an analysis of covariance with factors for treatment, pooled site, sex, and age group (<18 years vs. 18+ years). The baseline inflammatory lesion count will be included as a covariate. The p-values of the full model will be presented in a footnote. The final model will be reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response. (See Section 4.12 for sample code.) When reducing models, only the following covariates will be considered for deletion: age group, pooled site, and gender. Treatment group and baseline will always remain in the model.

4.6.1.2 Non-inflammatory Lesions

The analysis of treatment differences in the absolute change in non-inflammatory lesion counts will use the same method as the analysis of the inflammatory lesions. Covariates kept in the final model will be determined specifically for non-inflammatory lesions and may differ from the covariates retained in the model for inflammatory lesions.

4.6.1.3 Success on Dichotomized IGA Score

Subjects will be considered a success if their IGA score is clear (0) or almost clear (1) at Week 12/ET and is decreased by ≥ 2 grades from baseline.

Analysis of treatment differences in success at Week 12/ET will be conducted using a logistic regression model with factors for treatment, pooled site, sex, age group (<18 years vs. 18+ years), and with baseline IGA score as a covariate. The p-values of the full model will be presented in a footnote. The final model will be reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response. When reducing models, only the following covariates will be considered for deletion: age group, pooled site, and gender. Treatment group and baseline will always remain in the model. Missing IGA score will be imputed prior to determining the dichotomous success outcome. (See Section 4.12 for sample code.) To mitigate against models displaying separation or quasi-separation, Firth's penalized likelihood approach will be used. With samples as large as this study population, Firth's method has been shown to produce estimates that are nearly the same as the unconditional estimates [Heinze (2006, 1999) and Heinze and Schemper (2002)].

4.6.1.4 Efficacy Sensitivity Analyses

To assess the sensitivity of the primary efficacy analysis results to imputation methods, each co-primary outcome will be analyzed as described above, but with missing data imputed by last observation carried forward (LOCF) and baseline observation carried forward (BOCF) on the ITT population.

4.6.2 Secondary Efficacy Analyses

Secondary efficacy outcomes include the percent change in inflammatory and non-inflammatory lesion counts at Week 12/ET, the median time to 35% improvement in inflammatory lesions and the median time to a two (2) or more grade improvement in the IGA. Secondary efficacy endpoints will be assessed for the ITT population. Graphs of the secondary outcomes over time will be presented.

The percent change in lesion counts will be analyzed for treatment differences using the same models as described in the co-primary efficacy analyses.

The median time to 35% improvement in inflammatory lesions and time to a two or more grade improvement in the IGA will be analyzed for treatment differences using the Kaplan-Meier method of estimating median time to event where a subject will be censored at the date of last lesion assessment if improvement is not achieved by Week 12/ET (inclusive). If subjects came in later than 91 days after the start of study treatment (the upper range of that visit window) subjects will be right-censored on that day. The log-rank test will be used to test for significance of treatment group differences. A Cox regression model will be used to assess the impact of covariates on treatment difference. (See Section 4.12 for sample code.)

Analysis of the secondary efficacy outcomes will be adjusted for multiplicity using a hierarchical step-down procedure. These endpoints will be tested in the specified order with the rule that once a p-value exceeds 0.05, endpoints further down in the order are not tested and are assumed to show no statistically significant treatment difference. The order will be as follows:

1) Percent change in inflammatory lesions at Week 12/ET
2) Percent change in non-inflammatory lesions at Week 12/ET
3) Median time to achieve 35% reduction in inflammatory lesions
4) Median time to a two or more grade improvement in the IGA

4.6.3 Subgroup Analyses

Subgroup analysis of the primary efficacy endpoints will be performed on the ITT population for which MI methods were used to impute missing data. These analyses include stratification by age (<18 years vs 18+ years), gender, and females treated with Yaz/Bevaz, Estrostep and Ortho-Tri-Cyclen (or respective generic products) vs. females not treated with one of these oral contraceptive pills (OCP). This subgroup of specific OCPs will be denoted as OCPs with acne indications in the tables and listings. Other subgroup analyses may be developed if differences in baseline characteristics warrant further evaluations, or if covariate analyses indicate a covariate has significant influence on the variability of outcomes.

4.6.4 Exploratory Analyses

For the ITT population, exploratory analyses of treatment differences in the primary and secondary efficacy continuous and dichotomous endpoints at each study visit will be assessed as well. The continuous efficacy endpoints are: absolute change and percent change in inflammatory and non-inflammatory lesion counts. The dichotomous efficacy endpoints include: proportion of subjects with IGA success, proportion of subjects achieving 35% reduction in inflammatory lesions, and proportion of subjects with a two (2) or more grade improvement in IGA.

4.6.4.1 Continuous Efficacy End-Points

Analysis of the continuous efficacy end-points (lesion counts) will be conducted using a repeated measures analysis of covariance with factors for treatment, pooled site, sex, age, visit and treatment by visit interaction. The baseline assessment will be included as a covariate and subjects nested within pooled site will be the random repeated measure at each visit to adjust for the variability due to repeated visits. The final model will be reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response. The unstructured covariance structure will be specified initially. If the model fails to converge, the following covariance structures will be considered: CS, CSH. Of these models, the one with the smallest AIC score will be selected. If these models also have esimtation difficulties, variance diagnositcs will be performed to assess for collinearity and other model specification issues. Adjustments to the model will be made based on those findings. Absolute and percent change from baseline at each visit will be the dependent variable. Both the treatment difference overall and the treatment differences at each week will be displayed. (See Section 4.12 for sample code.) Should the repeated measures approach fail to converge or produce uninterpretable estimates, then the analyses will be performed for each visit.

4.6.4.2 Dichotomous Efficacy End-Points

Analysis of dichotomous efficacy-endpoints will be conducted using a repeated measures logistic general linear covariance model with factors for treatment, pooled site, sex, age, visit and treatment by visit interaction and with baseline score as a covariate. The final model will be reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response. (See Section 4.12 for sample code.) Missing data will be imputed prior to determining the dichotomous outcome. Should the repeated measures approach fail to converge or produce uninterpretable estimates, then the analyses will be performed using a logistic regression model for each visit.

4.7 Drug Exposure and Compliance

Drug exposure and compliance will be performed on the SAF population. The number of days that study drug was taken and study drug compliance will be summarized by treatment group.

Duration of exposure will be defined as:

Date of Last Drug Administration – Date of First Drug Administration + 1 day

The percent compliance for study drug will be calculated as follows:

$$\% \text{ Compliance} = 100 * \frac{\text{(Number of Doses Expected– Number of Doses Missed)}}{\text{(Number of Doses Expected)}}$$

where the number of doses expected is defined as the number of days from Baseline to the date of last dose. Subjects' diaries will be reviewed at each visit to report the number of doses that were missed.

Percent compliance will be summarized as a continuous variable using descriptive statistics, and dichotomously as well as: <80% vs. ≥80% compliant.

4.8 Tolerability

Cutaneous tolerability assessments (erythema, scaling, dryness, pruritus, burning/stinging) will be summarized by visit from Baseline to Week 12/ET by treatment group. Bubble charts of the proportion of subjects with each score on the cutaneous tolerability assessments will be presented for each visit.

4.9 Safety

4.9.1 Adverse Events

All AEs that occur during the study will be recorded and classified on the basis of Medical Dictionary for Regulatory Activities (MedDRA) terminology version 18.1. Treatment-emergent AEs (TEAEs) are defined as AEs with an onset on or after the date of the first study drug dose. Adverse events noted prior to the first study drug administration that worsen after Baseline will also be reported as TEAEs and included in the summaries.

All information pertaining to an AE noted during the study will be listed by subject, detailing verbatim term given by the Investigator or designee, preferred term, system organ class (SOC), onset date, resolution date, severity, seriousness, action taken, outcome, and drug relatedness. The event onset will also be shown relative (in number of days) to date of first dose. When summarizing AEs by severity and relationship, each subject will be counted only once, within a system organ class or a preferred term, by using the event with the highest severity and greatest relationship within each classification.

The following adverse event summaries will be produced:

- All TEAEs
- All treatment related TEAEs
- All TEAEs leading to treatment modification
- All treatment related TEAEs leading to treatment modification
- All TEAEs leading to treatment discontinuation
- All treatment related TEAEs leading to treatment discontinuation
- All SAEs
- All treatment related SAEs
- All TEAEs leading to death
- All treatment-related TEAEs leading to death
- All pregnancies

4.9.2 Vital Signs

Blood pressure and pulse will be summarized by treatment group from Baseline through Week 12/ET. Additionally, change from Baseline in vital signs will be summarized at Week 2, 4, 8, and 12/ET. Any clinically significant changes from Baseline will be documented as an AE.

4.9.3 Urine Pregnancy Tests (Female Subjects)

Urine pregnancy test (UPT) results for women of child-bearing potential (WOCBP) will be presented in data listings by subject.

4.9.4 Physical Exam and Concomitant Medical and Surgical Procedures

Physical exam and concomitant medical and surgical procedures will be presented in listings.

4.10 Concomitant Medication

Incidence of concomitant medication will be presented by treatment, drug class (i.e. ATC 2 classification) and preferred drug name. Coding will be done using the WHO March 2016 dictionary.

Concomitant medications are all medications taken during the study period, including those started before but on going at first dose.

Where a medication stop date is partially or fully missing, and it is unclear as to whether the medication is prior to or concomitant with study treatment, it will be assumed that it is concomitant.

4.11 Deviations from SAP

Any deviations from the original statistical plan will be described and justified in the final clinical study report.

4.12 Algorithms/SAS Codes

- **Example 1: For each continuous efficacy variable, the following imputation approach will be followed:**

```
This example illustrates the approach for inflammatory lesion
(paramcd='INFL'):
 proc transpose data=&data out=&data_t(drop=_name_ _label);
  by usubjid tmt agegr1 sex newsite base; var chg;
  where paramcd='INFL' and avisitn in (2,3,4,5,6) ;
  id avisitn;

/* for subjects with only baseline, change from baseline will be 0, so set all
visits to 0 */
/* only integer results */

proc mi data=&data_t out=mi nimpute=25 seed=12345 round=1.0  ;var base
chg3 chg4 chg5 chg6 ;
mcmc chain=single impute=full;
```

- **Example 2: For the dichotomous success efficacy variables, the following imputation approach will be followed:**

```
This example illustrates the approach for IGA success:
proc transpose data=&data out=&data_iga(drop=_name_ _label_);
by usubjid tmt agegr1 sex newsite base; var aval;
where paramcd='IGA' and avisitn in (2,3,4,5,6) ; id
avisitn;  run;

/* for subjects with only baseline, carry the baseline value forward */
/* the minimum for IGA score is 0 and the maximum is 4 */
/* only integer results */

proc mi data=&data out=mi2i nimpute=25 seed=12345 round=1.0  minimum=0
maximum=4 noprint;
var base _3 _4 _5 _6; mcmc
chain=single impute=full; run;

/* Once final IGA score has been imputed, the success variable
will be recomputed */
```

- **Example 3: Efficacy Endpoints analysis: Models of Differences in Lesion Counts at Week 12\ET;**

```
proc mixed data=data;
class usubjid tmt agegr1 sex poolsite;
where visit=12;
model inflam=tmt inflbas agegr1 sex poolsite  / solution covb noint;
lsmeans tmt  / pdiff cl;
run;
```

Example 4: Efficacy Endpoints analysis: Models of Differences at Week 12\ET in IGA;

```
proc logistic data=data descending;
class tmt agegr1 sex poolsite / param=glm;
   model success= tmt poolsite sex agegr1 IGABAS / noint covb firth;
run;
```

- **Example 5: Repeated measures analysis of continuous efficacy endpoints;**
  - **for each week:**

```
proc mixed data=data;
class usubjid tmt agegr1 sex poolsite visit;
model inflam=tmt poolsite agegr1 sex inflbas visit tmt*visit / solution covb;
repeated visit / subject=usubjid(poolsite) type=un;
random intercept;
lsmeans tmt*visit  / pdiff cl;
run;
```

  - **for the overall estimate:**

```
proc mixed data=data;
class usubjid tmt agegr1 sex poolsite visit;
model inflam=tmt poolsite agegr1 sex inflbas visit tmt*visit / solution covb;
repeated visit / subject=usubjid(poolsite) type=un;
random intercept;
lsmeans tmt / pdiff cl;
run;
```

- **Example 6: Repeated measures analysis of dichotomous efficacy endpoints;**

```
proc genmod data=igami2 descend;
class usubjid tmt agegr1 sex poolsite;
      model success=tmt agegr1 sex poolsite igabas / noint dist=bin;
      repeated subject=usubjid(poolsite) / corr=unstr corrw;
      estimate 'SB204 vs. Vehicle &visist' tmt*avisitn 1 -1 / e exp;
run;
```

- **Example 7: Cox proportional hazards models of time to event endpoints;**

```
proc phreg data=data;
class tmt poolsite agegr1 sex / param=glm;
model time*censor(0) = tmt poolsite agegr1 sex;
run;
```

5 References:

A SAS Macro to Automate the Process of Pooling Sites. Changhong Shi and Lili Chen, Merck & Co., Inc. Rahway, NJ. SESUG 2007

Paper SAS270-2014 Sensitivity Analysis in Multiple Imputation for Missing Data. Yang Yuan, SAS Institute Inc 2014.

Combining Type-III Analyses from Multiple Imputations Binhuan Wang, New York University School of Medicine; Yixin Fang, New York University School of Medicine; Man Jin, Forest Research Institute. 2014.

Heinze, G. (2006). "A Comparative Investigation of Methods for Logistic Regression with Separated or Nearly Separated Data." ***Statistics in Medicine***25:4216–4226.

Heinze, G., and Schemper, M. (2002). "A Solution to the Problem of Separation in Logistic Regression." ***Statistics in Medicine*** 21:2409–2419.

Heinze, G. (1999). ***The Application of Firth's Procedure to Cox and Logistic Regression***. Technical Report 10, updated January 2001, Department of Medical Computer Sciences, Section of Clinical Biometrics, University of Vienna

Protocol: NI-AC302

A Phase 3 Multi-Center, Randomized, Double-Blinded, Vehicle-Controlled, Parallel Group Study Comparing the Efficacy, Tolerability and Safety of Once Daily SB204 and Vehicle Gel in the Treatment of Acne Vulgaris.

Mock Data Displays- Tables
Final Version 1.0
Date: 22Dec2016

Prepared for:
Novan Inc.
4105 Hopson Road Morrisville, NC 27560

Prepared by:
Chiltern International
4000 CentreGreen Way, Suite 300, Cary, NC, 27513, United States

Contents

Table 14.1.1.1
Subject Disposition
All Randomized Subjects

	SB204 (N=XXX)	Vehicle (N=XXX)	Overall (N=XXX)
Randomized	xx	xx	xx
ITT Population	xx (xx.x)	xx (xx.x)	xx (xx.x)
SAF Population	xx (xx.x)	xx (xx.x)	xx (xx.x)
PP Population	xx (xx.x)	xx (xx.x)	xx (xx.x)
Completed Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued Early	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Reason for Study Discontinuation [a]			
Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lack of Efficacy as Determined by Investigator	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Subject	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physician Decision	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol Deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pregnancy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Worsening of Condition	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

Notes: Safety (SAF) Population includes all randomized subjects who received at least one dose (i.e. any application) of study medication and grouped by whether they ever received SB204 or not.
ITT (ITT) Population includes all study subjects who were randomized and dispensed study medication, and grouped by the treatment the subject was assigned at randomization.
Per-Protocol (PP) Population includes subjects in the SAF Population who complete the Week 12 evaluation without noteworthy protocol violations.
Unless stated otherwise, denominator is the number of subjects randomized.
[a]Denominator is the number of subjects who discontinued study.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.1.1.2
Summary of Protocol Deviations
ITT Population

Protocol Deviations	SB204 (N=XXX)	Vehicle (N=XXX)	Overall (N=XXX)
Subjects with Any Protocol Deviation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Subjects with a Major Protocol Deviation	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Deviation 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
…			
Deviation J	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
Subjects with a Minor Protocol Deviation			
Deviation 1	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
…			
Deviation J	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

Note (s): Percentages are based on the number of subjects in ITT population. Subjects may be counted in more than one category.
Reference: Listing 16.2.x

Table 14.1.2.1
Demographics
ITT Population

	SB204 (N=XXX)	Vehicle (N=XXX)	Overall (N=XXX)
Age (years)			
n	xxx	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Min, Max	x.x, xx.x	x.x, xx.x	x.x, xx.x
Age Group			
Juvenile (Age <18 years)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Adult (Age 18+ years)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race			
White	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or African American	xx (xx.x)	xx (xx.x)	xx (xx.x)
American Indian or Alaska Native	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity			
Hispanic or Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic or Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)
Sex			
Male	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note(s): Percentages are based on the number of subjects in ITT population.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.1.2.2
Child Bearing Potential and Contraceptive Use (Females Only)
ITT Population

	SB204 (N=XXX)	Vehicle (N=XXX)	Overall (N=XXX)
If Female, of Childbearing Potential?			
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)
If No to Childbearing Potential, Why			
Post-Menopausal	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hysterectomy or Bilateral Oophorectomy	xx (xx.x)	xx (xx.x)	xx (xx.x)
Surgically Sterilized	xx (xx.x)	xx (xx.x)	xx (xx.x)
If Yes to Childbearing Potential, Primary Method of Birth Control at Baseline			
Oral Contraceptive	xx (xx.x)	xx (xx.x)	xx (xx.x)
With Acne Indication [a]	xx (xx.x)	xx (xx.x)	xx (xx.x)
No Acne Indication	xx (xx.x)	xx (xx.x)	xx (xx.x)
Intra-Uterine Device	xx (xx.x)	xx (xx.x)	xx (xx.x)
Condom with Spermicide	xx (xx.x)	xx (xx.x)	xx (xx.x)
Diaphragm with Spermicide	xx (xx.x)	xx (xx.x)	xx (xx.x)
Implant	xx (xx.x)	xx (xx.x)	xx (xx.x)
Nuvaring	xx (xx.x)	xx (xx.x)	xx (xx.x)
Medroxyprogesterone Injection	xx (xx.x)	xx (xx.x)	xx (xx.x)
Transdermal Patch	xx (xx.x)	xx (xx.x)	xx (xx.x)
Abstinence	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note(s): Percentages are based on the number of female subjects in ITT population.
[a] Oral Contraceptive Pills (OCPs) with Acne Indications: Yaz/Bevaz, Estrostep and Ortho-Tri-Cyclen (or respective generic products). This includes women who used these OCPs after baseline so this number may be greater than the number indicating OCP method at baseline.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.1.3
Medical History by System Organ Class and Preferred Term
ITT Population

Body System Class Preferred Term	SB204 (N=XXX)	Vehicle (N=XXX)	Overall (N=XXX)
Subject with Any Medical History	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
.....			
Preferred Term n	xx (xx.x)	xx (xx.x)	xx (xx.x)
.....			
System Organ Class n	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
.....			
Preferred Term n	xx (xx.x)	xx (xx.x)	xx (xx.x)
	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class q	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
.....			

Note(s): All investigator terms were coded using MedDRA dictionary version 18.1.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.1.4
Concomitant Medications by WHO Drug Class and WHO Drug Preferred Name
ITT Population

Drug Class Preferred Name	SB204 (N=XXX)	Vehicle (N=XXX)
Subjects Who Took at Least One Concomitant Medication	xx (xx.x)	xx (xx.x)
Drug Class 1	xx (xx.x)	xx (xx.x)
Preferred Name 1	xx (xx.x)	xx (xx.x)
Preferred Name 2	xx (xx.x)	xx (xx.x)
Preferred Name 3	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)
Drug Class 2	xx (xx.x)	xx (xx.x)
Preferred Name 1	xx (xx.x)	xx (xx.x)
Preferred Name 2	xx (xx.x)	xx (xx.x)
Preferred Name 3	xx (xx.x)	xx (xx.x)
etc.	xx (xx.x)	xx (xx.x)
Drug Class 3	xx (xx.x)	xx (xx.x)
Preferred Name 1	xx (xx.x)	xx (xx.x)
Preferred Name 2	xx (xx.x)	xx (xx.x)
.....	xx (xx.x)	xx (xx.x)

Note(s): Subjects are counted only once at each level of summarization.
Concomitant medications are all medications taken during the study period, including those started before but ongoing at first dose. All medications were coded using WHO Drug dictionary version March 2016.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer's Note(s): Continue with all drug classes and preferred names which appear in the data. Sort drug classes and within drug classes, preferred terms by decreasing overall frequency.

Table 14.1.5.1
Baseline Inflammatory and Non-Inflammatory Lesions and IGA Score
ITT Population

Category	SB204 (N=XXX)	Vehicle (N=XXX)
Inflammatory Lesions		
N	XX	XX
Mean	XX.X	XX.X
SD	XX,XX	XX,XX
Median	XX,X	XX,X
Min. to Max.	XX to XX	XX to XX
Non-Inflammatory Lesions		
N	XX	XX
Mean	XX.X	XX.X
SD	XX,XX	XX,XX
Median	XX,X	XX,X
Min. to Max.	XX to XX	XX to XX
IGA		
0 - Clear	xx (xx.x)	xx (xx.x)
1 - Almost Clear	xx (xx.x)	xx (xx.x)
2 - Mild	xx (xx.x)	xx (xx.x)
3 - Moderate	xx (xx.x)	xx (xx.x)
4 - Severe	xx (xx.x)	xx (xx.x)

Note(s): IGA=Investigator's Global Assessment. Inflammatory includes papules/pustules and nodules/cysts.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Using shell for table 14.1.5.1, repeat for the following:

Table 14.1.5.2 Baseline Inflammatory and Non-Inflammatory Lesions and IGA Score, PP Population

Table 14.2.1.1
Primary Efficacy Analysis:
Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12\ET Using the MI Method
ITT Population

Absolute Change from Baseline	SB204 (N=XXX)	Vehicle (N=XXX)
N [a]	XX	XX
Mean [b]	XX.X	XX.X
SD	XX,XX	XX,XX
Median	XX,X	XX,X
Min. to Max.	XX to XX	XX to XX
LSMean [c]	XX.XX	XX.XX
LSSE	XX.XX	XX.XX
LSMEANS of Treatment Difference		XX.XX
P-value		0.XXX
P-values for Covariate Impact on Treatment Difference		
Gender		0.XXX
Age (<18 years vs 18+ years)		0.XXX
Pooled Site		0.XXX

Note(s):
[a] The number of subjects entering into the analysis, i.e. in the specified analysis population that have a baseline assessment. ITT subjects with only baseline assessments will have the baseline value carried forward across all visits.
[b] These summary statistics are based on the post-imputation data, using multiple imputation methodology (MCMC) for missing data. MCMC method: missing post-baseline results at each visit will be imputed separately for each treatment group using 25 iterations of a Markov chain Monte Carlo (MCMC) multiple imputation (MI) methodology, using SAS procedure MI
[c] The significance of each independent variable from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX), Treatment (0.XXX) and Baseline (0.XXX). The treatment LSM, SE, estimate of treatment difference, p-values and covariates displayed in the table are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer's Note: Footnotes may change if the modeling approach changes; however, this is the current planned approach. If a reduced model is used for the primary comparison, add the following footnote:

The significance of each covariate from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX).

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Using shell for table 14.2.1.1, repeat for the following:

Programmer's Note: For repeat tables, check the analysis population and imputation method and apply the appropriate footnote:

Table 14.2.1.2 Primary Efficacy Analysis: Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12\ET
Using LOCF Method
ITT Population

Programmer's Note: Change MI footnote to define LOCF as Last Observation Carried Forward:

[b] These summary statistics are based on the post-imputation data, using Last Observation Carried Forward imputation methodology (LOCF) for missing data.

Table 14.2.1.3 Primary Efficacy Analysis: Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12\ET
Using BOCF Method
ITT Population

Programmer's Note: Change MI footnote to define BOCF as Baseline Observation Carried Forward:

[b] These summary statistics are based on the post-imputation data, using Best Observation Carried Forward imputation methodology (BOCF) for missing data.

Table 14.2.1.4 Primary Efficacy Analysis: Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12
PP Population

Change footnotes as follows, removing footnote [b] and changing [c] to [b]:

[a] The number of subjects entering into the analysis, i.e. Per Protocol subjects with a Week 12\ET assessment.
[b] The significance of each independent variable from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX), Treatment (0.XXX) and Baseline (0.XXX). The treatment LSM, SE, estimate of treatment difference, p-values and covariates displayed in the table are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.

Table 14.2.2.1 Primary Efficacy Analysis: Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Week 12\ET
Using MI Method
ITT Population

Table 14.2.2.2 Primary Efficacy Analysis: Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Week 12\ET
Using LOCF Method
ITT Population

Programmer's Note: Change MI footnote to define LOCF as Last Observation Carried Forward.

Table 14.2.2.3 Primary Efficacy Analysis: Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Week 12\ET
Using BOCF Method
ITT Population

Programmer's Note: Change MI footnote to define BOCF as Baseline Observation Carried Forward.

Table 14.2.2.4 Primary Efficacy Analysis: Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Week 12
PP Population

Change footnotes as follows:

[a] The number of subjects entering into the analysis, i.e. Per Protocol subjects with a Week 12\ET assessment. Summary statistics are based on this population.
[b] The significance of each independent variable from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX), Treatment (0.XXX) and Baseline (0.XXX). The treatment LSM, SE, estimate of treatment difference, p-values and covariates displayed in the table are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.

Table 14.2.3.1
Primary Efficacy Analysis:
Proportion of Subjects with Success at Week 12\ET Using MI Method
ITT Population

Dichotomized Investigator's Global Assessment - Clear or Almost Clear and at Least 2 Grades Less than Baseline	SB204 (N=XXX)	Vehicle (N=XXX)	p-value
N [a]	XXXX	XXXX	
Success	XXX (XX.X%)	XXX (XX.X%)	
Failure	XXX (XX.X%)	XXX (XX.X%)	
Post-Imputation Success Percentage [b] [c]	(XX.X%)	(XX.X%)	0.XXX
P-values for Covariate Impact on Treatment Difference			
Gender		0.xxx	
Age (<18 years vs 18+ years)		0.xxx	
Pooled Site		0.xxx	

Note(s):
A subject will be considered an IGA Success if the IGA is clear (IGA=0) or almost clear (IGA=1) at Week 12\ET and is at least 2 grades less than Baseline.
[a] N, frequency and percentages are based on the raw, unimputed data, and the denominator for those percentages is the number of subjects with an IGA result at Week 12\ET.
[b] Post-Imputation Success Percentage is the aggregate result following multiple imputation (MCMC) for missing data. MI method: missing post-baseline results at each visit will be imputed separately for each treatment group using 25 iterations of a Markov chain Monte Carlo (MCMC) multiple imputation (MI) methodology, using SAS procedure MI. ITT subjects with only baseline assessments will have the baseline value carried forward across all visits. The denominator is all subjects in the analysis population who have a baseline assessment.
[c] Analysis will be based on a logistic regression model with factors for treatment, pooled site, sex, age, and Baseline IGA score as covariates. The covariates displayed are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer's Note: Footnotes may change if the modeling approach changes; however, this is the current planned approach. If a reduced model is used for the primary comparison, add the following footnote:

The significance of each covariate from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX), etc.

Using shell for table 14.2.3.1, repeat for the following:

Programmer's Note: For repeat tables, check the analysis population and imputation method and apply the appropriate footnote:

Table 14.2.3.2 Primary Efficacy Analysis: Proportion of Subjects with Success at Week 12\ET Using LOCF Method, ITT Population

Programmer's Note:

- *Remove the Post-Imputation Success Percentage row, this was only for MI method.*
- *Change footnotes as follows, deleting footnote [b] and changing [c] to [b]:*

[a] N, frequency and percentages are calculated using Last Observation Carried Forward imputation methodology (LOCF). ITT subjects with only baseline assessments will have the baseline value carried forward across all visits. The denominator is all subjects in the analysis population who have a baseline assessment.

[b] Analysis will be based on a logistic regression model with factors for treatment, pooled site, sex, age, and Baseline IGA score as covariates. The covariates displayed are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.

Table 14.2.3.3 Primary Efficacy Analysis: Proportion of Subjects with Success at Week 12\ET Using BOCF Method, ITT Population

Programmer's Note:

- *Remove the Post-Imputation Success Percentage row, this was only for MI method.*
- *Change footnote [a] to define BOCF as Baseline Observation Carried Forward.*

Table 14.2.3.4 Primary Efficacy Analysis: Proportion of Subjects with Success at Week 12, PP Population

Change footnote [a] as follows, deleting footnote [b] and changing [c] to [b]::

[a] N, frequency and percentages are calculated using all subjects in the per protocol population. The denominator is the number of subjects in the per protocol population, and, by definition, who have a Week 12\ET visit.

Table 14.2.4.1
Efficacy Subgroup Analysis:
Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12\ET, Using MI Method, by Gender
ITT Population

	Males (N=XXX)		Females (N=XXX)	
Absolute Change from Baseline	SB204 (N=XXX)	Vehicle (N=XXX)	SB204 (N=XXX)	Vehicle (N=XXX)
N [a]	XX	XX	XX	XX
Mean [b]	XX.X	XX.X	XX.X	XX.X
SD	XX,XX	XX,XX	XX,XX	XX,XX
Median	XX,X	XX,X	XX,X	XX,X
Min. to Max.	XX to XX	XX to XX	XX to XX	XX to XX
LSMean [c]	XX.XX	XX.XX	XX.XX	XX.XX
LSSE	XX.XX	XX.XX	XX.XX	XX.XX
LSMEANS of Treatment Difference		XX.XX		XX.XX
P-value for Treatment Difference		0.XXX		0.XXX
P-values for Covariate Impact on Treatment Difference				
Age (<18 years vs 18+ years)		0.xxx		0.xxx
Pooled Site		0.xxx		0.xxx

Note(s):
[a] The number of subjects entering into the analysis, i.e. in the specified analysis population that have a baseline assessment. Subjects with only baseline assessments will have the baseline value carried forward across all visits.
[b] These summary statistics are based on the post-imputation data, using multiple imputation methodology (MCMC) for missing data. MCMC method: missing post-baseline results at each visit will be imputed separately for each treatment group and subgroup using 25 iterations of a Markov chain Monte Carlo (MCMC) multiple imputation (MI) methodology, using SAS procedure MI.
[c] The significance of each independent variable from the full model are as follows:
The p-values from the full model for males are as follows: pooled site (0.XXX), Age (0.XXX).
The p-values from the full model for females are as follows: pooled site (0.XXX), Age (0.XXX).
The treatment LSM, SE, estimate of treatment difference, p-values and covariates displayed in the table are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer's Note: Footnotes may change if the modeling approach changes; however, this is the current planned approach.

Using shell for table 14.2.4.1, repeat for the following:

Table 14.2.4.2 Efficacy Subgroup Analysis: Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12\ET, using MI Method, by Age (<18 Years vs. 18+ Years), ITT Population

Programmer's Note: Omit age from the list of covariates and include age group. Modify the footnotes as follows:

The covariates displayed are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
The p-values from the full model for the < 18 group are as follows: pooled site (0.XXX), Gender (0.XXX).
The p-values from the full model for the 18+ group are as follows: pooled site (0.XXX), Gender (0.XXX).
The treatment LSM, SE, estimate of treatment difference, p-values and covariates displayed in the table are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.

Table 14.2.4.3 Efficacy Subgroup Analysis: Absolute Change from Baseline in Inflammatory Lesion Counts at Week 12\ET, Using MI Method, in Females treated with OCP/acne indication vs all other females, ITT Population

The p-values from the full model for females who used OCPs with acne indication are as follows: pooled site (0.XXX), Age (0.XXX).
The p-values from the full model for females who did not use OCPs with acne indication are as follows: pooled site (0.XXX), Age (0.XXX).

Programmer's Note: Omit age from the list of covariates and include age group. Modify the footnotes as follows:

Programmer's Note: For table 14.2.4.3, remove GENDER from the model and from the footnote.

Using shell for table 14.2.1.1, repeat for the following:

Table 14.2.5.1 Secondary Efficacy Analysis: Percent Change from Baseline in Non-Inflammatory Lesion Counts at Week 12\ET, Using MI Method
ITT Population

Table 14.2.5.2 Secondary Efficacy Analysis: Percent Change from Baseline in Non-Inflammatory Lesion Counts at Week 12\ET, Using LOCF Method, ITT Population

Table 14.2.5.3 Secondary Efficacy Analysis: Percent Change from Baseline in Non-Inflammatory Lesion Counts, at Week 12\ET Using BOCF Method, ITT Population

Table 14.2.5.4 Secondary Efficacy Analysis: Percent Change from Baseline in Non-Inflammatory Lesion Counts, at Week 12\ET, PP Population

Table 14.2.5.5
Secondary Efficacy Analysis:
Time to a 35% Reduction in Inflammatory Lesion Counts
ITT Population

	SB204 (N=XXX)	Vehicle (N=XXX)
Subjects achieving 35% improvement in Inflammatory Lesions [a]		
Yes	xx (xx.x)	xx (xx.x)
Censored	xx (xx.x)	xx (xx.x)
Quartiles (Days) (95% CI)		
25%	x.x [xx.x, xx.x]	x.x [xx.x, xx.x]
50% (Median)	x.x [xx.x, xx.x]	x.x [xx.x, xx.x]
75%	x.x [xx.x, xx.x]	x.x [xx.x, xx.x]
p-value[b]		0.xxx
Treatment Difference (Standard Error) [c]		xx (xx.x)
		0.xxx
P-values for Covariate Impact on Time to Improvement [c]		
Gender		0.xxx
Age (<18 years vs 18+ years)		0.xxx
Pooled Site		0.xxx

[a] A subject is censored at date of last lesion assessment if a 35% improvement is not observed by Week 12\ET.
[b] Difference in median event is measured using a log-rank test. Confidence intervals based on the identify transformation are displayed. If an estimate cannot be computed, NE is displayed.
[c] A Cox Model was fit to assess the impact of the specified covariates on time to improvement and treatment differences in the time to improvement. The p-values from that model are displayed. Treatment difference is based on the estimate the marginal means over a balanced population.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Using shell for table 14.2.5.5, repeat for the following:

Table 14.2.5.6
Secondary Efficacy Analysis: Time to a Two (2) or More Grade Improvement in IGA, ITT Population

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Table 14.2.6.1
Exploratory Efficacy Analysis:
Absolute Change from Baseline in Inflammatory Lesion Counts, by Study Visit
ITT Population

Visit	SB204 (N=XXX)	Vehicle (N=XXX)
Week 2		
N [a]	xxx	xxx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x
Min, Max	x.x, xx.x	x.x, xx.x
LSMean [b]	xx.xx	xx.xx
LSSE	xx.xxx	xx.xxx
LSMEANS of Treatment Difference		xx.xx
p-value		0.xxx
Etc. to Week 12\ET		
Treatment Difference Overall		xx.xx
Overall p-value		0.xxx
P-values for Covariate Impact on Treatment Difference		0.xxx
Gender		0.xxx
Age (<18 years vs 18+ years)		0.xxx
Pooled Site		

Note(s):
[a] These summary statistics are based on the assessments present at this visit.
[b] The significance of each independent variable from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX), Treatment (0.XXX) and Baseline (0.XXX). The treatment LSM, SE, estimate of treatment difference, p-values and covariates displayed in the table are from the final model which was reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer's Note: Footnotes may change if the modeling approach changes; however, this is the current planned approach. If a reduced model is used for the primary comparison, add the following footnote:

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

The significance of each covariate from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX), visit (0.XXX), visit by treatment interactions (0.XXX), etc.

Using shell for table 14.2.6.1, repeat for the following:

Table 14.2.6.2 Exploratory Efficacy Analysis: Absolute Change from Baseline in Non-Inflammatory Lesion Counts, by Study Visit, ITT Population

Table 14.2.6.3 Exploratory Efficacy Analysis: Percent Change from Baseline in Inflammatory Lesion Counts, by Study Visit, ITT Population

Table 14.2.6.4 Exploratory Efficacy Analysis: Percent Change from Baseline in Non-Inflammatory Lesion Counts, by Study Visit, ITT Population

Table 14.2.6.5
Exploratory Efficacy Analysis:
Proportion of Subjects with Success, by Study Visit
ITT Population

Dichotomized Investigator's Global Assessment - Clear or Almost Clear and at Least 2 Grades Less than Baseline	SB204 (N=XXX)	Vehicle (N=XXX)
Week 2		
N	XXXX	XXXX
Success	XXX (XX.X%)	XXX (XX.X%)
Failure	XXX (XX.X%)	XXX (XX.X%)
P-value [a]		0.XXX
Week 4		
N	XXXX	XXXX
Success	XXX (XX.X%)	XXX (XX.X%)
Failure	XXX (XX.X%)	XXX (XX.X%)
P-value		0.XXX
Etc. to Week 12\ET		
Overall p-value [b]		
P-values for Covariate Impact on Treatment Difference		
Gender		0.xxx
Age (<18 years vs 18+ years)		0.xxx
Pooled Site		0.xxx

Note(s): A subject will be considered an IGA Success if the IGA is clear (IGA=0) or almost clear (IGA=1) at Week 12\ET and is at least 2 grades less than Baseline.
[a] Count and percentages are based on the assessments available at each visit. The p-values are from comparison of treatment differences at each study visit from a repeated measures logistic general linear covariance model with factors for treatment, pooled site, sex, age, visit and treatment by visit interaction and with baseline score as a covariate. The final model will has been reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
[b] The GEE parameter estimate p-values from a repeated measures logistic general linear covariance model specified in the footnote above.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer's Note: Footnotes may change if the modeling approach changes; however, this is the current planned approach. If a logistic model by visit is used instead, use the following footnote:

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

[a] Count and percentages are based on the assessments available at each visit. The p-values are the Wald chi-square p-values from the type 3 analysis of effect of treatment from a logistic regression model, by study visit, with factors for treatment, pooled site, sex, age, visit and treatment by visit interaction and with baseline score as a covariate. The final model will has been reduced to only contain covariates that have a significant (i.e. p-value < 0.05) impact on the response.
[b] Wald chi-square p-values from the type 3 analysis of effect of treatment from a logistic regression model with the same covariates as the model in the footnote above, but rather than fitting the model by visit, a single overall model has been specified, and study visit has been included in the model.

If a reduced model is used for the primary comparison, add the following footnote:

The significance of each covariate from the full model are as follows: pooled site (0.XXX), Gender (0.XXX), Age (0.XXX).

Using shell for table 14.2.6.5, repeat for the following:

Table 14.2.6.6 Exploratory Efficacy Analysis: Proportion of Subjects with a two (2) or more grade improvement in IGA, by Study Visit, ITT Population

Programmer's Note: Change column 1 header to 'A two or more grade improvement in IGA' and remove success footnote.

Table 14.2.6.7 Exploratory Efficacy Analysis: Proportion of Subjects with a 35% Reduction in Inflammatory Lesions, by Study Visit, ITT Population

Programmer's Note: Change column 1 header to '35% Reduction in Inflammatory Lesions' and remove success footnote.

Table 14.3.1.1
Summary of Drug Exposure and Compliance
Safety Population

	SB204 (N=XXX)	Vehicle (N=XXX)
Overall Duration of Exposure (Days) [a]		
Number of Subjects with Exposure	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x
Min, Max	x.x, xx.x	x.x, xx.x
Duration Unknown	Xx (xx.xx%)	Xx (xx.xx%)
Overall % Compliance [b]		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x
Min, Max	x.x, xx.x	x.x, xx.x
< 80%	xx (xx.x)	xx (xx.x)
>= 80%	xx (xx.x)	xx (xx.x)
Compliance Undefined	Xx (xx.xx%)	Xx (xx.xx%)
Total Missed Doses		
n	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x
Min, Max	x.x, xx.x	x.x, xx.x

[a] Duration of Exposure = Date of Last Drug Administration - Date of First Drug Administration + 1 day
[b] % Compliance = 100*((Number of Doses Expected - Number of Doses Missed) / (Number of Doses Expected)), where number of doses missed is assumed to be 1 dose per date of missed dose reported and number of expected doses is defined as 1 dose * duration of exposure. For subjects who are lost-to-follow-up or who did not return diaries but reported an unknown number of missed doses, exposure duration is defined as unknown and compliance is considered undefined.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.3.2.1
Cutaneous Tolerability Evaluation - Erythema - Summarized by Study Visit
Safety Population

Study Visit	SB204 (N=XXX)	Vehicle (N=XXX)
Baseline	xx	xx
0 - None	xx (xx.x)	xx (xx.x)
1 - Mild	xx (xx.x)	xx (xx.x)
2 - Moderate	xx (xx.x)	xx (xx.x)
3 - Severe	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Week 2	xx	xx
0 - None	xx (xx.x)	xx (xx.x)
1 - Mild	xx (xx.x)	xx (xx.x)
2 - Moderate	xx (xx.x)	xx (xx.x)
3 - Severe	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Week 4	xx	xx
0 - None	xx (xx.x)	xx (xx.x)
1 - Mild	xx (xx.x)	xx (xx.x)
2 - Moderate	xx (xx.x)	xx (xx.x)
3 - Severe	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Week 8	xx	xx
0 - None	xx (xx.x)	xx (xx.x)
1 - Mild	xx (xx.x)	xx (xx.x)
2 - Moderate	xx (xx.x)	xx (xx.x)
3 - Severe	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Week 12\ET	xx	xx
0 - None	xx (xx.x)	xx (xx.x)
1 - Mild	xx (xx.x)	xx (xx.x)
2 - Moderate	xx (xx.x)	xx (xx.x)
3 - Severe	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Note: Percentages are based on the number of subjects who completed each visit.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Using shell 14.3.2.1, repeat table for the following:

Table 14.3.2.2 Cutaneous Tolerability Evaluation - Scaling - Summarized by Study Visit, Safety Population

Table 14.3.2.3 Cutaneous Tolerability Evaluation - Dryness - Summarized by Study Visit, Safety Population

Table 14.3.2.4 Cutaneous Tolerability Evaluation - Pruritus - Summarized by Study Visit, Safety Population

Table 14.3.2.5 Cutaneous Tolerability Evaluation - Burning/Stinging - Summarized by Study Visit, Safety Population

Table 14.3.3.1
Shift from Baseline in Cutaneous Tolerability Evaluation - Erythema, by Treatment and Study Visit
Safety Population

Study Visit / Cutaneous Tolerability Score	SB204 Cutaneous Tolerability Score at Baseline					Vehicle Cutaneous Tolerability Score at Baseline				
	0 - None	1 - Mild	2 - Moderate	3 - Severe	Missing	0 - None	1 - Mild	2 - Moderate	3 - Severe	Missing
Week 2										
0 - None	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1 - Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2 - Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3 - Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Missing	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Week 4										
0 - None	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1 - Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2 - Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3 - Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Missing	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Week 8										
0 - None	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1 - Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2 - Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3 - Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Missing	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Week 12										
0 - None	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
1 - Mild	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
2 - Moderate	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
3 - Severe	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Missing	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Using shell 14.3.3.1, Repeat table for the following:

Table 14.3.3.2 Shift from Baseline in Cutaneous Tolerability Evaluation - Scaling - Summarized Continuously by Study Visit, Safety Population

Table 14.3.3.3 Shift from Baseline in Cutaneous Tolerability Evaluation - Dryness - Summarized Continuously by Study Visit, Safety Population

Table 14.3.3.4 Shift from Baseline in Cutaneous Tolerability Evaluation - Pruritus - Summarized Continuously by Study Visit, Safety Population

Table 14.3.3.5 Shift from Baseline in Cutaneous Tolerability Evaluation - Burning/Stinging - Summarized Continuously by Study Visit, Safety Population

Table 14.3.4.1
Treatment Emergent Adverse Events (TEAE) Overview
Safety Population

Number of Subjects / Number of Events	SB204 (N=XXX)	Vehicle (N=XXX)
Any TEAE	xx (xx.x)	xx (xx.x)
Number of TEAEs	xx	xx
Treatment-Related TEAE	xx (xx.x)	xx (xx.x)
Number of Treatment-Related TEAEs	xx	xx
TEAE Leading to Treatment Modification	xx (xx.x)	xx (xx.x)
Number of TEAE Leading to Treatment Modification	xx	xx
Treatment-Related TEAE Leading to Treatment Modification	xx (xx.x)	xx (xx.x)
Number of TRTEAE Leading to Treatment Modification	xx	xx
TEAE Leading to Treatment Discontinuation	xx (xx.x)	xx (xx.x)
Number of TEAE Leading to Treatment Discontinuation	xx	xx
Treatment-Related TEAE Leading to Treatment Discontinuation	xx (xx.x)	xx (xx.x)
Number of TRTEAE Leading to Treatment Discontinuation	xx	xx
Serious TEAE	xx (xx.x)	xx (xx.x)
Number of Serious TEAEs	xx	xx
Treatment-Related Serious TEAE	xx (xx.x)	xx (xx.x)
Number of Treatment-Related Serious TEAEs	xx	xx
TEAE Leading to Death	xx (xx.x)	xx (xx.x)
Number of TEAE Leading to Death	xx	xx
Treatment-Related TEAE Leading to Death	xx (xx.x)	xx (xx.x)
Number of Treatment-Related TEAE Leading to Death	xx	xx
Pregnancies	xx (xx.x)	xx (xx.x)

Note: Adverse events were coded using MedDRA 18.1. TR=Treatment-Related.
Treatment modification includes reduction, interruption, or discontinuation of Study Drug.

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Table XXXXXXX.rtf
Novan Inc: NI-AC302/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Table 14.3.4.2
Treatment Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	SB204 (N=XXX)	Vehicle (N=XXX)
Number of Subjects with at Least One Event	xx (xx.x)	xx (xx.x)
Number of Events	xx	xx
System Organ Class 1	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)
System Organ Class 2	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)

Note(s): Adverse event terms were coded using MedDRA dictionary version 18.1. Subjects are counted once within each level of summary.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer Note: Order SOC by decreasing frequency and preferred term by decreasing frequency within SOC based on overall incidence.

Using shell 14.3.4.2, repeat table for the following:

Table 14.3.4.3 Treatment-Related Emergent Adverse Events by System Organ Class and Preferred Term, Safety Population

Programmer's Note: subset on TEAEs related to study treatment. If there are no events, note within the table:

"No treatment-related treatment emergent AEs were reported"

Table 14.3.4.4 Treatment Emergent Adverse Events Leading to Treatment Modification, Safety Population

Programmer's Note: subset on TEAEs leading to treatment modification. Add the following footnote:

Note: Treatment modification includes reduction, interruption, or discontinuation of Study Drug

If there are no events, note within the table:

"No treatment emergent AEs leading to treatment modification were reported"

Table 14.3.4.5 Treatment-Related Treatment Emergent Adverse Events Leading to Treatment Modification, Safety Population

Programmer's Note: subset on Treatment-Related TEAEs leading to treatment modification. Add the following footnote:

Note: Treatment modification includes reduction, interruption, or discontinuation of Study Drug.

If there are no events, note within the table:

"No treatment-related treatment emergent AEs leading to treatment modification were reported"

Table 14.3.4.6 Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug, Safety Population

Programmer's Note: subset on TEAEs leading to discontinuation of Study Drug.

If there are no events, note within the table:

"No treatment emergent AEs leading to discontinuation of study drug were reported"

Table 14.3.4.7 Treatment-Related Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug, Safety Population

Programmer's Note: subset on Treatment-Related TEAEs leading to discontinuation of Study Drug.

If there are no events, note within the table:

"No treatment-related treatment emergent AEs leading to discontinuation of study drug were reported"

Table 14.3.4.8 Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term, Safety Population

Programmer's Note: subset on Serious TEAEs.

If there are no events, note within the table:

"No treatment emergent SAEs were reported"

Table 14.3.4.9 Treatment-Related Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term, Safety Population

Programmer's Note: subset on Treatment-Related Serious TEAEs.

If there are no events, note within the table:

"No treatment-related treatment emergent SAEs were reported"

Table 14.3.4.10 Treatment Emergent Adverse Events Leading to Death, Safety Population

Programmer's Note: subset on TEAEs with fatal outcome.

If there are no events, note within the table:

"No treatment emergent AEs leading to death were reported"

Table 14.3.4.11 Treatment-Related Treatment Emergent Adverse Events Leading to Death, Safety Population

Programmer's Note: subset on treatment related TEAEs with fatal outcome.

If there are no events, note within the table:

"No treatment-related treatment emergent AEs leading to death were reported"

Table 14.3.4.12 Summary of Pregnancies, Safety Population

Programmer's Note: subset on Pregnancies.

If there are no events, note within the table:

"No pregnancies were reported"

Table 14.3.4.13
Summary of Treatment Emergent Adverse Events (TEAE) by Highest Severity, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Severity	SB204 (N=XXX)	Vehicle (N=XXX)
Subjects with at least one event	Mild	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)
Number of events	Mild	xx	xx
	Moderate	xx	xx
	Severe	xx	xx
System Organ Class 1	Mild	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)
Preferred Term 1	Mild	xx (xx.x)	xx (xx.x)
	Moderate	xx (xx.x)	xx (xx.x)
	Severe	xx (xx.x)	xx (xx.x)

Note(s): Adverse event terms were coded using MedDRA dictionary version 18.1. Subjects are counted once within each level of summary. If a Subject has multiple events, the event with highest severity will be considered.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer Note: Order SOC by decreasing frequency and preferred term by decreasing frequency within SOC based on overall incidence.

Using shell 14.3.4.13, repeat table for the following:

Table 14.3.4.14 Summary of Treatment-Related Emergent Adverse Events (TEAE) by Severity, System Organ Class and Preferred Term, Safety Population

Programmer's Note: subset on related TEAEs

Table 14.4.1
Summary of Vital Signs
Safety Population

<Parameter> (<units>)

	SB204 (N=XXX)		Vehicle (N=XXX)	
Timepoint	Actual	Change from Baseline	Actual	Change from Baseline
Baseline				
n	xx		xx	
Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)	
Median	xx.x		xx.x	
Min, Max	xx, xx		xx, xx	
Missing	xx		xx	
Week 2				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Missing	xx	xx	xx	xx
Week 4				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
....		xx	xx	xx

Note(s): Baseline is defined as the last assessment prior to/on the date of the first study treatment.
Source: Listing xx.x.x.x.x, Program: xxxxx.sas, Output: T_xx.x_x_x_xxxx.rtf, Generated on: DDMMMYYYY HH:MM

Programmer Note: Include all vital signs parameters (e.g. SBP, DBP, Pulse) and all available post-baseline visits. Missing not presented if no missing values.

Protocol: NI-AC302

A Phase 3 Multi-Center, Randomized, Double-Blinded, Vehicle-Controlled, Parallel Group Study Comparing the Efficacy, Tolerability and Safety of Once Daily SB204 and Vehicle Gel in the Treatment of Acne Vulgaris.

Mock Data Displays- Listings
Final Version 1.0
Date:22Dec2016

Prepared for:
Novan Inc.
4105 Hopson RoadMorrisville, NC 27560

Prepared by:
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Table of Contents

Listing 16.2.1.1
Subject Disposition
All Randomized Subjects

Treatment Group	Subject ID	Met All Inc/Exc Criteria	Date of: Informed Consent	Date of Completion or Discontinuation	Treatment Duration (days)	Final Study Disposition	In ITT	In SAF	In PP
xxxxxxx	xxxxxxx	Yes	DDMMMYYYY	DDMMMYYYY	XX	Completed	Yes	Yes	Yes
xxxxxxxx	xxxxxxxx	Yes	DDMMMYYYY	DDMMMYYYY	XX	Withdrawal by Subject	Yes	Yes	No

Programmer's Note(s): All listings will be sorted by treatment group (SB204 and then Vehicle) and then by Subject ID.

Listing 16.2.1.2
Subjects With Photography Consent
All Randomized Subjects

Treatment Group	Subject ID	Site	Date of: Photography Consent	Photo May be Used for: Commercial Purposes	Photo May be Used for: Medical/ Scientific Purposes
xxxxxxx	xxxxxxx	XXXXXXX	DDMMMYYYY	Yes	Yes
xxxxxxxx	xxxxxxxx	XXXXXXX	DDMMMYYYY	Yes	No
xxxxxxxx	xxxxxxxx	XXXXXXX			

s<nnn>xxxx yyyymmddthh:mm

Programmer's Note(s): Restrict to subjects who consented to photography.

Listing 16.2.2
Protocol Violations/Deviations
All Randomized Subjects

Treatment Group	Subject ID	Date of Violation/ Deviation /Day	Major/Minor Violation /Deviation	Type of Violation	Details of Violation/Deviation	Resulted in Removal of Subject from Population? If yes, specify population
xxxxxxx	xxxxxxx	DDMMMYYYY/xx	Minor	ICF Issue	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	No
xxxxxxxx	xxxxxxxx	DDMMMYYYY/xx	Minor	Assessment not Performed per Protocol	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	Yes: Per Protocol
xxxxxxxx	xxxxxxxx	DDMMMYYYY/xx	Major	Non-compliance with IP	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	Yes : PP

Note(s): *Day = Day relative to the date of first dose of study medication.*
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.3
Inclusion/Exclusion Criteria not Met
ITT Population

Treatment Group	Subject ID	Criteria Not Met	Description of Criteria
xxxxxxx	xxxxxxx	INCXX	XXXXXXXXXXXXXXXXXXXXX
xxxxxxxx	xxxxxxxx	EXCLXX	XXXXXXXXXXXXXXXXXXXXX

Listing 16.2.4.1
Demographics
ITT Population

Treatment Group	Subject ID	Study Center	Pooled Study Center	Date of Birth	Age (years)	Gender	Ethnicity	Race
xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	DDMMMYYYY	xx.x	Male	Not Hispanic or Latino	xxxxxx
xxxxxxxx	xxxxxxxx	xxxxxxx	xxxxxxx	DDMMMYYYY	xx.x	Female	Not Hispanic or Latino	xxxxx
xxxxxxxx	xxxxxxxx	xxxxxxx	xxxxxxx	DDMMMYYYY	xx.x	Female	Not Hispanic or Latino	Other: xxxxxx

Note(s): Age is calculated as the interval between date of birth and date of baseline visit.
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.4.2
Child Bearing Potential and Pregnancy Test Results
ITT Population (Females only)

Treatment Group	Subject ID	Of Child-Bearing Potential?	If no, why?	If Yes, Method of Birth Control	OCP with Acne Indication? [a]	Visit	Collection Date / Day	Pregnancy Test Result
XXXXXXX	XXXXXXX	Yes		XXXXXXXXXX	Yes	Screening	DDMMMYYYY /XX	Negative
XXXXXXX	XXXXXXX	No	XXXXXXXXXXX			Screening	DDMMMYYYY /XX	Negative

Note(s): *Day = Day relative to the date of first dose of study medication.*
[a] OCPs with Acne Indications: Yaz/Bevaz, Estrostep and Ortho-Tri-Cyclen (or respective generic products).
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.4.3
Medical History
ITT Population

Treatment Group	Subject ID	SOC / Preferred Term / Verbatim Term	Onset / End
xxxxxxx	xxxxxxx	Xxxxxxxx / Xxxxxxxx / xxxxxxxx	DDMMYYYY / DDMMYYYY
xxxxxxxx	xxxxxxxx	Xxxxxxxx / Xxxxxxxx / xxxxxxxx	DDMMYYYY / Ongoing

Listing 16.2.4.4
Physical Exam
Safety Population

Treatment Group	Subject ID	Visit	Date	Body System	Evaluation	Abnormality
XXXXXXX	XXXXXXX	Screening	DDMMMYYYY	General Appearance	Normal	
				Respiratory	Normal	
				Cardiovascular	Normal	
				Other: XXXXXXXx	ANCS	XXXXXXXXXXXXXXXXXXX
		Baseline	DDMMMYYYY	General Appearance	ACS	XXXXXXXXXXXXXXXXXXX
				Respiratory	Normal	
				Cardiovascular	Normal	
		Etc.				
XXXXXXX	XXXXXXX	Screening	DDMMMYYYY	General Appearance	Normal	
				Respiratory	Normal	

Note(s):ANCS = Abnormal, Not clinically significant; ACS = Abnormal, Clinically Significant. If a finding was determined to be clinically significant, it is also reported as an adverse event, or, if it occurred prior to study start, it is reported in medical history.
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.5.1
Study Drug Management
ITT Population

Treatment Group	Subject ID	Visit	Date/ Day	Was Pump dispensed?	If yes, Pump number	Was previous pump returned?	If no. Reason why:
xxxxxxx	xxxxxxx	Baseline	DDMMMYYYY/xx	Yes	XXXXXX		
		Week 4	DDMMMYYYY/xx	No		No	XXXXXXXXXX
		Week 8	DDMMMYYYY/xx	Yes	XXXXXX		
		Week 12	DDMMMYYYY/xx	Yes	XXXXXX		
xxxxxxxx	Xxxxxxx	Baseline	DDMMMYYYY/xx	Yes	XXXXXX		
		Week 4	DDMMMYYYY/xx	Yes	XXXXXX		
		Week 8	DDMMMYYYY/xx	Yes	XXXXXX	Yes	
		Week 12	DDMMMYYYY/xx	Yes	XXXXXX		
xxxxxxxx	xxxxxxx	Baseline	DDMMMYYYY/xx	Yes	XXXXXX		
		Week 4	DDMMMYYYY/xx	Yes	XXXXXX	Yes	
		Week 8	DDMMMYYYY/xx	Yes	XXXXXX		
		Week 12	DDMMMYYYY/xx	No			

Note(s): *Day = Day relative to the date of first dose of study medication.*
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.5.2
Study Drug Compliance
ITT Population

Treatment Group	Subject ID	Overall Compliance (%)	Dates of Missed Doses, if any:
xxxxxxx	xxxxxxx	XX.X	DDMMYYYY, DDMMYYYY
xxxxxxx	xxxxxxx	XX.X	
xxxxxxxx	Xxxxxxx	XX.X	DDMMYYYY, DDMMYYYY, DDMMYYY, etc.
xxxxxxx	xxxxxxx	XX.X	
xxxxxxxx	xxxxxxx	XX.X	

Note(s): *Day = Day relative to the date of first dose of study medication.*
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.6.1.1
Lesion Counts : Total Inflammatory and Non-Inflammatory Lesions
ITT Population

Treatment Group	Subject ID	Visit	Date	Counter's Initials	Inflammatory Lesions			Non-Inflammatory Lesions		
					Count	Change from Baseline	Percent Change from Baseline	Count	Change from Baseline	Percent Change from Baseline
xxxxxxx	xxxxxxx	Screening	DDMMMYYYY	XXXX	XX			XX		
		Baseline	DDMMMYYYY	XXXX	XX			XX		
		Week 2	DDMMMYYYY	XXXX	XX	XX	XX	XX	XX	XX
		Week 4	DDMMMYYYY	XXXX	XX	XX	XX	XX	XX	XX
		Week 8	DDMMMYYYY	XXXX	XX	XX	XX	XX	XX	XX
		Week 12\ET	DDMMMYYYY	XXXX	XX	XX	XX	XX	XX	XX
xxxxxxx	xxxxxxx	Screening	DDMMMYYYY	XXXX	XX			XX		
		Baseline	DDMMMYYYY	XXXX	XX			XX		
		Week 2	DDMMMYYYY	XXXX	XX	XX	XX	XX	XX	XX
		Week 4	DDMMMYYYY	XXXX						
		Week 8	DDMMMYYYY	XXXX						
		Week 12\ET	DDMMMYYYY	XXXX	XX	XX	XX	XX	XX	XX

Note: Inflammatory Lesions includes: papules/pustules + nodules/cysts.
s<nnn>xxxx yyyymmddthh:mm

Novan Inc
Protocol Number: NI-AC302

Listing 16.2.6.1.2
Lesion Counts: Papules, Pustules, Nodules, and Cysts
ITT Population

Treatment Group	Subject ID	Visit	Date	Counter's Initials	Papules/Pustules	Nodules/Cysts
xxxxxxx	xxxxxxx	Screening	DDMMMYYYY	XXXX	XXX	XXX
		Baseline	DDMMMYYYY	XXXX	XXX	XXX
		Week 2	DDMMMYYYY	XXXX	XXX	XXX
		Week 4	DDMMMYYYY	XXXX	XXX	XXX
		Week 8	DDMMMYYYY	XXXX	XXX	XXX
		Week 12\ET	DDMMMYYYY	XXXX	XXX	XXX
xxxxxxx	xxxxxxx	Screening	DDMMMYYYY	XXXX	XXX	XXX
		Baseline	DDMMMYYYY	XXXX	XXX	XXX
		Week 2	DDMMMYYYY	XXXX	XXX	XXX
		Week 4	DDMMMYYYY	XXXX	XXX	XXX
		Week 8	DDMMMYYYY	XXXX	XXX	XXX
		Week 12\ET	DDMMMYYYY	XXXX	XXX	XXX

Listing 16.2.6.2
Investigator Global Assessment (IGA)
ITT Population

Treatment Group	Subject ID	Visit	Evaluator's Initials	Date	Global Assessment	Shift from Baseline	Success?
xxxxxxx	xxxxxxx	Screening	XXXX	DDMMMYYYY	3: Moderate		
		Baseline	XXXX	DDMMMYYYY	4: Severe		
		Week 2	XXXX	DDMMMYYYY	3: Moderate	X	No
		Week 4	XXXX	DDMMMYYYY	2: Mild	-X	No
		Week 8	XXXX	DDMMMYYYY	2: Mild	-X	No
		Week 12	XXXX	DDMMMYYYY	2: Mild	X	No
				DDMMMYYYY			
xxxxxxxx	xxxxxxxx	Screening	XXXX	DDMMMYYYY	4:Severe		
		Baseline	XXXX	DDMMMYYYY	4: Severe		
		Week 2	XXXX	DDMMMYYYY	3: Moderate	-X	No
		Week 4	XXXX	DDMMMYYYY	2: Mild	-X	No
		Week 8	XXXX	DDMMMYYYY	1: Almost Clear	-X	Yes
		Week 12	XXXX	DDMMMYYYY	0: Clear	-X	Yes

Note(s): For Shift from Baseline, negative values represent improvement.s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.6.3
Cutaneous Tolerability
Safety Population

Treatment Group	Subject ID	Visit	Date	Erythema	Scaling	Dryness	Pruritus	Burning/ Stinging
xxxxxxx	xxxxxxx	Screening	DDMMMYYYY	1: Mild	1: Mild	2: Moderate	0: None	0: None
		Baseline	DDMMMYYYY	1: Mild	1: Mild	2: Moderate	0: None	0: None
		Week 2	DDMMMYYYY	1: Mild	1: Mild	2: Moderate	0: None	0: None
		Week 4	DDMMMYYYY	1: Mild	1: Mild	2: Moderate	0: None	0: None
		Week 8	DDMMMYYYY	1: Mild	1: Mild	2: Moderate	0: None	0: None
		Week 12	DDMMMYYYY	1: Mild	1: Mild	2: Moderate	0: None	0: None
xxxxxxxx	xxxxxxxx	Screening	DDMMMYYYY	xxxx	xxxx	xxxx	xxxx	xxxx
		Baseline	DDMMMYYYY	xxxx	xxxx	xxxx	xxxx	xxxx
		Week 2	DDMMMYYYY	xxxx	xxxx	xxxx	xxxx	xxxx
		Week 4	DDMMMYYYY	xxxx	xxxx	xxxx	xxxx	xxxx
		Week 8	DDMMMYYYY	xxxx	xxxx	xxxx	xxxx	xxxx
		Week 12	DDMMMYYYY	xxxx	xxxx	xxxx	xxxx	xxxx

Note(s):
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.6.4
Vital Signs
Safety Population

Treatment Group	Subject ID	Visit	Date/ Day	Systolic BP (mmHg)	Diastolic BP (mmHg)	Pulse (bpm)	Evaluation	If Abnormal and Clinically Significant, provide MH or AE term
xxxxxxx	xxxxxxx	Screening	DDMMMYYYY/xx	xxx	xxx	xxx	Normal	
		Baseline	DDMMMYYYY/xx	xxx	xxx	xxx	Normal	
		Week 2	DDMMMYYYY/xx	xxx	xxx	xxx	Abnormal, NCS	
		Week 4	DDMMMYYYY/xx	xxx	xxx	xxx	Normal	
		Week 8	DDMMMYYYY/xx	xxx	xxx	xxx	Normal	
		Week 12\ET	DDMMMYYYY/xx	xxx	xxx	xxx	Normal	
xxxxxxxx	xxxxxxxx	Screening	DDMMMYYYY/xx	xxx	xxx	xxx	Abnormal, CS	XXXXXXXXXXXXX

Note(s): *Day = Day relative to the date of first dose of study medication.* NCS = Not clinically significant; CS = Clinically Significant. If a post-baseline finding was determined to be clinically significant, it is also reported as an adverse event.
s<nnn>xxxx yyyymmddthh:mm

Novan Inc
Protocol Number: NI-AC302

Listing 16.2.6.5
Concomitant Medications
ITT Population

Treatment Group	Subject ID	Drug Class/ Preferred Name/ Reported Term	Indication	Start Date (Day)/ End Date (Day)	Dose (Unit) / Frequency / Route	If for AE or MH, Primary Term
xxxxxxx	xxxxxxx	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	Adverse Event	DDMMMYYYY (XX)/ Ongoing		
xxxxxxxx	xxxxxxxx	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	Medical History	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXX.X (XXXXX) / XXX / XXXXXXXXXX	XXXXXXXXX
xxxxxxx	xxxxxxx	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	Prophylaxis	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXX.X (XXXXX) / XXX / XXXXXXXXXX	
xxxxxxxx	xxxxxxxx	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	Dietary Supplement	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXX.X (XXXXX) / XXX / XXXXXXXXXX	XXXXXXXXX
xxxxxxxx	xxxxxxxx	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	Contraception	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXX.X (XXXXX) / XXX / XXXXXXXXXX	
xxxxxxxx	xxxxxxxx	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	Other: XXXXXXXXXX	DDMMMYYYY (XX)/ DDMMMYYYY (XX)	XXX.X (XXXXX) / XXX / XXXXXXXXXX	

Note(s): *Day = Day relative to the date of first dose of study medication.*
Coding will be done using the WHO March 2016 dictionary. Drug Class corresponds to ACT level 2.
s<nnn>xxxx yyyymmddthh:mm

Listing 16.2.7.1
Adverse Events
Safety Population

Treatment Group	Subject ID	System Organ Class/ Preferred Term/ Reported Term	TEAE	First Dose Date/ Start Date/ End Date / (Days)	Cause Study Discon-tinuation?	Severity / Relationship	Action / Treatment / Final Outcome	SAE?	SAE Criteria
xxxxxxx	xxxxxxx	XXXXXXXXXXXXXXX / XXXXXXXXXXXXXX / XXXXXXXXXXXXXXX		DDMMMYYY / DDMMMYYY / DDMMMYYYY / XX	No	Mild / Unlikely	Dose Not Changed / XXXXXXXX / XXXXXXXXXXX XX	No	
xxxxxxxx	xxxxxxxx	XXXXXXXXXXXXXXX / XXXXXXXXXXXXXX / XXXXXXXXXXXXXXX		DDMMMYYY / DDMMMYYY / DDMMMYYYY / XX	Yes	XXXXXXX / XXXXXXX	XXXXXXXX / XXXXXXXX / XXXXXXXXXXX XX	Yes	XXXXXXXXXXX XX

Note(s): TEAE=Treatment-emergent Adverse Event. Days = (Adverse event end date - event start date)+1
Adverse events were coded using MedDRA 18.1
s<nnn>xxxx yyyymmddthh:mm

Repeat Listing 16.2.7.1 for:

Listing 16.2.7.2 Treatment-Emergent Adverse Events Leading to Treatment Modification, Safety Population
Listing 16.2.7.3 Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug, Safety Population
Listing 16.2.7.4 Treatment-Emergent Serious Adverse Events, Safety Population
Listing 16.2.7.5 Treatment-Emergent Adverse Events Leading to Death, Safety Population

Programmer's Note(s): If there are no TEAE leading to Death, add the following statement in the body of the listing:

No Treatment-Emergent Adverse Events leading to death were reported.

Listing 16.2.7.6 Pregnancies, Safety Population

Programmer's Note(s): If there are no pregnancies, add the following statement in the body of the listing:

No pregnancies were reported.

Listing 16.2.7.7
Concomitant Medical and Surgical Procedures
ITT Population

Treatment Group	Subject ID	Verbatim Term	Start Date (Day) / End Date (Day)	Was it for an AE/SAE?
xxxxxxx	xxxxxxx	XXXXXXXXXXXXXXXXXXXX	DDMMYYYY (XX) / DDMMYYYY (XX)	No
xxxxxxxx	xxxxxxxx	XXXXXXXXXXXXXXXXXXXX	DDMMYYYY (XX) / Ongoing	No

Protocol: NI-AC302

A Phase 3 Multi-Center, Randomized, Double-Blinded, Vehicle-Controlled, Parallel Group Study Comparing the Efficacy, Tolerability and Safety of Once Daily SB204 and Vehicle Gel in the Treatment of Acne Vulgaris

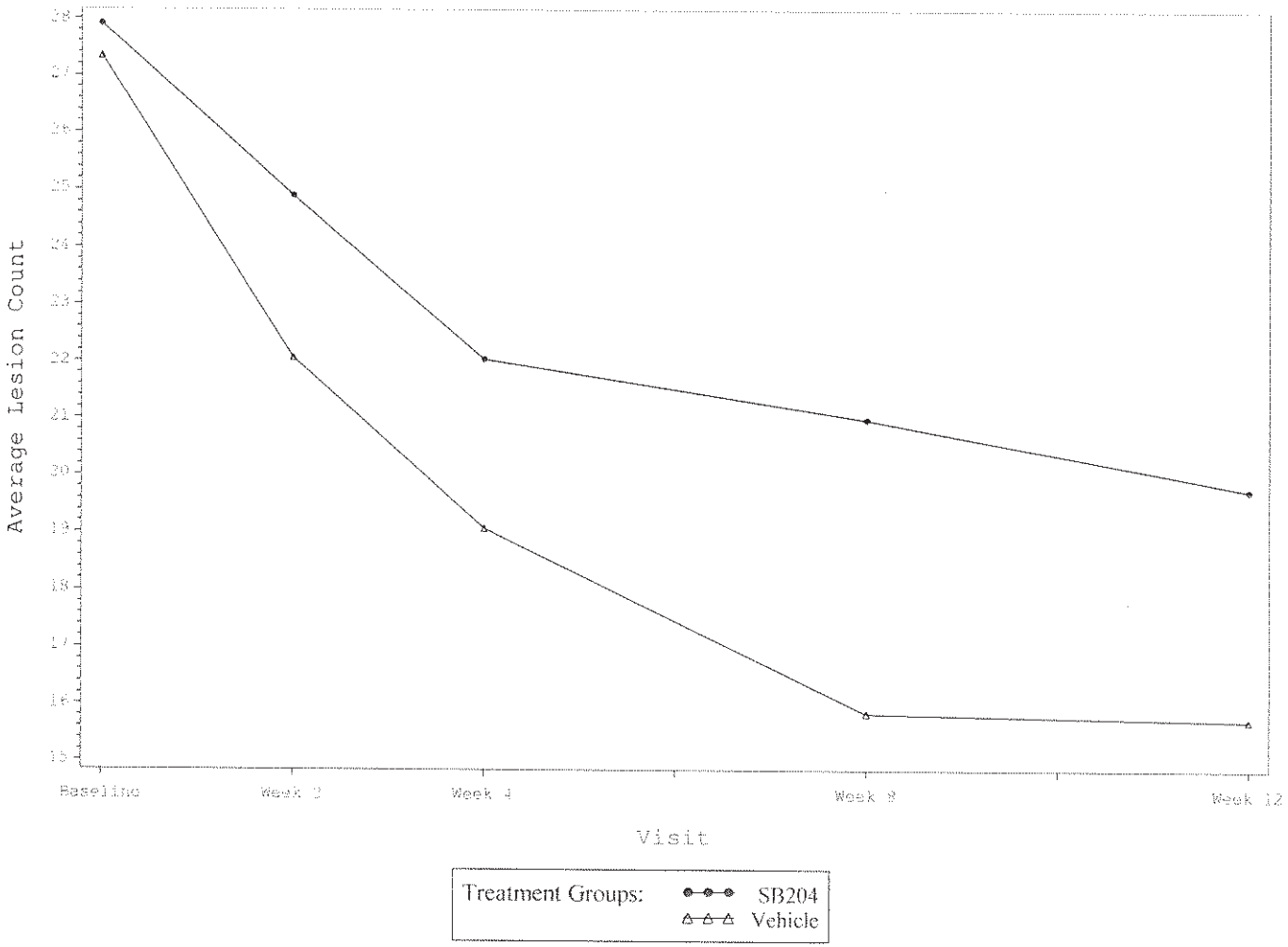
Mock Data Displays- Figures
Final Version 1.0
Date: 22Dec2016

Prepared for:
Novan Inc.
4105 Hopson Road Morrisville, NC 27560

Prepared by:
Chiltern International
4000 CentreGreen Way, Suite 300, Cary, NC, 27513, United States

Contents

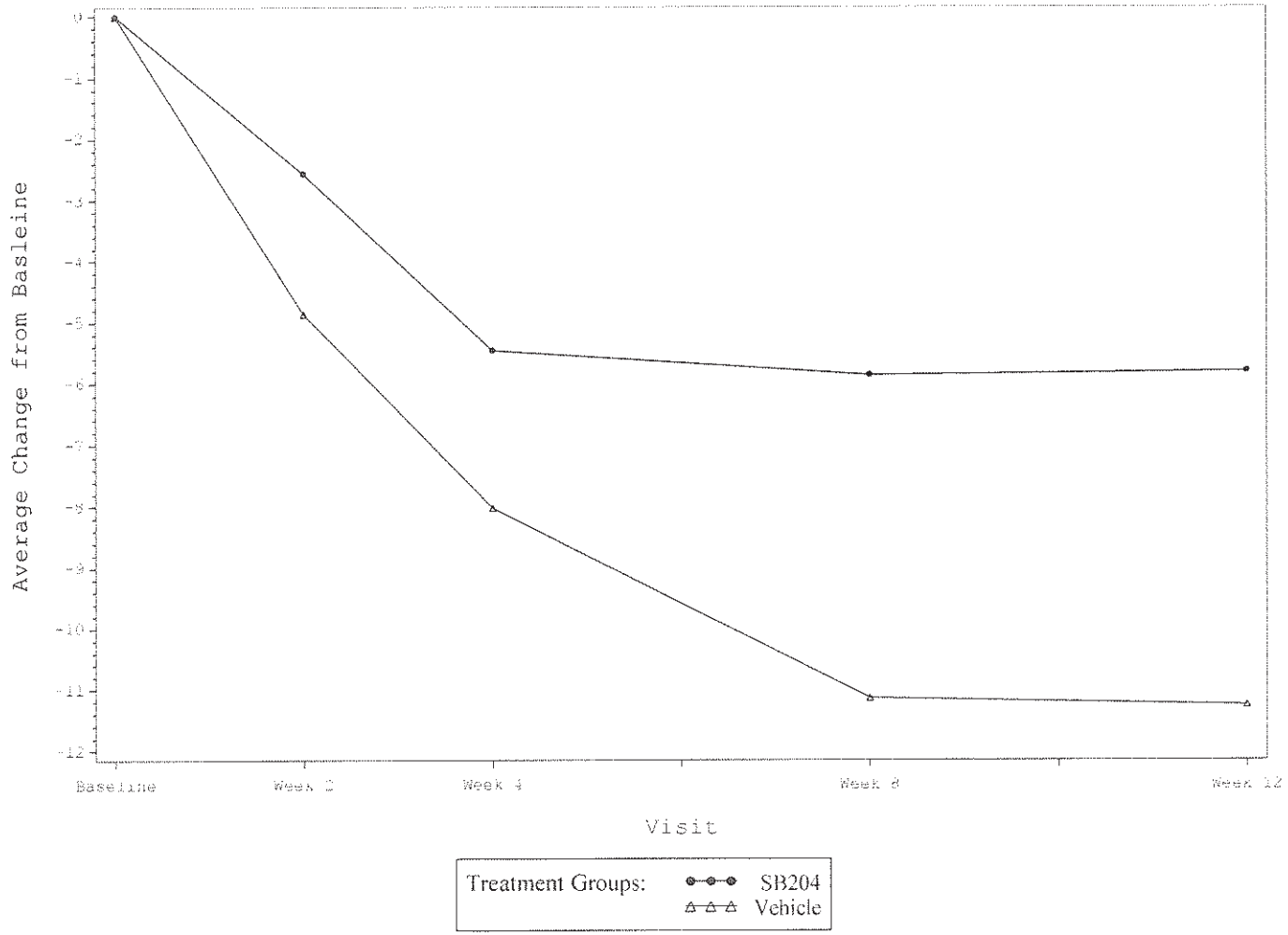
Figure 14.1.1 Average Inflammatory Lesion Count Over Time
ITT Population



Programmer's Note(s): In final output, the unmarked tick marks will not appear.

Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Figure XXXXXXX.rtf
Novan Inc: NI-AC301/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Figure 14.1.2 Average Change from Baseline in Inflammatory Lesion Count Over Time
ITT Population



Programmer's Note(s): In final output, the unmarked tick marks will not appear.
Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Figure XXXXXXX.rtf
Novan Inc: NI-AC301/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Using shell for Figure 14.1.2 repeat for the following:

Figure 14.1.3 Average Percent Change in Inflammatory Lesion Count Over Time, ITT Population

Figure 14.1.4 Average Percent Change in Inflammatory Lesion Count Over Time, PP Population

Using shell for Figure 14.1.1, repeat for the following:

Figure 14.2.1 Average Non-Inflammatory Lesion Count Over Time, ITT Population

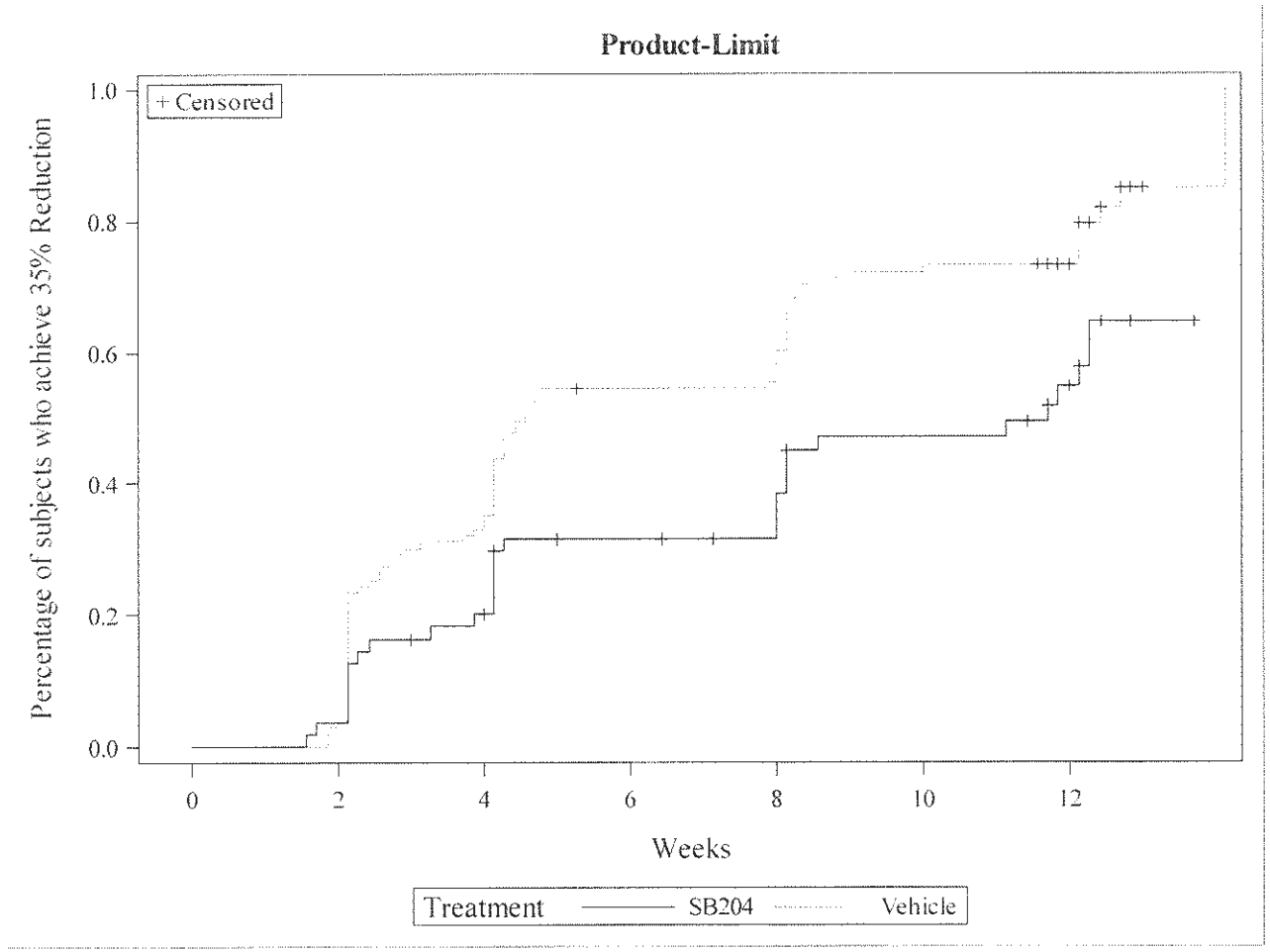
Using shell for Figure 14.1.2 repeat for the following:

Figure 14.2.2 Average Change from Baseline in Non-Inflammatory Lesion Count Over Time, ITT Population

Figure 14.2.3 Average Percent Change in Non-Inflammatory Lesion Count Over Time, ITT Population

Figure 14.2.4 Average Percent Change in Non-Inflammatory Lesion Count Over Time, PP Population

Figure 14.3.1 Secondary Efficacy Analysis: Time to 35% Improvement in Inflammatory Lesion Count
ITT Population



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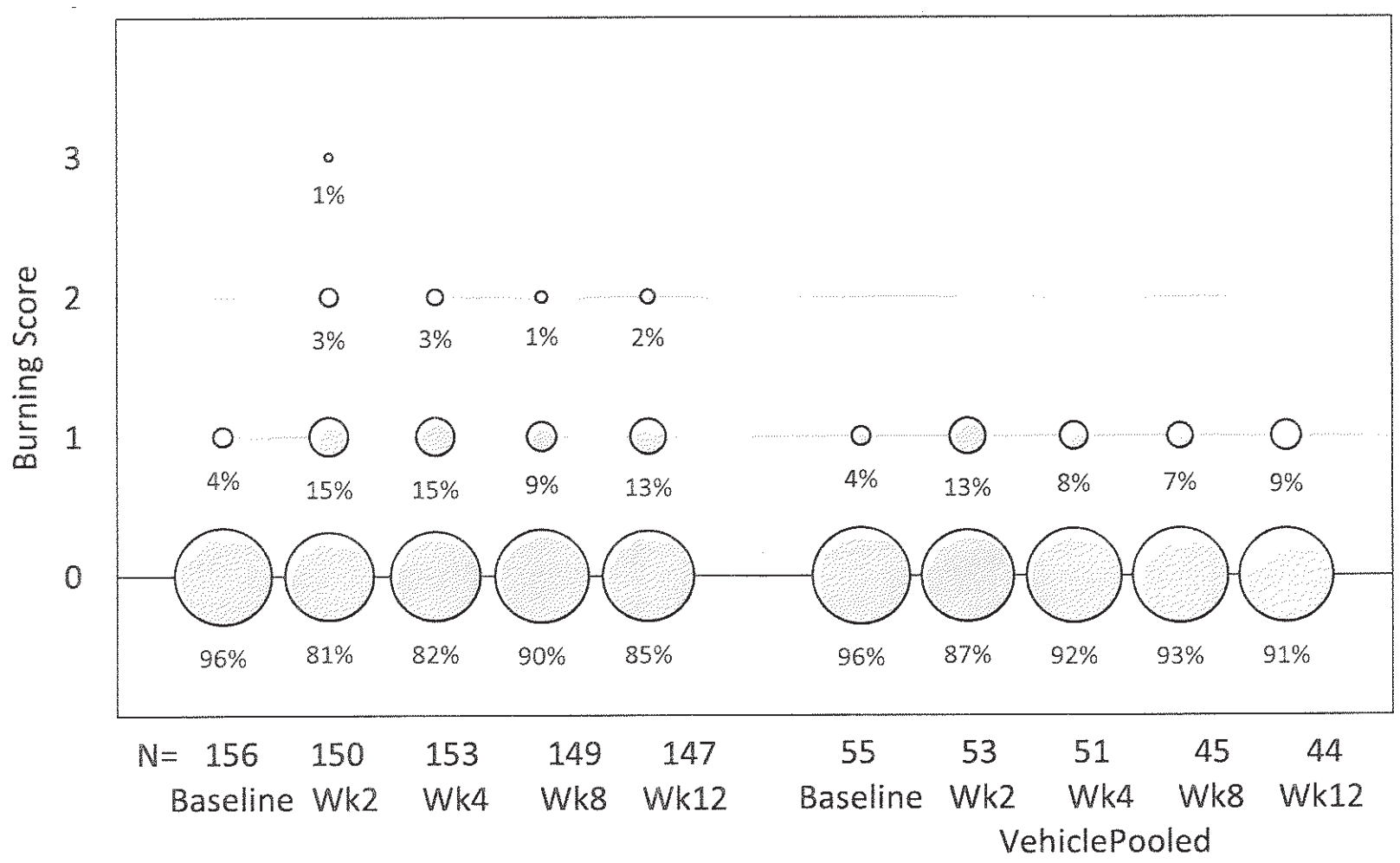
Novan Inc: NI-AC301/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Using shell for Figure 14.3.1, repeat for the following:

Figure 14.3.2 Secondary Efficacy Analysis: Time to 2 or More Grade Improvement in IGA Score, ITT Population

Figure 14.4.1 Distribution of Erythema Scores by Treatment and Visit
Safety Population



Source: Listing XX.X.X.X, Program: XXXXXXXXX.sas, Output: Figure XXXXXXX.rtf
Novan Inc: NI-AC301/CIL-AS/DRAFT
Produced: 5 October 2016, 16:33
Data Cut: DDMMMYYYY; Status: Blinded/Dummy Treament Data, Draft Output

Using shell for Figure 14.4.1, repeat for the following:

Figure 14.4.2 Distribution of Dryness Scores by Treatment and Visit, Safety Population

Figure 14.4.3 Distribution of Scaling Scores by Treatment and Visit, Safety Population

Figure 14.4.4 Distribution of Pruritus Scores by Treatment and Visit, Safety Population

Figure 14.4.5 Distribution of Burning/stinging Scores by Treatment and Visit, Safety Population