Statistical Analysis Plan

Protocol Title	A Phase 2, Open Label Study to Evaluate the Safety, Efficacy and Systemic Exposure of VP-102 Topical Film Forming Solution [0.7% (w/v) cantharidin] in Subjects (2 years and older) with Molluscum Contagiosum
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This study will be conducted in compliance with the protocol, Good Clinical Practice and all other applicable regulatory requirements, including the archiving of essential documents.

SAP Document History

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List of Abbreviations

AE	Adverse Event
ANCOVA	Analysis of Covariance
ATC Class	Anatomical/Therapeutic/Chemical Class
BMI	Body Mass Index
CDLQI	Children's Dermatology Life Quality Index
CSR	Clinical Study Report
EDC	Electronic Data Capture
EOS	End of Study
ERT	Evaluation of Response to Treatment
GC/MS	Gas Chromatography/Mass Spectrometry
IRB	Institutional Review Board
ITT	Intent to Treat
LLOQ	Lower Limit of Quantification
LOCF	Last Observation Carried Forward
LSR	Local Skin Reactions
MedDRA	Medical Dictionary for Regulatory Activities
mm	Millimeter
MMRM model	Mixed Model, Repeat Measures model
PERIT	Patient Evaluation of Response to Investigational Treatment
RTF	Rich Text Format
SERT	Safety Evaluation of Response Treatment
TEAE	Treatment Emergent Adverse Event
TFL	Tables, Figures, Listings

WHO	World Health Organization

1. Introduction

Verrica Pharmaceuticals, Inc. is conducting a study under the protocol name "A Phase 2, Open-Label Study to Evaluate the Safety, Efficacy and Systemic Exposure of VP-102 Topical Film Forming Solution [0.7% (w/v) cantharidin] in Subjects (2 years and older) with Molluscum Contagiosum". The study background, design and subject assessments for the study are described in the study specific protocol.

The statistical methods to be implemented during the analyses of data collected within the scope of this study (VP-102-103) will be outlined in this document. The purpose of this plan is to provide specific guidelines from which the statistical analysis will proceed. Any deviations from this plan will be documented in the clinical study report.

2. Study Rationale and Objectives

2.1. Study Rationale

The protocol states: "For many dermatologists, 0.7% w/v cantharidin has been the treatment of choice for molluscum for decades. However, cantharidin remains an unapproved drug, and there is no reliable or controlled source on the market. This study will evaluate VP-102, a controlled, highly-pure, standardized form of topical cantharidin manufactured under good manufacturing practices in order to address the problems associated with currently available compounded cantharidin products and the needs of patients and medical professionals."

2.2. Study Objectives

2.2.1. Primary Objectives

The primary objective of this study is to determine the presence or absence of systemic cantharidin exposure from a single 24-hour dermal application of VP-102 topical film-forming solution [0.7% (w/v) cantharidin] (VP-102) when applied to molluscum contagiosum (molluscum) lesions on pediatric subjects 2 years old and older.

2.2.2. Secondary Objectives

The secondary objectives of this study are:

- to assess the safety of VP-102, when applied once every 21 days for up to 4 applications, to treated molluscum lesions on subjects 2 years old and older by assessing adverse events including expected local skin reactions, physical examinations and concomitant medications throughout the study compared to baseline.
- To assess the efficacy of VP-102 in the treatment of molluscum lesions as assessed by clearance or reduction of treated molluscum lesions as compared to baseline.

- To assess the impact of VP-102 treatment on quality of life of subjects as assessed via the administration of the Children's Dermatology Life Quality Index (CDLQI).

3. Study Design

This is a Phase 2 study that will be conducted in the United States to determine the systemic exposure, efficacy, safety and impact on quality of life of VP-102 (0.7% cantharidin) following treatment of molluscum lesions for up to 4 treatments, 21 days apart, with VP-102 in up to 40 subjects (2 years or older). Subjects to be included in the Exposure group must have at least 21 lesions treated at Day 1 to qualify. The Standard treatment group will consist of subjects with fewer than 21 lesions treated at Day 1. Duration of molluscum lesions prior to Day 1 will be recorded but will not be an inclusion/exclusion requirement.

Study drug, VP-102, will be supplied in single-use applicators, with one applicator sufficient to treat at least 50 molluscum lesions. If required due to the number and size of lesions, a second single-use applicator may be used. No more than 2 applicators will be permitted per subject per treatment. In the Exposure group, blood samples for systemic exposure evaluation will be collected on Day 1, prior to the Study drug application (T=0), and 2 (± 30 minutes), 6 (± 1 hour) and 24 (±3 hours) hours post-application. The film-forming Study drug solution will be applied and left on the lesions for approximately 24 hours before the subject and/or parent/guardian washes the dried film off the lesions with soap and warm water. For those subjects in the Exposure group, the dried film will be removed after the 24-hour blood draw is obtained. Study drug treatment may be removed prior to the 24-hour time point in the event significant blistering, uncontrollable pain or treatment emergent AEs are experienced.

Molluscum lesions will be treated without occlusion in all anatomic areas including the face, trunk, back, arms, legs, hands, feet, genital region and buttocks as long as the physician feels it is safe to do so.

The study duration from Day 1 through the EOS visit is up to 12 weeks. Pre-study screening for eligibility (informed consent, inclusion/exclusion criteria and medical history) will occur up to 14 days before, or on Day 1/Study drug administration. Subjects will be treated with application to molluscum lesions every 21 days (± 4 days) for a maximum of 4 treatment sessions. Subjects that completely clear prior to ~Day 84 will

complete their EOS visit on that day. In the event of scheduling conflicts in subsequent visits after the Day 1 treatment, subjects may be scheduled on 21 ± 4 days following their previous treatment. The next study visit should then be scheduled 21 days after the previous treatment.

Assessment of local skin reactions (LSR) will be performed by the investigator or trained member of the research team at each treatment visit and the EOS visit. LSRs will be recorded as adverse events. LSRs will include the following adverse events: blistering, pain, pruritus, erythema, edema, erosion/ulcerations, flaking/scaling/dryness, scabbing/crusting and pigmentation changes. A Skin Quality Assessment will also be performed as part of the review of LSRs and will assess erythema, flaking/scaling/dryness, scabbing/crusting, hyperpigmentation, hypopigmentation and scarring, if applicable.

Parent/subject quality of life and measure of impact of skin disease will be assessed with the CDLQI prior to application of Study drug at each treatment session and at the EOS visit. Subjects will also complete a Safety Monitoring Questionnaire at Visits 2-5.

Subjects will be given a 24-hour phone number to call the investigator or a clinical research team member in the event of questions or AEs. Evaluations will also be provided by the subject or parent/guardian using the Patient Evaluation of Response to Investigational Treatment (PERIT) form the following day after Study drug application. Parents will also be asked to take and send photos via text or e-mail to the study team for assessment during the 24-hour follow-up call. All observed AEs, local skin reactions and parent-reported AEs will be recorded.

Parents or guardians must provide informed consent, and pediatric subjects older than 5 years must provide assent as required by the IRB before any study procedures are conducted. Subjects must meet all study eligibility criteria through a complete review of pertinent medical history, a symptom/sign evaluation, and limited physical examination.

4. Determination of Sample Size

The primary objective of the study is to determine the presence or absence of systemic cantharidin exposure from application of VP-102. Thus, power calculations were not performed. There will be up to 40 subjects enrolled with the goal of 16 completing all blood draws in the Exposure group. Any subject in the Exposure group who does not

complete all blood draws may continue to receive treatment, but will be replaced. At least 3 subjects in the Exposure group will be from 2-5 years of age.

5. Statistical Methods

The statistical analyses will be reported using summary tables, figures and listings (TFLs). Numbering for TFLs will be based on the recommended numbering convention provided by the International Conference on Harmonization. Continuous variables will be summarized with means, standard deviations, medians, minimums and maximums. Categorical variables will be summarized by counts and percent of subjects in corresponding categories. Where appropriate, 95% confidence intervals will be included. Missing values are not considered for percent calculations, unless stated otherwise. In those cases, footnotes will specify the percent basis. All summary tables will present a summary of the Exposure treatment group and Standard treatment group. In addition, an overall/total summary will be provided that will include subjects who were replaced.

Individual subject data obtained via the electronic data capture (EDC) system and from external vendors will be presented in listings.

The analyses described in this plan are considered *a priori*, in that they have been defined prior to database lock. Any analysis added after the database lock will be considered *post hoc* and exploratory. *Post hoc* analyses will be labeled as such on the output and identified in the CSR. All analyses and tabulations will be performed using SAS® version 9.3 or higher. Tables and listings will be presented in .rtf or .pdf format. Upon completion, all SAS programs will be validated by an independent programmer. The validation process will be used to confirm that statistically valid methods have been implemented and that all data manipulations and calculations are accurate. Checks will be made to ensure accuracy, consistency with this plan, consistency with tables and consistency between tables and corresponding data listings.

6. Analysis Populations

The Intent to Treat population (ITT) will include all subjects who meet the screening eligibility criteria and are enrolled in the study. A subject will be considered enrolled in the study when they have signed informed consent and received at least 1 treatment of study medication.

The Safety population will include subjects who meet the screening eligibility criteria for the study and receive at least one application of Study drug.

The Exposure population will include those subjects who are assigned to the Exposure cohort and have successfully completed all blood draws (Pre-Application and 2hr, 6hr and 24hr post-application on Day 1). Subjects assigned to the Exposure cohort without successfully completing all blood draws will be replaced and not included in the Exposure population, but will be included in the Intent to Treat and Safety populations.

7. Study Population

7.1. Subject Disposition

Information regarding subject disposition will be summarized for all subjects by treatment group. Summaries will include: number of subjects enrolled, number of subjects in each analysis population, number of subjects completing the study, and number of subjects who discontinue the study early. For those who discontinue early, the primary reason for discontinuation will be summarized.

7.2. Protocol Deviations

Protocol deviations will be collected throughout the duration of the study. Protocol deviations will be assigned a sponsor-defined category type. Each deviation will be defined as major or minor. A tabular summary of all major deviations will be generated. In addition, a by-subject listing of all protocol deviations (major and minor) will be produced.

7.3. Demographic and Baseline Characteristics

Demographics variables will include: age, sex, ethnicity and race. Age will be calculated by comparing date of birth to date of informed consent.

Baseline characteristics will include: medical history, molluscum history, height, weight and body mass index (BMI). BMI will be calculated by weight (kg) / height (m^2). Molluscum history variables that will be summarized include time since clinical diagnosis (as compared to informed consent), age at diagnosis and any previous treatments for molluscum lesions. Medical history will not be summarized in a table, but will be displayed in a listing.

Continuous variables will be summarized using descriptive statistics. Categorical variables will be summarized using counts and percentages. Demographics, baseline characteristics and molluscum history will be summarized for all 3 analysis populations (ITT, Safety, Exposure).

8. Exposure Analysis

Plasma samples from the Exposure group will be analyzed at each time point using a GC/MS assay method that was previously validated by Pacific Bio Labs (Study number 14I0376R-A03). Samples will be listed as either below or above the LLOQ (1 ng/ml).

An overall and by time point summaries of concentration results above and below the LLOQ will be provided using the Exposure population. Concentration levels above LLOQ will be considered evidence of the presence of systemic cantharidin (primary objective). A listing will be generated which will show results of LLOQ as well as any results reported above LLOQ.

9. Efficacy Analysis

The ITT and Exposure population will be used for efficacy analysis. Results will be summarized using descriptive statistics and counts/percentages. Where appropriate, 95% confidence intervals may be generated as well.

For the purposes of the analyses, all lesions reported in the study will be considered treatable. Although the protocol specifies study objectives and efficacy variables in terms of treated lesions, actual analysis will be carried out on treatable lesions. The reason to carry out analysis on treatable lesions is to avoid any bias or confusion with determining whether a lesion was treated. This is also in alignment with other studies in this clinical program per regulatory feedback. As a result, considering treatable lesions instead of treated lesions will be a more conservative approach when analyzing study results.

9.1. Efficacy Variables

Efficacy endpoints to be analyzed are:

- Proportion of subjects exhibiting complete clearance of all treated molluscum lesions (baseline and new) on or before Week 12 (EOS).
- Proportion of subjects exhibiting a 90% or greater reduction of all molluscum lesions (baseline and new) at the EOS visit.
- Percent reduction of molluscum lesions from baseline at the EOS visit.
- Change from baseline in the number of molluscum lesions at the EOS visit.
- Change from baseline in the quality of life and impact of skin disease as measured by the Children's Dermatology Life Quality Index (CDLQI) assessment at the EOS visit.
- Subject reported spread to siblings as measured by any new occurrence of molluscum in siblings of subject.

9.2. Baseline Values

Unless otherwise noted, baseline is defined as the last non-missing value recorded prior to the first application of study drug. When applicable, unscheduled visits will be used in the determination of baseline values.

9.3. Adjustments for Covariates

No statistical analysis is planned for this study; as a result, no adjustment for covariates will be made.

9.4. Handling of Dropouts or Missing Data

All subjects who receive treatment will be evaluated in the ITT population. Subjects who do not complete all of the scheduled blood draws will be replaced. In the event a subject requests to be removed from the study due to study related adverse events or additional spreading of disease, data will be collected and analyzed as a treatment failure and not replaced.

Unless described otherwise in subsequent sections, analyses will be carried out with the data available using no imputation for missing data. A description of how missing data will be handled for the primary endpoint and secondary endpoints is included below.

9.4.1. Handling of Missing Data for Complete Clearance Endpoint

The efficacy endpoint, proportion of subjects exhibiting complete clearance of all treatable lesions, is to be assessed a maximum of four times during the study. Assessments are to be done at Day 21, Day 42, Day 63 and Day 84 (EOS).

Subjects who do not have an assessment of complete clearance of all treatable lesions at any of the scheduled assessments will be considered to have missing data for this endpoint. Since the endpoint is complete clearance on or before Week 12, a subject will be considered to have met the condition of complete clearance if that subject has at least one assessment of complete clearance, regardless of what other assessments of clearance may be missing. If a subject has only non-missing assessments of not achieving clearance, then that subject will not be considered to have cleared. If a subject is missing all assessments of clearance, then that subject will be considered to have not cleared.

9.4.2. Handling of Missing Data for Select Endpoints

Assessment of number of treatable lesions is planned for the baseline visit, the EOS visit and each visit where treatment is applied. Endpoints that are based on these assessments include percent reduction from baseline of treatable lesions, change from baseline in treatable lesions and proportion of subjects exhibiting 90% or greater reduction of treatable lesions from baseline. If the EOS assessment of number of treatable lesions is not available, the number of treatable lesions will be imputed from earlier assessments of lesions count using last observation carried forward (LOCF). The LOCF method uses

information from the last available assessment of the measurement to include subjects with missing data in analysis. Similarly, LOCF will be used to impute other post baseline visit where lesion count is not available. One exception is if only the baseline lesion count is available for a subject. In that instance, the baseline value will not be carried forward and the number of treatable lesions will be left as missing.

Missing composite CDLQI scores at the EOS visit will be handled using the same method of LOCF as described above for imputing missing lesion counts. For handling individual questions with missing responses, see Section 10.4 for more details.

9.5. Interim Analysis and Data Monitoring

No formal interim analysis or data monitoring is planned for this study.

9.6. Multiple Comparison/Multiplicity

No formal statistical comparisons are planned; thus, no adjustment for multiple comparisons is needed.

9.7. Examination of Subgroups

Analyses based on subgroups of interest may be carried out for exploratory purposes. Possible analyses include the following:

- Baseline Lesion Count: 1-20 lesions, 21-40 lesions, 41 or more lesions. Note: lesion count categories may be adjusted based on distribution of baseline lesion counts.
- Age: 2-5 years old, 6-11 years old, 12 years or older.
- Gender: Female, Male.
- Subjects 12 or older with genital lesions being 50% or greater percent of lesions at baseline. A separate analysis will be run for those subjects who do not qualify for this subgroup.
- Presence or absence of atopic dermatitis.

10. Methods of Efficacy Analysis

10.1. Complete Clearance of Treatable Lesions

Counts and percent of subjects who have complete clearance of all treatable molluscum lesions on or before EOS will be displayed by treatment group. Complete clearance will be defined as no lesions (lesion count=0) reported for a subject per the Skin Examination form. Summaries of complete clearance will also be provided by visit. Note: all lesions reported on the Skin Examination form will be considered treatable. Number of inflamed lesions, number of lesions not treated and reasons why lesions were not treated will be displayed in listings.

The EOS visit is scheduled to occur on Day 84 and 21 days (+/- 4 days) after their last treatment visit. For the analyses of this endpoint, only visits that occur prior to Day 100 will be considered for determining complete clearance. Subjects without an assessment of lesion count within this visit window will be counted as not cleared.

10.2. Lesion Percent (%) Reduction at EOS

At the EOS visit, the number of lesions will be reported. The percent change in number of lesions will be calculated as described in Section 10.3. Based on the percent reduction of lesions at EOS, subjects will be assessed and assigned to one of 2 categories: ≥ 90% reduction of lesions, <90% reduction in lesions. Subject counts and percentage of subject for each of these categories will be displayed by treatment group over the entire study and by visit.

10.3. Change and Percent Change in Number of Lesions

Number of lesions present will be recorded at each treatment visit as well as EOS. For each post baseline treatment visit, the change in number of lesions from baseline will be calculated. Summary statistics of number of lesions will be displayed for each treatment visit by treatment group. Summary statistics of change in number of lesions from baseline will also be displayed.

Percent change of lesions will be calculated at each post baseline visit. Percent change will be calculated using the following formula (in formula below, lesions refers to treatable lesions):

$$\text{Percent (\%) Change} = \left(\frac{Lesions\ at\ Post\ Baseline\ Visit - Lesions\ at\ Baseline\ Visit}{Lesions\ at\ Baseline\ Visit}\right) * 100$$

Analysis of percent change in number of lesions will be carried in the same manner as change in number of lesions.

10.4. Children's Dermatology Life Quality Index (CDLQI)

At each study visit, the CDLQI will be administered with specific instruction to focus on the impact of molluscum and not any other possible concomitant skin ailments. The CDLQI is a 10-item questionnaire completed by subject/parent to assess skin condition over the past week. From responses to that questionnaire, a composite score is calculated. The calculated composite score is the sum of the individual 10 items of the CDLQI and can range from 0-30. For each item on the CDLQI, a score of 0-3 is assigned using the following scores per response:

- Not at all= 0
- Only a little= 1
- Quite a lot= 2
- Very much (or Prevented School, Question 7 only) = 3

Larger composite CDLQI scores indicate skin condition is having more effect on subjects' lives. If one question is left unanswered, it is scored 0 for the total composite score. If two or more questions are left unanswered, the questionnaire is not scored and will be counted as missing. Question 7 has 2 parts: one applicable if the subject is in school; the other if the subject is on vacation (holiday). Subjects are supposed to only respond to 1 of these questions. Should the subject respond to both questions, the higher of the 2 scores will be counted.

The composite score from the CDLQI will be treated as a continuous variable. Descriptive statistics of the composite score will be displayed by visit and EOS for each treatment group considering all subjects. The CDLQI has only been validated for subjects between 4-16 years old age. As a result, analyses will only consider subjects 4-16 years old.

Descriptive statistics for each of the individual items (questions) in the CDLQI will be generated by visit. The CDLQI has a series of domains, each with its own score. The domain scores are calculated based on responses to specific question(s) within the CDLQI. Descriptive statistics of each domain score will be provided by visit. Those domains along with the questions used to derive and the maximum score for each domain are include in Table 1 below:

Table 1

Domain	CDLQI Question(s)	Maximum Domain Score
Symptoms and Feelings	1,2	6
Leisure	4,5,6	9
School or Holidays	7	3
Personal Relationship	3,8	6
Sleep	9	3
Treatment	10	3

In addition, a sensitivity analysis of the composite CDLQI score will be performed to support the findings of the analyses described above. For the sensitivity analysis, the same methods described above with the only exception that all subjects enrolled in the study will be included in the analysis. That means subjects below 4 years of age as well as subject greater than 16 years of age will be considered. This analysis will be included so that summaries will be available that include all subjects enrolled in the study.

10.5. Subject Reported Spread of Molluscum Lesions

Sibling information will be collected for subjects enrolled in the study. Subjects who have at least one sibling who does not exhibit molluscum lesions at baseline will be considered for this analysis. For those subjects, the count and percent of subjects who had a sibling who was clear at baseline but showed lesions post baseline will be

summarized by treatment group. Note: subjects who do not have a sibling free of molluscum lesions at baseline will not be considered for this analysis.

11. Safety Analysis

All safety analysis will be based on the Safety Population. Analysis using the Safety population will be based on the treatment received.

11.1. Extent of Exposure

The total number of lesions treated will be collected by visit over the duration of the study. For each visit, the number of lesions treated will be determined by subtracting the reported number of lesions not treated from the total number of lesions reported. Summary statistics of number of lesions treated at visits Day 1, Day 21, Day 42 and Day 63 will be generated by treatment group. In addition, the total number of treatment visits and total number of lesions treated will be displayed.

11.2. Adverse Events

Adverse events summaries will only consider Treatment Emergent Adverse Events (TEAEs). TEAEs are defined as those adverse events that occurred after dosing and those existing adverse events that worsened during the study. If it cannot be determined whether the adverse event is treatment emergent due to an incomplete (partial) onset date, the adverse event will be considered to be treatment emergent. Verbatim terms entered into the clinical database via the EDC system will be mapped to preferred terms and system organ classes using the most current version of Medical Dictionary for Regulatory Activities (MedDRA) available.

Each adverse event summary will be displayed by treatment group. Summaries that are displayed by system organ class and preferred terms will be ordered by descending order of incidence of system organ class and preferred term within each system organ class. Summaries of the following types will be presented:

- Overall summary of the TEAEs which contain an overview of each item below.
- Subject count and incidence rate of TEAEs by MedDRA system organ class and preferred term.
- Subject count and incidence rate of TEAEs by MedDRA system organ class, preferred term and highest severity. At each level of subject summarization, a subject is classified according to the highest severity if the subject reported one or more events.
- Subject count and incidence rate of TEAEs by MedDRA system organ class, preferred term and closest relationship to study drug (Related/Not Related). Related AEs are those reported as “Definitely”, “Probable” or “Possibly”. At each level of subject summarization, a subject is classified according to the

closest relationship if the subject reported one or more events. Adverse events with missing relationship will be considered related for this summary.
- Subject count and incidence rate of Serious TEAEs by MedDRA system organ class and preferred term.
- Subject count and incidence rate of TEAEs leading to study discontinuation by MedDRA system organ class and preferred term.

11.3. Targeted Adverse Events- Local Skin Reactions

Local skin reactions (LSRs) to treatment reported by investigators and subjects will be recorded as adverse events. LSRs will include the following adverse events: blistering, pain, pruritus, erythema, edema, erosion/ulcerations, flaking/scaling/dryness, scabbing/crusting and pigmentation changes. LSRs will be identified via a medical review of adverse events reported. LSRs will be coded and summarized using similar methods as described in Section 11.2 for adverse events.

Summaries of LSRs will include the following:

- Subject count and incidence rate of LSRs by MedDRA system organ class and preferred term.
- Subject count and incidence rate of LSRs by MedDRA system organ class, preferred term and highest severity. At each level of subject summarization, a subject is classified according to the highest severity if the subject reported one or more events.
- Subject count and incidence rate of LSRs by MedDRA system organ class, preferred term and closest relationship to study drug (Related/Not Related). Related LSRs are those reported as “Definitely”, “Probable” or “Possibly”. At each level of subject summarization, a subject is classified according to the closest relationship if the subject reported one or more events. LSRs with missing relationship will be considered related for this summary.
- Subject count and incidence rate of serious LSRs by MedDRA system organ class and preferred term.
- Subject count and incidence rate of LSRs by LSR types described in the first paragraph of this section.

In addition, information from a study specific from of assessment of local skin reactions (LSRs) will be collected 1, 7 and 14 days after each treatment and at the EOS visit. The following clinical responses will be recorded: blistering, erythema, edema, erosion/ulcerations, flaking/scaling/dryness, scabbing/crusting and pigmentation changes (hyperpigmentation or hypopigmentation) and scaring. Possible graded responses for each of these LSRs are: None, Mild, Moderate, Severe. Only the most severe reaction grade will be recorded at each assessment. This grading of LSRs is on a distinct scale

based on the descriptions in the LSR guide and severity of these reactions are not the same as the adverse analyses described in Section 11.2. Overall counts and percentages for each of the reactions will be displayed by treatment group. Summaries of each reaction by highest severity and last observed assessment will be shown.

11.4. Patient Evaluation of Response to Treatment (PERIT)

Twenty-four (24) hours after each treatment, an assessment of treated skin appearance will be carried out. Possible assessments include: No Response, Redness Only, Blistering at application site, Excessive blistering at application site and beyond.

Overall counts and percentages will be displayed by treatment group for each treatment visit. In addition, a summary of the highest severity will be shown.

11.5. Vital Signs

Heart rate and temperature will be collected at each visit. Change from baseline will be calculated for each post baseline visit temperature and pulse rate. Height will be recorded only at baseline. Weight will be collected at baseline and at the EOS visit.

Summary statistics for each vital sign and change from baseline result will be displayed by treatment group and visit for temperature and pulse rate. Baseline height and weight will be summarized as part of the baseline summary. Any other collection of height and weight will be included in by subject listings.

11.6. Physical Examination

Physical examinations results will be displayed in by subject listings. No summary tables of physical examination are planned.

11.7. Prior and Concomitant Medications

Prior and concomitant medication verbatim terms captured via the EDC system will be mapped to Anatomical/Therapeutic/Chemical (ATC) class and Preferred Names using the most current versions of the World Health Organization (WHO) Drug Dictionary Enhanced available.

Prior and concomitant medications will be summarized for each treatment group by WHO ATC class and preferred name. These summaries will present the number and percent of subjects using each medication. Subjects may have more than one medication per ATC class and preferred name. At each level of subject summarization, a subject is counted once if one or more medications at that level is reported for the subject. Each summary will be ordered by descending order of incidence of ATC class and preferred term.