STATISTICAL ANALYSIS PLAN (SAP)

Protocol Number:	GEN-003-005
Protocol Title:	A Randomized, Placebo-controlled, Double-blind Study to Assess the Efficacy and Safety of a Maintenance Dose of GEN-003 in Subjects with Genital Herpes Infection
Product Name or Number:	GEN-003
Sponsor:	Genocea Biosciences, Inc. Cambridge Discovery Park 100 Acorn Park Drive, 5th Floor Cambridge, MA 02140
SAP Prepared by:	Thomas H. Oliphant, PhD Andrew Kampfschulte, MS Biostatistician Innovative Analytics, Inc. 161 East Michigan Ave. Kalamazoo, MI 49007 USA
SAP Version Number (Date):	Version 1.0 (February 7, 2018)

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1 LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation or Term	Definition
AE	adverse event
AESI	adverse event of special interest
DMC	Data Monitoring Committee
EQ-5D-5L	EuroQol – 5 Domains – 5 Levels
IA	interim analysis
IM	intramuscular
MAAE	medically attended adverse event
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified intent-to-treat
MM2	Matrix-M2 adjuvant
PP	Per protocol
PT	Preferred term
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SOC	System Organ Class

2 STUDY OVERVIEW

This study is a randomized, double-blind, placebo-controlled clinical trial of GEN-003 in subjects who have received previous doses of GEN-003. Subjects who completed Study GEN-003-003 and received all 3 doses, reported data in daily electronic reporting period on at least 80% of days, and had no important protocol deviation in that trial were offered enrollment in this study. Subjects who met all inclusion and no exclusion criteria and provided written informed consent for this study were randomized within 11 to 18 months after the last active GEN-003 dose in a 1:1 ratio to receive 1 intramuscular (IM) dose (the maintenance dose) of GEN-003 or placebo. Randomization was stratified on the basis of the GEN-003 dose received by the subject in Study GEN-003-003.

Subjects were to use a daily electronic tool for reporting the presence or absence of genital herpes lesions and severity of genital herpes symptoms from Day 1 until the Month 6 visit.

Subjects were to complete the EuroQol – 5 Domains – 5 Levels (EQ-5D-5L) questionnaire on each day of the first recurrence after the maintenance dose through Month 6.

Local reactions and systemic events were to be recorded for the first 7 days after the maintenance dose on a paper Diary Card; if any event was ongoing after Day 8, it was to be followed until resolution. All adverse events (AEs) and concomitant medications were to be recorded from Day 1 to Day 29/Month 1. After Day 29/Month 1 to the end of the study, only serious AEs (SAEs), AEs of special interest (AESIs), medically attended AEs (MAAEs), antiviral medications, and vaccines were to be recorded. All AEs were to be graded in accordance with the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials from Grade 1 (mild) to Grade 4 (life-threatening).

From Month 2 to Month 6, the investigational site was to contact each subject monthly by telephone or site visit for review of daily electronic reporting tool data and assessment of SAEs, AESIs, and antiviral medication use (through Month 6).

A Data Monitoring Committee (DMC) was to review safety data at intervals of a minimum of 3 months until all subjects have completed the GEN-003/placebo dosing period. Any additional meetings and the specific safety monitoring plan were to be detailed in the DMC charter.

3 STUDY OBJECTIVES

3.1 Primary Efficacy Objective

The primary efficacy objective is as follows:

- To evaluate the efficacy of GEN-003 versus placebo administered as a maintenance dose in reduction of genital herpes lesion rate

3.2 Secondary Efficacy Objectives

The secondary efficacy objectives are as follows:

- To evaluate the efficacy of GEN-003 versus placebo administered as a maintenance dose on genital herpes recurrence through Month 6:
- Reduction of genital herpes recurrence frequency
- Increase of proportion of subjects who are genital herpes recurrence-free
- Increase of time to first genital herpes recurrence
- Reduction of genital herpes recurrence duration

3.3 Safety Objective

- To evaluate the safety and tolerability of a maintenance dose of GEN-003 versus placebo

4 ANALYSIS POPULATIONS

4.1 Modified Intent-to-Treat Population

The Modified Intent-to-Treat (mITT) population includes all randomized subjects who received the maintenance dose. Subjects will be analyzed according to the treatment to which they were randomized.

4.2 Safety Population

The Safety population includes all randomized subjects who received the maintenance dose. Subjects will be analyzed according to the treatment received.

4.3 Per Protocol Population

The Per Protocol (PP) population includes subjects who received the maintenance dose, reported data during the daily electronic reporting period on at least 80% of days, and had no important protocol deviations. Subjects will be analyzed according to the treatment received.

5 STATISTICAL METHODOLOGY

5.1 Summarization of Data

Study results will be summarized in tabular format by treatment group (GEN-003, Placebo), with descriptive statistics and/or in subject listings. In general, descriptive statistics for continuous variables will consist of subject count, mean, standard deviation (SD), median, and range; and descriptive statistics for categorical variables will consist of subject counts and percentages. Time-to-event data will be analyzed by the Kaplan-Meier life test method, and results will be summarized by 25th, 50th (median), and 75th percentiles with associated 2-sided 95% confidence intervals (CIs), as well as the percentage of censored observations.

The efficacy analyses described in this Statistical Analysis Plan (SAP) will be performed for the mITT and PP populations. The safety analyses will be performed for the safety population.

5.2 Sample Size Justification

Sample size in this study is dependent on the enrollment in GEN-003-003. No formal sample size calculations were performed for this study.

5.3 Randomization

Eligible subjects were randomized in a 1:1 ratio to receive 1 IM dose of GEN-003 (60 μg each antigen and 50 μg MM2) or placebo. Randomization was stratified on the basis of the GEN-003 dose received by the subject in Study GEN-003-003.

5.4 Unblinding

5.4.1 At Subject Level

Unblinding of treatment assignment is discouraged. If a medical emergency occurrs for which the identity of the treatment assignment is critical to the care of a subject, the Investigator will call the Medical Monitor to discuss. If unblinding is deemed necessary, a designated unblinded study team member (unblinded statistician) will provide the treatment assignment to the Medical Monitor who will provide the information to the Investigator.

5.4.2 Interim Analysis

The Sponsor and members of the study team will be unblinded to the treatment arms at the interim analysis time point. Only the DMC members and unblinded statistician will have access to unblinded safety data at the subject level and only at specified intervals throughout the study or as necessary to perform the task of overall safety monitoring.

5.4.3 Final Analysis

After database lock at the end of the study, individual subject treatment assignments will be unblinded and available to all study team personnel, including the lead, blinded statistician.

5.5 Data Handling

5.5.1 Method for Handling Missing Data

No imputation of missing data will be performed. All available safety and efficacy data will be included in data listings and summaries.

5.5.2 Definition of Baseline Values

Unless otherwise specified, Baseline values are defined as the values collected on Day 1 of GEN-003-005.

5.5.3 Windowing of Visits

All data will be categorized based on the scheduled visit at which it was collected. These visit designators are predefined values that appear as part of the visit tab in the electronic case report form.

5.5.4 Justification of Pooling

All data from all sites will be pooled. Study center or treatment-by-center interaction will generally not be included in statistical analyses.

5.5.5 Withdrawals, Dropouts, Loss to Follow-up

Time-to-event variables will be censored if a subject withdraws, drops out, or is lost to follow-up before the documentation of the time to the first subject-reported recurrence after the maintenance dose.

If a subject withdraws, drops out, or is lost to follow-up before the first recurrence after the maintenance dose is recorded, the subject will be censored at the last documented time without recurrence recorded; if no record is available after the maintenance dose, the subject will be censored at Day 1.

5.6 Output Production and Validation

All analyses will be performed using SAS V 9.2 or higher (SAS Institute, Inc, Cary, North Carolina, USA). Validation and quality control of the tables, listings, and figures that display the results of the statistical analysis of the data from this study will follow the appropriate Innovative Analytics standard operating procedures.

6 SUBJECT DISPOSITION

A breakdown of the number and percentage of subjects enrolled by site and treatment group will be provided. The number of subjects who complete the study will be summarized in tabular format for the safety population. Reasons for discontinuation from the study will also be summarized. A summary of analysis populations table by treatment group will be presented, and a subject listing of protocol deviations will be produced.

7 DEMOGRAPHIC CHARACTERISTICS

Demographic and baseline characteristics will be summarized by treatment group.

For quantitative variables, summary statistics (number [n], mean, SD, minimum, median, and maximum) will be presented for all subjects. For qualitative variables, results will be summarized as counts and percentages for all subjects.

8 MEDICAL HISTORY

All medical history events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) coding system. Medical history events (past and current medical disorders) will be presented by treatment group for the safety population, summarized by MedDRA system organ class (SOC) and preferred term (PT).

9 CONCOMITANT MEDICATIONS

All medications will be coded using the World Health Organization (WHO) Drug Dictionary. Frequency tables will be presented by treatment group that summarize the prior and concomitant medications taken during the course of the study. A subject listing of medications will also be provided.

10 ELECTRONIC DIARY COMPLIANCE

Summary statistics will be presented by treatment group for the electronic diary compliance after the maintenance dose.

11 EFFICACY ANALYSIS

11.1 Genital Herpes Lesion Rate

Lesion rate (days) is defined as number of days with lesions divided by the time period of follow-up for lesions (in days). The days with lesions will be collected continuously throughout the study via an electronic lesion diary, and lesion rates will be calculated for the following periods: Baseline and Day 1 to 183 (post-dosing). For the purposes of determining days with lesions, a diary entry of missing will be treated the same as a diary entry of “no,” except in the following case: if 1 or 2 consecutive instances of missing is flanked by “yes” values on both sides, those missing values will be treated as a “yes” value.

Lesion rate will be analyzed with descriptive summary tables for overall and individual lesion rates calculated for the periods noted above. Individual subject lesion rates will be compared for the active treatment group vs. placebo using the Wilcoxon rank sum test.

11.2 Frequency of Genital Herpes Recurrences

The frequency of genital herpes recurrences in the 6-month period after the maintenance dose will be calculated as the number of recurrences reported using the daily electronic lesion diary, and will be summarized by mean, SD, median, and range. The median frequencies of recurrences will be compared between treatment groups using the Wilcoxon rank sum test.

11.3 Proportion of Subjects Recurrence-Free

The proportion of subjects in each treatment group who are genital herpes recurrence-free at 6 months after the maintenance dose will be tabulated and compared using a chi-square test for homogeneity of proportions.

11.4 Time to First Genital Herpes Recurrence

Time to the first subject-reported recurrence in the 6 month period after the maintenance dose will be estimated via Kaplan-Meier approach. The log rank test will be used to compare time to first recurrence between the GEN-003 and placebo arms.

11.5 Duration of Genital Herpes Recurrences

Mean lesion outbreak duration is defined as the average number of days with lesions per outbreak for those who have lesion outbreaks (recurrences).

Mean lesion outbreak duration will be presented in a similar descriptive summary table as done for lesion rate as described above. Individual subject mean outbreak duration will be summarized by treatment arm over 6 months (Days 1 to 183) after the maintenance dose. A Wilcoxon rank sum test will be used to test the hypothesis that the median mean lesion outbreak durations are the same between treatment groups at 6 months after the maintenance dose.

11.6 Antiviral Medication Use

Antiviral medications will be coded using the most current WHO Drug Dictionary and summarized by anatomical therapeutic chemical class and preferred term with results presented by treatment group. Antiviral medication use (Y/N) during the 6 months following the maintenance dose will be summarized by treatment group.

12 SAFETY ANALYSES

12.1 Reactogenicity

Frequency counts will be presented for systemic events and local reactions for the safety population. This will be done for events occurring within the first 7 days following the maintenance dose. Results will be presented by treatment group and maximum severity. Duration, in days, of events will also be summarized with n, median, minimum and maximum. All analyses will be done for the safety population.

Antipyretic and analgesic medications taken within 7 days after the maintenance dose will also be summarized by treatment group.

12.2 Adverse Events

All AEs will be coded using the MedDRA coding system. Frequency tables will be presented by treatment group for all AEs by SOC and PT. Frequency tables will be produced for AEs leading to discontinuation of dosing, by severity, by causality, for most common (≥5% in any group) AEs, SAEs, MAAEs, and AESIs. Subject listings of all AEs by study day will also be provided.

In all displays, AEs will be displayed by MedDRA SOC and PT, with subjects who have the same AE counted only once for that event and with subjects who have more than 1 AE within a SOC counted only once in that SOC.

13 SUBJECT LISTINGS

All data that are collected and entered into the study database will be presented in subject listings by GEN-003-005 treatment group.

14 INTERIM ANALYSIS

An interim analysis (IA) will be conducted after all subjects should have completed the Month 6 visit and will include analysis of lesion rates. The tables to be produced for this interim analysis are noted in the List of Statistical Tables Table of Contents (TOC) with an ‘X’ in the IA column.

15 FINAL SIGN-OFF FOR GENOCEA BIOSCIENCES, INC PROTOCOL GEN-003-005 STATISTICAL ANALYSIS PLAN

Thomas H Oliphant
Thomas H Oliphant (Feb 22, 2018)

Feb 22, 2018

Thomas H. Oliphant, PhD
Biostatistician
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Date

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Tingting Ge, PhD
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Date

16 REVISIONS TO STATISTICAL ANALYSIS PLAN

Date	Revision	Statistician's Signature
•	•	•
•	•	•
•	•	•
•	•	•
•	•	•
•	•	•

17 APPENDIX

17.1 Conventions for Statistical Tables and Listings

The following conventions are used in the mockups for the statistical tables:

[Sponsor] = [Genocea Biosciences]

[Protocol] = [GEN-003-005]

[Drug name] = [GEN-003]

In general, font size will be Courier 9-point and all margins will be 1 inch.

Treatment Groups

GEN-003 Antigens 60 µg / M2 50 µg

Placebo

List of Statistical Tables for GEN-003-005

Table No.	Table Title	Analysis Population	IA
14.1.1	Number and Percentage of Enrolled Subjects by Site and Treatment Group	Safety	
14.1.2	Demographic and Baseline Characteristics by Treatment Group	Safety	x
14.1.3	Summary of Analysis Populations by Treatment Group		
14.1.4	Subject Disposition by Treatment Group	Safety	
14.1.5	Frequency of Medical History Events by Treatment Group	Safety	
14.1.6	Prior Medications by Treatment Group	Safety	
14.1.7	Concomitant Medications by Treatment Group	Safety	
14.1.8	Summary of Antiviral Medications Taken During the Study by Treatment Group, Drug Class and Preferred Term	Safety	
14.2.1	Summary Statistics for Electronic Diary Compliance After Maintenance Dose by Treatment Group	mITT	
14.2.2.1	Descriptive Summary of Overall Lesion Rates by Treatment Group and Observation Period	mITT	x
14.2.2.2	Descriptive Summary of Overall Lesion Rates by Treatment Group and Observation Period	PP	
14.2.3.1	Descriptive Summary of Individual Subject Lesion Rates by Treatment Group and Observation Period	mITT	x
14.2.3.2	Descriptive Summary of Individual Subject Lesion Rates by Treatment Group and Observation Period	PP	

Table No.	Table Title	Analysis Population	IA
14.2.4.1	Frequency of Recurrences at 6 Months After Maintenance Dose by Treatment Group	mITT	x
14.2.4.2	Frequency of Recurrences at 6 Months After Maintenance Dose by Treatment Group	PP	
14.2.5.1	Proportion of Subjects Who Are Recurrence Free at 6 Months After Maintenance Dose	mITT	x
14.2.5.2	Proportion of Subjects Who Are Recurrence Free at 6 Months After Maintenance Dose	PP	
14.2.6.1	Time to First Recurrence After Maintenance Dose	mITT	x
14.2.6.2	Time to First Recurrence After Maintenance Dose	PP	
14.2.7.1	Descriptive Summary and Analysis of Mean Lesion Outbreak Duration Over 6 Months After Maintenance Dose	mITT	x
14.2.7.2	Descriptive Summary and Analysis of Mean Lesion Outbreak Duration Over 6 Months After Maintenance Dose	PP	
14.2.8.1	Summary of Antiviral Medication Use After Maintenance Dose	mITT	
14.2.8.2	Summary of Antiviral Medication Use After Maintenance Dose	PP	
14.3.1.1	Frequency Table of All Adverse Events by SOC, Preferred Term, and Treatment	Safety	
14.3.1.2	Frequency Table of All Adverse Events by SOC, Preferred Term, Treatment, and Severity	Safety	
14.3.1.3	Frequency Table of All Adverse Events by SOC, Preferred Term, Treatment, and Causality	Safety	

Table No.	Table Title	Analysis Population	IA
14.3.1.4	Frequency Table of All Adverse Events Leading to Discontinuation of Dosing by SOC, Preferred Term and Treatment	Safety	
14.3.1.5	Frequency Table of Subjects with Adverse Events of Special Interest by SOC, Preferred Term, and Treatment	Safety	
14.3.1.6	Frequency Table of All Adverse Events with ≥ 5% Occurrence by SOC, Preferred Term, and Treatment	Safety	
14.3.1.7	Summary of Local Reactions and Systemic Events Occurring Within 7 Days Postdose by Treatment and Maximum Severity	Safety	
14.3.1.8	Descriptive Summary of Duration (days) of Systemic Events and Local Reactions by Treatment	Safety	
14.3.1.9	Summary of Antipyretic/Analgesic Medications Taken Within 7 Days after Maintenance Dose by Treatment Group, Drug Class, and Preferred Term	Safety	
14.3.2.1	Frequency Table of Subjects with Serious Adverse Events by SOC, Preferred Term, and Treatment	Safety	
14.3.2.2	Frequency Table of Subjects with Medically Attended Adverse Events by SOC, Preferred Term, and Treatment	Safety	

Table 14.1.1: Number and Percentage of Enrolled Subjects by Site and Treatment Group

Safety Population

Site	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Site 1	n (x.x%)	n (x.x%)
Site 2	n (x.x%)	n (x.x%)
Site 3	n (x.x%)	n (x.x%)
Site 4	n (x.x%)	n (x.x%)
etc.		
Site X	n (x.x%)	n (x.x%)
All Sites	n (x.x%)	n (x.x%)

Program: Date Produced: mm/dd/yy

Table 14.1.2: Demographic and Baseline Characteristics by Treatment Group

Safety Population

Variable	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx	Total N=xx
Age (years)			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx
Median	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Sex			
Male	n (x.x%)	n (x.x%)	n (x.x%)
Female	n (x.x%)	n (x.x%)	n (x.x%)
Race			
American Indian or Alaska Native	n (x.x%)	n (x.x%)	n (x.x%)
Asian	n (x.x%)	n (x.x%)	n (x.x%)
Black	n (x.x%)	n (x.x%)	n (x.x%)
Hawaiian or Pacific Islander	n (x.x%)	n (x.x%)	n (x.x%)
White	n (x.x%)	n (x.x%)	n (x.x%)
Other	n (x.x%)	n (x.x%)	n (x.x%)
Ethnicity			
Hispanic or Latino	n (x.x%)	n (x.x%)	n (x.x%)
Not Hispanic or Latino	n (x.x%)	n (x.x%)	n (x.x%)
Weight (lbs)			
n	xx	xx	xx
Mean	xx.xx	xx.xx	xx.xx
SD	xx.xxx	xx.xxx	xx.xxx
Median	xx.xx	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x

Table 14.1.3: Summary of Analysis Populations by Treatment Group

Population	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Modified Intent-to-Treat[a]	n (x.x%)	n (x.x%)
Safety[b]	n (x.x%)	n (x.x%)
Per Protocol[c]	n (x.x%)	n (x.x%)

[a] Includes all randomized subjects who received the maintenance dose.

[b] Includes all randomized subjects who received the maintenance dose.

[c] Includes all subjects in the mITT Population who reported 80% of daily electronic reporting data, and who had no major protocol deviations

Table 14.1.4: Subject Disposition by Treatment Group

Safety Population

Disposition	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Subject completed the study	n (x.x%)	n (x.x%)
Primary Reason for Discontinuation from Study		
Withdrew consent for reason other than AE	n (x.x%)	n (x.x%)
Withdrew consent due to solicited or unsolicited AEs		
Lost to Follow-up	n (x.x%)	n (x.x%)
Non-compliance	n (x.x%)	n (x.x%)
Investigator discretion	n (x.x%)	n (x.x%)
Sponsor request	n (x.x%)	n (x.x%)
Death	n (x.x%)	n (x.x%)
Site termination	n (x.x%)	n (x.x%)
Study termination	n (x.x%)	n (x.x%)

Table 14.1.5: Frequency of Medical History Events by Treatment Group

Safety Population

Medical History Events	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
SOC1	n (x.x%)	n (x.x%)
Preferred Term for MH Event1	n (x.x%)	n (x.x%)
Preferred Term for MH Event2	n (x.x%)	n (x.x%)
Preferred Term for MH Event3	n (x.x%)	n (x.x%)
SOC2	n (x.x%)	n (x.x%)
Preferred Term for MH Event4	n (x.x%)	n (x.x%)
Preferred Term for MH Event5	n (x.x%)	n (x.x%)
Preferred Term for MH Event6	n (x.x%)	n (x.x%)
	n (x.x%)	n (x.x%)
SOC3	n (x.x%)	n (x.x%)
Preferred Term for MH Event7	n (x.x%)	n (x.x%)
Preferred Term for MH Event8	n (x.x%)	n (x.x%)
ETC...		

Program: Date Produced: mm/dd/yy

Programming Notes:

- Data comes from Medical History module
- Sort by SOC and preferred terms
- These data will be coded in MedDRA.

Table 14.1.6: Prior Medications by Treatment Group

Safety Population

ATC Text Level 2 Preferred Name	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
ATC Text Level 2	n (x.x%)	n (x.x%)
Preferred Name1	n (x.x%)	n (x.x%)
Preferred Name2	n (x.x%)	n (x.x%)
Preferred Name3	n (x.x%)	n (x.x%)
ATC Text Level 2	n (x.x%)	n (x.x%)
Preferred Name1	n (x.x%)	n (x.x%)
Preferred Name2	n (x.x%)	n (x.x%)
Preferred Name3	n (x.x%)	n (x.x%)
ATC Text Level 2	n (x.x%)	n (x.x%)
Preferred Name1	n (x.x%)	n (x.x%)
Preferred Name2	n (x.x%)	n (x.x%)
Preferred Name3	n (x.x%)	n (x.x%)

Note: Prior Medication mapping was based on WHODRUG.
Program: Date Produced: mm/dd/yy
Programming Note:

- Prior medications are those medications with a start date BEFORE date of maintenance dose (Day 1).

Table 14.1.7: Concomitant Medications by Treatment Group

Safety Population

ATC Text Level 2 Preferred Name	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
ATC Text Level 2	n (x.x%)	n (x.x%)
Preferred Name1	n (x.x%)	n (x.x%)
Preferred Name2	n (x.x%)	n (x.x%)
Preferred Name3	n (x.x%)	n (x.x%)
ATC Text Level 2	n (x.x%)	n (x.x%)
Preferred Name1	n (x.x%)	n (x.x%)
Preferred Name2	n (x.x%)	n (x.x%)
Preferred Name3	n (x.x%)	n (x.x%)
ATC Text Level 2	n (x.x%)	n (x.x%)
Preferred Name1	n (x.x%)	n (x.x%)
Preferred Name2	n (x.x%)	n (x.x%)
Preferred Name3	n (x.x%)	n (x.x%)

Note: Concomitant Medication mapping was based on WHODRUG.
Program: Date Produced: mm/dd/yy
Programming Note:

- Concomitant medications are those medications with a start date on or after date of maintenance dose (Day 1), or with a start date before Day 1 and continue beyond Day 1.

Table 14.1.8: Summary of Antiviral Medications Taken During the Study by Treatment Group, Drug Class and Preferred Term

Safety Population
Day 1 to Month 6

Preferred Term	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Any Antiviral Medication	n (x.x%)	n (x.x%)
Preferred Term 1	n (x.x%)	n (x.x%)
Preferred Term 2	n (x.x%)	n (x.x%)
Preferred Term 3	n (x.x%)	n (x.x%)
etc.		

Program: Date Produced: mm/dd/yy

Programming Notes:

- Antiviral medications are defined as medications with an ATC2 Class of 'ANTIVIRALS FOR SYSTEMIC USE'

Table 14.2.1: Summary Statistics for Electronic Diary Compliance After Maintenance Dose by Treatment Group

mITT Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Days with Entry		
n	xx	xx
Mean	xx.xx	xx.xx
SD	xx.xxx	xx.xxx
Median	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x
Days without Entry		
n	xx	xx
Mean	xx.xx	xx.xx
SD	xx.xxx	xx.xxx
Median	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x
Percent Compliance		
n	xx	xx
Mean	xx.xx	xx.xx
SD	xx.xxx	xx.xxx
Median	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x

Note: Days with Entry are days from Day 1 to Month 6 visit or date of discontinuation with an entry of 'Yes' or 'No'
Days without Entry are days from Day 1 to Month 6 visit or date of discontinuation with an entry of blank

Program: Date Produced: mm/dd/yy

Programming Notes:

- Use Day 1 as start date
- Use earliest of Month 6 visit and date of completion or early termination (dsdtdat) from Subject Disposition form as cutoff date
- Percent Compliance = Days with Entry/(Days with Entry + Days without Entry) * 100%

Table 14.2.2.1: Descriptive Summary of Overall Lesion Rates by Treatment Group and Observation Period

mITT Population

Variable Visit Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Overall lesion rate (days)		
Days with lesions/followup time(%)		
Baseline	xx/xx (%)	xx/xx (%)
Days 1-183	xx/xx (%)	xx/xx (%)

Note: Lesion rate (days) is defined as number of days with lesions divided by the number of days in the observation period.

Note: The overall rate is presented where numerator and denominator are summed across subjects.

Program: Date Produced: mm/dd/yy

Programming Notes:

- Present results for Baseline and Days 1-183.
- A day with lesions is a day for which LESIONS='Yes'.
- Number this table 14.2.2.1 and produce a similar table (14.2.2.2) for the PP population

Table 14.2.3.1: Descriptive Summary of Individual Subject Lesion Rates by Treatment Group and Observation Period

mITT Population

Visit Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Baseline		
n	xx	xx
Mean	xx.xx	xx.xx
SD	xx.xxx	xx.xxx
Median	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x
Total subjects w/ at least 1 day of lesions	n (%)	n (%)
Days 1-183		
n	xx	xx
Mean	xx.xx	xx.xx
SD	xx.xxx	xx.xxx
Median	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x
Total subjects w/ at least 1 day of lesions	n (%)	n (%)
Change from Baseline (Days 1-183)		
n	xx	xx
Mean	xx.xx	xx.xx
SD	xx.xxx	xx.xxx
Median	xx.xx	xx.xx
Min, Max	xx.x, xx.x	xx.x, xx.x
P-Value (vs. Placebo)[1]	0.xxxx	

Note: Lesion rate (days) is defined as number of days with lesions divided by the number of days in the observation period.
[1]P-value based on Wilcoxon rank sum test.

Program: Date Produced: mm/dd/yy
Programming Notes:

- Present results for Baseline and Days 1-183.
- A day with lesions is a day for which LESIONS='Yes'.
- Number this table 14.2.3.1 and produce a similar table (14.2.3.2) for the PP population

Table 14.2.4.1: Frequency of Recurrences at 6 Months After Maintenance Dose by Treatment Group

mITT Population

Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx	P-value[1]
Number of Recurrences at 6 Months after Maintenance Dose			0.xxxx
n	xx	xx	
Mean	xx.xx	xx.xx	
SD	xx.xxx	xx.xxx	
Median	xx.xx	xx.xx	
Min, Max	xx.x, xx.x	xx.x, xx.x	

Note: Recurrences refer to subject-reported recurrences.
[1]P-value based on Wilcoxon rank sum test.

Program: Date Produced: mm/dd/yy
Programming Notes:

- Number this table 14.2.4.1 and produce a similar table (14.2.4.2) for the PP population

Table 14.2.5.1: Proportion of Subjects Who Are Recurrence Free at 6 Months After Maintenance Dose

mITT Population

Variable Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx	P-value[1]
Recurrence Free at 6 Months after Maintenance Dose*			0.xxxx
Yes	n (%)	n (%)	
No	n (%)	n (%)	
Unknown	n (%)	n (%)	

* 'Yes' includes subjects who do not have a recurrence from Maintenance Dose through 6 months after Maintenance Dose. 'No' includes subjects who do have a recurrence from Maintenance Dose through 6 months after Maintenance Dose. 'Unknown' includes subjects who discontinue prior to 6 months after Maintenance Dose and have not had a recurrence prior to discontinuation.
[1] From a chi-square test of homogeneity of proportions (excluding Unknown counts).

Program: Date Produced: mm/dd/yy
Programming Notes:

- Number this table 14.2.5.1 and produce a similar table (14.2.5.2) for the PP population

Table 14.2.6.1: Time to First Recurrence After Maintenance Dose

mITT Population

Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Number with recurrence (%)	xx(xx.x)	xx(xx.x)
Number Censored (%)	xx(xx.x)	xx(xx.x)
Time to first recurrence*		
25th Percentile (95% CI)	xx(xx.x,xx.x)	xx(xx.x,xx.x)
Median (95% CI)	xx(xx.x,xx.x)	xx(xx.x,xx.x)
75th Percentile (95% CI)	xx(xx.x,NE)	xx(xx.x,NE)
Min, Max	xx,xx	xx,xx
K-M Estimate[1] (95% CI)	x.xxx(x.xxx,x.xxx)	x.xxx(x.xxx,x.xxx)
Log rank test vs. Placebo p-value	0.xxxx	

* The number of days from Maintenance Dose to the day the subject experienced a recurrence, or the censoring day that the subject was last known to be recurrence-free.
NE = Not Estimable CI = Confidence Interval K-M = Kaplan-Meier
[1] Percent of event-free subjects

Program: Date Produced: mm/dd/yy

Programming Notes:

- Number this table 14.2.6.1 and produce a similar table (14.2.6.2) for the PP population

Table 14.2.7.1: Descriptive Summary and Analysis of Mean Lesion Outbreak Duration Over 6 Months After Maintenance Dose

mITT Population

Visit Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo	P-value [1]
6 Months After Maintenance Dose			0.xxxx
n	xx	xx	
Mean	xx.xx	xx.xx	
SD	xx.xxx	xx.xxx	
Median	xx.xx	xx.xx	
Min, Max	xx.x, xx.x	xx.x, xx.x	
Total subjects w/ at least 1 day of lesions	n (%)	n (%)	

Note: Mean lesion outbreak duration is defined for each subject as the average number of days with lesions per outbreak (recurrence) during the period of interest. Subjects with no recurrences during the period of interest are excluded from the analysis.
[1]P-value based on Wilcoxon rank sum test.

Program: Date Produced: mm/dd/yy
Programming Notes:

- A day with lesions is a day for which LESIONS='Yes'.
- Number this table 14.2.7.1 and produce a similar table (14.2.7.2) for the PP population

Table 14.2.8.1: Summary of Antiviral Medication Use After Maintenance Dose

mITT Population

Variable Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Antiviral Medication Use After Maintenance Dose		
Yes	n (%)	n (%)
No	n (%)	n (%)

Program: Date Produced: mm/dd/yy

Programming Notes:

- Antiviral medications are defined as medications with an ATC2 Class of 'ANTIVIRALS FOR SYSTEMIC USE'
- Number this table 14.2.8.1 and produce a similar table (14.2.8.2) for the PP population

Table 14.3.1.1: Frequency Table of All Adverse Events by SOC, Preferred Term, and Treatment

Safety Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With AEs	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same event more than once are counted only once for the Preferred Term. Subjects who have more than one adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Table 14.3.1.2: Frequency Table of All Adverse Events by SOC, Preferred Term, Treatment, and Severity

Safety Population
Severity: Grade 1 (Mild)

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With AEs	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same event more than once are counted only once for the Preferred Term. Subjects who have more than one adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Programming Note: Produce a subtable for each level of severity (Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4=Potentially Life-threatening).

Table 14.3.1.3: Frequency Table of All Adverse Events by SOC, Preferred Term, Treatment, and Causality

Safety Population
Relationship to Investigational Product: Likely

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With AEs	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same event more than once are counted only once for the Preferred Term. Subjects who have more than one adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Programming Note: Produce a subtable for each level of causality/relationship to vaccine (Likely, Unlikely).

Table 14.3.1.4: Frequency Table of All Adverse Events Leading to Discontinuation of Dosing by SOC, Preferred Term and Treatment

Safety Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With AEs	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same event more than once are counted only once for the Preferred Term. Subjects who have more than one adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Table 14.3.1.5: Frequency Table of Subjects with Adverse Events of Special Interest by SOC, Preferred Term and Treatment

Safety Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With an Adverse Event of Special Interest	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same event of Special Interest more than once are counted only once for the Preferred Term. Subjects who have more than one adverse event of Special Interest within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Table 14.3.1.6: Frequency Table of All Adverse Events with ≥ 5% Occurrence by SOC, Preferred Term, and Treatment

Safety Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With AEs	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same event more than once are counted only once for the Preferred Term. Subjects who have more than one adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Programming Notes:

- Include all SOC/PT where the active treatment group has a ≥ 5% occurrence rate for that SOC/PT.

Table 14.3.1.7: Summary of Local Reactions and Systemic Events Occurring Within 7 Days Postdose by Treatment and Maximum Severity

Safety Population

Local Reactions and Systemic Events	Grade [1]	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Any Local Reaction or Systemic Event	Any	n (x.x%)	n (x.x%)
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
Any Local Reaction	Any	n (x.x%)	n (x.x%)
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
Pain	Any	n (x.x%)	n (x.x%)
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
Tenderness	Any	n (x.x%)	n (x.x%)
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
Swelling	Any	n (x.x%)	n (x.x%)
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
Swelling (mm)	Any	n (x.x%)	n (x.x%)

Local Reactions and Systemic Events	Grade [1]	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
	Any	n (x.x%)	n (x.x%)
	1	n (x.x%)	n (x.x%)
	2	n (x.x%)	n (x.x%)
	3	n (x.x%)	n (x.x%)
	4	n (x.x%)	n (x.x%)
Redness (mm)			
Any Systemic Event	ETC	n (x.x%)	n (x.x%)
Fever	ETC	n (x.x%)	n (x.x%)
Headache	ETC	n (x.x%)	n (x.x%)
Chills	ETC	n (x.x%)	n (x.x%)
Fatigue	ETC	n (x.x%)	n (x.x%)
Nausea	ETC	n (x.x%)	n (x.x%)
Diarrhea	ETC	n (x.x%)	n (x.x%)
Vomiting	ETC	n (x.x%)	n (x.x%)
Muscle aches	ETC	n (x.x%)	n (x.x%)
Any Local Reaction or Systemic Event		n (x.x%)	n (x.x%)
Any Local Reaction		n (x.x%)	n (x.x%)
Pain		n (x.x%)	n (x.x%)
ETC			

Program: Date Produced: mm/dd/yy

Programming Notes:

- Information comes from the Diary Card
- If a subject has multiple of the same events, take the maximum severity.
- During the 7 day period after the (Days 1-7) a subject should only be counted one time. If a subject has a sign/symptom at least once during that 7 day interval the subject is counted for that sign/symptom.
- Watch page breaks. Please try and keep all the grades together for a sign/symptom.
- Do not include Grade=0 as Grades of 0 imply "None" or no event.
- Fever is based on Temperature (F) which is collected on the Diary Card. See Appendix 2 in the protocol for grade definitions. Grade 1 = 100.4-101.1; Grade 2 = 101.2-102.0; Grade 3 = 102.1-104; Grade 4 >104.

- For Redness (mm) and Swelling (mm), see also Appendix 2 in the protocol. For both redness and swelling: Grade 1 = 2.5-5 cm; Grade 2 = 5.1-10 cm; Grade 3 = >10cm; Grade 4 is Necrosis or exfoliative dermatitis, which we won't be able to determine and will be handled separately as an AE.

Table 14.3.1.8: Descriptive Summary of Duration (days) of Systemic Events and Local Reactions by Treatment

Safety Population

Systemic Events and Local Reactions	Statistic	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Fever	N	xx	xx
	Median	xx.x	xx.x
	Minimum	xx	xx
	Maximum	xx	xx
Headache	N	xx	xx
	Median	xx.x	xx.x
	Minimum	xx	xx
	Maximum	xx	xx
Chills	N	xx	xx
	Median	xx.x	xx.x
	Minimum	xx	xx
	Maximum	xx	xx
Fatigue	N	xx	xx
	Median	xx.x	xx.x
	Minimum	xx	xx
	Maximum	xx	xx
Nausea	N	xx	xx
	Median	xx.x	xx.x
	Minimum	xx	xx
	Maximum	xx	xx
Dairrhea	N		
	Median		
ETC...	ETC...		

Program: Date Produced: mm/dd/yy

Programming Notes:

- Information comes from the Diary Card
- For start date, use the date from when the symptom is first recorded on the card (severity >0). For the stop date, use the date when the symptom is last present on the card (severity > 0). If a stop date is not available, then this needs to be given to the CDM.

Table 14.3.1.9: Summary of Antipyretic/Analgesic Medications Taken Within 7 Days after Maintenance Dose by Treatment Group, Drug Class and Preferred Term

Safety Population

Preferred Term	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
Any Anti-Fever/Anti-Pain Medication	n (x.x%)	n (x.x%)
Preferred Term 1	n (x.x%)	n (x.x%)
Preferred Term 2	n (x.x%)	n (x.x%)
Preferred Term 3	n (x.x%)	n (x.x%)
etc.		

Program: Date Produced: mm/dd/yy

Programming Note:

- Antipyretic/analgesic medications are defined as medications with an ATC2 Class of 'ANALGESICS' or 'ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS'

Table 14.3.2.1: Frequency Table of Subjects with Serious Adverse Events by SOC, Preferred Term and Treatment

Safety Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With a Serious AE	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same serious adverse event more than once are counted only once for the Preferred Term. Subjects who have more than one serious adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

Table 14.3.2.2: Frequency Table of Subjects with Medically Attended Adverse Events by SOC, Preferred Term and Treatment

Safety Population

	GEN-003 60 ug/ M2 50 ug N=xx	Placebo N=xx
MedDRA SOC Preferred Term		
Total Number (%) of Subjects With a Medically Attended AE	x (x.x)	x (x.x)
SOC1	x (x.x)	x (x.x)
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOC2		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

SOCn		
PT1	x (x.x)	x (x.x)
PT2	x (x.x)	x (x.x)

Note: Adverse event mapping was based on the MedDRA Version xx.x thesaurus.
Note: Subjects who have the same medically attended adverse event more than once are counted only once for the Preferred Term. Subjects who have more than one medically attended adverse event within a System Organ Class are counted only once in that System Organ Class.

Program: Date Produced: mm/dd/yy

List of Statistical Listings for GEN-003-005

Listing No.	Listing Title	Analysis Population
16.2.1	Subject Disposition and Reasons for Discontinuation From Study	Safety
16.2.2.1	Protocol Deviations by Subject	Safety
16.2.2.2	Randomization and Analysis Populations by Subject	Safety
16.2.3	Subjects Excluded from the Per Protocol Analysis Population	Safety
16.2.4.1	Baseline Demographics by Subject	Safety
16.2.4.2	Medical History by Subject	Safety
16.2.4.3	Prior Medications by Subject	Safety
16.2.4.4	Concomitant Medications by Subject	Safety
16.2.5.1	Dosing Status by Subject	Safety
16.2.5.2	Dosing Date/Time by Subject	Safety
16.2.6.1	Electronic Diary Data by Subject	Safety
16.2.6.2	EQ-5D-5L Data by Subject	Safety
16.2.7.1	Systemic Events (Diary Card) by Subject	Safety
16.2.7.2	Local Reactions (Diary Card) by Subject	Safety
16.2.7.3	Adverse Events by Subject	Safety
16.2.7.4	Serious Adverse Events by Subject	Safety
16.2.7.5	Adverse Events Associated with Discontinuation of Dosing by Subject	Safety
16.2.7.6	Adverse Events Leading to Death by Subject	Safety
16.2.7.7	Medically Attended Adverse Events by Subject	Safety
16.2.7.8	Adverse Events of Special Interest by Subject	Safety
16.2.8.1	Urine Pregnancy Test Results by Subject	Safety
16.2.8.2	Pregnancy Results by Subject	Safety

Listing 16.2.1: Subject Disposition and Reasons for Discontinuation From Study

Safety Population

Treatment	Subject Number	Subject Status	Disposition Date	Reason(s) for Discontinuation	Discontinuation Explanation
GEN-003 60 ug / M2 50 ug	xxxx		ddmmmyyyy	Completed	
	xxxx			Withdrew consent due to AE	
	xxxx			Withdrew consent not due to AE	
	xxxx			Lost to Follow-up	
				Non-compliance	
Placebo	xxxx			Investigator discretion	
	xxxx			Sponsor request	
	xxxx			Death	
	xxxx			Site termination	
	xxxx			Study termination	
	xxxx				

Program: Date Produced: mm/dd/yy

Programming Note

- "Subject Status": If DSDECOD = "Subject completed" then "Subject Status" = "Completed study". If DSDECOD is ≠ "Subject completed" then "Subject Status" = "Did not complete study".
- Sort by treatment, subject number.

Listing 16.2.2.1: Protocol Deviations by Subject

Safety Population

Treatment	Subject Number	Deviations Date	Deviation Type - Subject	Deviation Type - Site	Description of Deviation	Site Corrective Action
GEN-003 60 ug / M2 50 ug	xxxx	ddmmmyyyy	Subject did not meet eligibility criteria	Missed procedure		
		ddmmmyyyy	Subject received wrong treatment or incorrect dose	Out of window procedure		
		ddmmmyyyy	Subject received prohibited concomitant medication	Consent process error		
			Subject received a vaccine in excluded time period	Noncompliance		
			Subject used suppressive antiviral therapy	Other		
Placebo	xxxx		Consent process error			
	xxxx		Noncompliance			
	xxxx		Other			
	xxxx					
	xxxx					
	xxxx					
	xxxx					
	xxxx					

Program: Date Produced: mm/dd/yy

Programming Note:

- Deviation information will come from the Protocol Deviations CRF.
- Sort by treatment, subject number, and deviations date.

Listing 16.2.2.2: Randomization and Analysis Populations by Subject

Safety Population

Treatment	Subject Number	Informed Consent Date	Randomization Date	Did Subject Meet all of the Eligibility Criteria	If no, Criteria Not Met	mITT Population	Safety Population	Per Protocol Population
GEN-003 60 ug / M2 50 ug	xxxx	ddmmmyyyy	ddmmmyyyy	Yes		Yes	Yes	Yes
	xxxx			No		No	No	No
	xxxx							
Placebo	xxxx							
	xxxx							
	xxxx							
	xxxx							
	xxxx							

Program: Date Produced: mm/dd/yy

Programming Note:

- Sort by treatment, subject number.
- Information comes from Randomization and Eligibility-Demographics CRFs.

Listing 16.2.3: Subjects Excluded from the Per Protocol Analysis Population

Safety Population

Treatment	Subject Number	Reason for Exclusion from Per Protocol Population
GEN-003 60 ug / M2 50 ug	xxxx	Inclusion/exclusion criteria not met
	xxxx	Daily electronic diary noncompliance
	xxxx	Had an important protocol deviation
Placebo	xxxx	
	xxxx	
	xxxx	
	xxxx	
	xxxx	
	xxxx	
	xxxx	
	xxxx	
	xxxx	

Program: Date Produced: mm/dd/yy

Programming Note:

- More than one reason may be listed for a subject.
- Sort by treatment and subject number.

Listing 16.2.4.1: Baseline Demographics by Subject

Safety Population

Treatment	Subject Number	Age	Sex	Ethnicity	Race	Weight (lbs)
GEN-003 60 ug / M2 50 ug	xxxx			Hispanic	White	
	xxxx			Non-Hispanic	Black or African American	
	xxxx				Asian	
	xxxx				American Indian or Alaska Native	
	xxxx				Native Hawaiian or Other Pacific Islander	
Placebo	xxxx				Other, specify	
	xxxx					
	xxxx					

Program: Date Produced: mm/dd/yy

Programming Notes:

- Data comes from the Eligibility-Demographics CRF.
- Sort by treatment, subject number.

Listing 16.2.4.2: Medical History by Subject

Safety Population

Treatment	Subject Number	SOC	Preferred Term	Verbatim	Status
GEN-003 60 ug / M2 50 ug	xxxx				Ongoing
	xxxx				Intermittent
	xxxx				Resolved
Placebo	xxxx				
	xxxx				
	xxxx				

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject number, SOC and Preferred Term.

Listing 16.2.4.3: Prior Medications by Subject

Safety Population

Treatment	Subject Number	ATC Text Level 2/ Preferred Name/ Medication	Route	Start Date	Stop Date	Ongoing
GEN-003 60 ug / M2 50 ug	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Oral	ddmmmyyyy	ddmmmyyyy	
	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Topical			
	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Subcutaneous			
		Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Transdermal			
Placebo	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Intraocular			
	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Intramuscular			
	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Inhalation			
		Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Intraperitoneal			
	...	...	Nasal			
	xxxx	Xxxxxxxxxxxx/ Ppppppppppppp/ mmmmmmmmmmmmmmm	Vaginal			

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject, start date, stop date, and medication.
- Prior meds are any meds with a start date BEFORE date of maintenance dose (Day 1).
- Prior Meds will be coded.
- Please try to keep subject data together. Depending on number of con meds per subject, this may not be possible.

Listing 16.2.4.4: Concomitant Medications by Subject

Safety Population

Treatment	Subject Number	ATC Text Level 2/ Preferred Name/ Medication	Route	Start Date	Stop Date	Ongoing
GEN-003 60 ug / M2 50 ug	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Oral	ddmmmyyyy	ddmmmyyyy	
	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Topical			
	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Subcutaneous			
		Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Transdermal			
Placebo	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Intraocular			
	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Intramuscular			
	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Inhalation			
		Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Intraperitoneal			
	...	...	Nasal			
	xxxx	Xxxxxxxxxxxx/ Pppppppppppppp/ mmmmmmmmmmmmmmmm	Vaginal			

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject, start date, stop date, and medication.
- Concomitant meds are any meds which started on or after the date of maintenance dose (Day 1), or which started before date of maintenance dose and continued beyond date of maintenance dose.
- Concomitant Meds will be coded.
- Please try to keep subject data together. Depending on number of con meds per subject, this may not be possible.

Listing 16.2.5.1: Dosing Status by Subject

Safety Population

Treatment	Subject Number	Was Dose Temporarily Delayed?	Reason for Temporary Delay
GEN-003 60 ug / M2 50 ug	xxxx	Yes	Fever
		No	Other acute illness
Placebo	xxxx		

Programming Notes:

- Sort by treatment, subject.
- Data collected on Study Drug Discontinuation CRF.

Listing 16.2.5.2: Dosing Date/Time by Subject

Safety Population

Treatment	Subject Number	Dose Date	Dose Time	Location
GEN-003 60 ug / M2 50 ug	xxxx	ddmmmyyyy	hh:mm	Left deltoid
				Right deltoid
	xxxx	ddmmmyyyy	hh:mm	
Placebo	xxxx	ddmmmyyyy	hh:mm	
	xxxx	ddmmmyyyy	hh:mm	

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject.
- Data collected on Study Immunization CRF.

Listing 16.2.6.1: Electronic Diary Data by Subject

Safety Population

Treatment	Subject Number	Date	Lesions	# Lesions	Open Lesion	Prodrome	Itching Score	Pain Score	Pain During Urination Score	Draining or Discharge Score	Swelling Score
GEN-003 60 ug / M2 50 ug	xxxx	ddmmmyyyy	Yes	xx	Yes	Yes	x	x	x	x	x
			No		No	No					
Placebo	xxxx										
	xxxx										

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject, date.
- Data comes from Signs and Symptoms diary.

Listing 16.2.6.2: EQ-5D-5L Data by Subject

Safety Population

Treatment	Subject Number	Date	Mobility	Self-Care	Usual Activities	Pain/ Discomfort	Anxiety/Depression	Health Rating
GEN-003 60 ug / M2 50 ug	xxxx	ddmmmyyyy	No problems	No problems	No problems	No pain	Not anxious	xx
			Slight problems	Slight problems	Slight problems	Slight pain	Slightly anxious	
			Moderate problems	Moderate problems	Moderate problems	Moderate pain	Moderately anxious	
			Severe problems	Severe problems	Severe problems	Severe pain	Severely anxious	
			Unable to walk	Unable to wash/dress	Unable to do usual activities	Extreme pain	Extremely anxious	
Placebo	xxxx							
	xxxx							

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject, date.
- Data comes from EQ-5D-5L CRF.

Listing 16.2.7.1: Systemic Events (Diary Card) by Subject

Safety Population

Treatment	Subject Number	Visit	Date	Temperature (F)	Headache	Chills	Fatigue	Nausea	Etc.
GEN-003 60 ug / M2 50 ug	xxxx	Day 1 Pre	ddmmmyyyy	xx.x	0	0	0	0	
		Day 1 (1hr)			1	1	1	1	
		Day 1			2	2	2	2	
		Day 2			3	3	3	3	
		Day 3							
		Day 4							
		Day 5							
		Day 6							
		Day 7							
Placebo	xxxx								

Grade 0 = None; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject, and visit.
- Data comes from Body Symptoms-Reactions Log CRF; for visit and time information, use the variable DCNOMDAT.
- Diary Cards are filled out for the 7 days following the maintenance dose.
- Page break by subject.
- Always include the first 7 days after the maintenance dose; if additional days are captured and the symptoms are all = 0 (None), then do not present on listing.

Listing 16.2.7.2: Local Reactions (Diary Card) by Subject

Safety Population

Treatment	Subject Number	Visit	Date	Pain	Tenderness	Swelling	Swelling (mm)	Redness (mm)
GEN-003 60 ug / M2 50 ug	xxxx	Day 1 Pre	ddmmmyyyy	0	0	0	xxx	xxx
		Day 1 (1hr)		1	1	1		
		Day 1		2	2	2		
		Day 2		3	3	3		
		Day 3						
		Day 4						
		Day 5						
		Day 6						
		Day 7						
Placebo	xxxx							

Grade 0 = None; Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by treatment, subject, and visit.
- Diary Cards are filled out for the 7 days following the maintenance dose.
- Data comes from Body Symptoms-Reactions Log CRF; for visit and time information, use the variable DCNOMDAT.
- Page break by subject.
- Always include the first 7 days after the maintenance dose; if additional days are captured and the symptoms are all = 0 (None), then do not present on listing.

Listing 16.2.7.3: Adverse Events by Subject

Safety Population
Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	MedDRA SOC/ Preferred Term/ AE Verbatim	Start Date/ Day	Stop Date/ Day	Severity [1]	Outcome	Action Taken with Study Drug	AE Related To Study Drug	Serious	AESI	MAAE
xx-xxx		ddmmmyyyy / xxx	ddmmmyyyy / xxx	1	Fatal	None	Likely	Not Serious	Yes	Yes
				2	Not recovered	Dose delayed	Unlikely	Death	No	No
				3	Recovered	Drug withdrawn		Life Threatening		
				4	Recovered w/ sequelae			Hospitalization		
								Significant Disability		
								Congenital Anomaly or Birth Defect		
								Other medically important event		

Note: Adverse event coding was done using the MedDRA Version xx.x dictionary.
[1] Severity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening
AESI = Adverse Event of Special Interest
MAAE = Medically Attended Adverse Event

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by Treatment, Subject number, start date, stop date, SOC, PT.
- If "Ongoing" is checked, then AE Stop Date should be missing. Put "Ongoing" in the Stop Date column.
- May need to use an 8-point font for this listing

Listing 16.2.7.4: Serious Adverse Events by Subject

Safety Population
Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	MedDRA SOC/ Preferred Term/ AE Verbatim	Start Date/ Day	Stop Date/ Day	Severity [1]	Outcome	Action Taken with Study Drug	AE Related To Study Drug	Serious	AESI	MAAE
xx-xxx		ddmmmyyyy/ xxx	ddmmmyyyy/ xxx	1	Fatal	None	Likely	Death	Yes	Yes
				2	Not recovered	Dose delayed	Unlikely	Life Threatening	No	No
				3	Recovered	Drug withdrawn		Hospitalization		
				4	Recovered w/ sequelae			Significant Disability		
								Congenital Anomaly or Birth Defect		
								Other medically important event		

Note: Adverse event coding was done using the MedDRA Version xx.x dictionary.
[1] Severity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening
AESI = Adverse Event of Special Interest
MAAE = Medically Attended Adverse Event

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by Treatment, Subject number, start date, stop date, SOC, PT.
- If "Ongoing" is checked, then AE Stop Date should be missing. Put "Ongoing" in the Stop Date column.
- List out all AEs EXCEPT where Serious = 'No'.
- May need to use an 8-point font for this listing

Listing 16.2.7.5: Adverse Events Associated with Discontinuation of Dosing by Subject

Safety Population
Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	MedDRA SOC/ Preferred Term/ AE Verbatim	Start Date/ Day	Stop Date/ Day	Severity [1]	Outcome	Action Taken with Study Drug	AE Related To Study Drug	Serious	AESI	MAAE
xx-xxx		ddmmmyyyy/ xxx	ddmmmyyyy/ xxx	1	Fatal	Drug withdrawn	Likely	Not Serious	Yes	Yes
				2	Not recovered		Unlikely	Death	No	No
				3	Recovered			Life Threatening		
				4	Recovered w/ sequelae			Hospitalization		
								Significant Disability		
								Congenital Anomaly or Birth Defect		
								Other medically important event		

Note: Adverse event coding was done using the MedDRA Version xx.x dictionary.
[1] Severity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening
AESI = Adverse Event of Special Interest
MAAE = Medically Attended Adverse Event

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by Treatment, Subject number, start date, stop date, SOC, PT.
- If "Ongoing" is checked, then AE Stop Date should be missing. Put "Ongoing" in the Stop Date column.
- List out all AEs where Action Taken = Drug withdrawn.
- May need to use an 8-point font for this listing

Listing 16.2.7.6: Adverse Events Leading to Death by Subject

Safety Population
Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	MedDRA SOC/ Preferred Term/ AE Verbatim	Start Date/ Day	Stop Date/ Day	Severity [1]	Outcome	Action Taken with Study Drug	AE Related To Study Drug	Serious	AESI	MAAE
xx-xxx		ddmmmyyyy/ xxx	ddmmmyyyy/ xxx	1	Fatal	None	Likely	Death	Yes	Yes
				2		Dose delayed	Unlikely		No	No
				3		Drug withdrawn				
				4						

Note: Adverse event coding was done using the MedDRA Version xx.x dictionary.
[1] Severity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening
AESI = Adverse Event of Special Interest
MAAE = Medically Attended Adverse Event

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by Treatment, Subject number, start date, stop date, SOC, PT.
- If "Ongoing" is checked, then AE Stop Date should be missing. Put "Ongoing" in the Stop Date column.
- List out all AEs where Outcome=Fatal OR Serious=Death.
- May need to use an 8-point font for this listing

Listing 16.2.7.7: Medically Attended Adverse Events by Subject

Safety Population
Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	MedDRA SOC/ Preferred Term/ AE Verbatim	Start Date/ Day	Stop Date/ Day	Severity [1]	Outcome	Action Taken with Study Drug	AE Related To Study Drug	Serious	AESI	MAAE	MAAE Type
xx-xxx		ddmmmyyyy / xxx	ddmmmyyyy / xxx	1	Fatal	None	Likely	Not Serious	Yes	Yes	ER Visit
				2	Not recovered	Dose delayed	Unlikely	Death	No		Other visit
				3	Recovered	Drug withdrawn		Life Threatening			
				4	Recovered w/ sequelae			Hospitalization			
								Significant Disability			
								Congenital Anomaly or Birth Defect			
								Other medically important event			

Note: Adverse event coding was done using the MedDRA Version xx.x dictionary.
[1] Severity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening
AESI = Adverse Event of Special Interest
MAAE = Medically Attended Adverse Event

Program: Date Produced: mm/dd/yy

Programming Notes:

- Sort by Treatment, Subject number, start date, stop date, SOC, PT.
- If "Ongoing" is checked, then AE Stop Date should be missing. Put "Ongoing" in the Stop Date column.
- List out all AEs where MAAE=Yes.
- May need to use an 8-point font for this listing

Listing 16.2.7.8: Adverse Events of Special Interest by Subject

Safety Population
Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	MedDRA SOC/ Preferred Term/ AE Verbatim	Start Date/ Day	Stop Date/ Day	Severity [1]	Outcome	Action Taken with Study Drug	AE Related To Study Drug	Serious	AESI	MAAE
xx-xxx		ddmmmyyyy / xxx	ddmmmyyyy / xxx	1	Fatal	None	Likely	Not Serious	Yes	Yes
				2	Not recovered	Dose delayed	Unlikely	Death		No
				3	Recovered	Drug withdrawn		Life Threatening		
				4	Recovered w/ sequelae			Hospitalization		
								Significant Disability		
								Congenital Anomaly or Birth Defect		
								Other medically important event		

Note: Adverse event coding was done using the MedDRA Version xx.x dictionary.
[1] Severity: Grade 1 = Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Potentially life-threatening
AESI = Adverse Event of Special Interest
MAAE = Medically Attended Adverse Event

Program:

Date Produced: mm/dd/yy

Programming Notes:

- Sort by Treatment, Subject number, start date, stop date, SOC, PT.
- If "Ongoing" is checked, then AE Stop Date should be missing. Put "Ongoing" in the Stop Date column.
- List out all AEs where AESI=Yes.
- May need to use an 8-point font for this listing

Listing 16.2.8.1: Urine Pregnancy Test Results by Subject

Safety Population

Treatment	Subject Number	Date	Results
GEN-003 60 ug / M2 50 ug	xxxx	ddmmmyyyy	Negative
			Positive
			Not done
Placebo			

Program: Date Produced: mm/dd/yy

Programming Note:

- Sort by Treatment, Subject number.

Listing 16.2.8.2: Pregnancy Results by Subject

Safety Population

Treatment: GEN-003 60 ug / M2 50 ug

Subject Number	Date	Date of Last Menstrual Period	Expected Date of Delivery	Date of Ultrasound	Date of Amniocentesis	Date of Chorionic Villus Sampling	Date of MSAFP/ Serum Markers	Other	Pregnancy Outcome	Status	Describe	Compli-cations
xxxx	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy	ddmmmyyyy		Unknown	Healthy Baby		Yes
									Full term	Sick Baby (describe)	X	No
									Premature Birth	Stillbirth		
									Spontaneous Miscarriage	Congenital Anomaly/ Birth defect (describe)	X	
									Elective termination	Multiple Births(#)		

Program: Date Produced: mm/dd/yy

Programming Note:

- Sort by Treatment, Subject number.