STATISTICAL ANALYSIS PLAN

Protocol PRO 2018-02

Version 1.0
January 16, 2019

A Multicenter, Double-Blind, Randomized, Controlled Study of the Safety and Effectiveness of PN40082 for Lip Augmentation

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Statistical Analysis Plan

1 Purpose of Statistical Analysis Plan

The purpose of the statistical analysis plan is to describe in detail all the data, statistical methods, and summary tables required to implement the statistical analysis of Clinical Study Protocol PRO 2018-02 (Section 8 in the study protocol version 4.0, dated October 02, 2018).

This plan has also incorporated responses to the FDA review comments on the Abbreviated SAP version 2.0, two consideration points in particular as follows:

(1) Use of As-Treated (AT) population for safety instead of Intent-to-Treat population
(2) For the primary efficacy endpoint, due to the likeliness that there will be a large number of ties in the ranked data, use the Wilcoxon Mann-Whitney test and the associated confidence interval for the median differences to test the non-inferiority hypothesis.

2 Study Objectives

To compare the safety and efficacy profile of PN40082 versus Restylane Silk Injectable Gel with 0.3% lidocaine (Restylane Silk) for lip augmentation.

3 Study Design and Sample Size Determination

3.1 Study Design

For the purpose of exploring the above objectives, the study will be conducted as a multicenter, double-blind, randomized, controlled study in subjects seeking lip augmentation. Subjects will be randomized 1:1 to treatment with either PN40082 or Restylane Silk. The treating investigator will be performing assessments at baseline to confirm inclusion/exclusion criteria entry. The Evaluating Investigator and subject will be blinded to the treatment. Injections of the study device will be performed by an unblinded Treating Investigator. At each visit, the blinded Evaluating Investigator and subject evaluations of the treated areas will be performed and recorded. Visits will occur at:

- Visit 1 / Week 0 (Day 1) – baseline and treatment
- Visit 2 / Day 28 (±2 days) / Month 1 – interim visit (touch-up if necessary)
- Visit 3 / Day 56 (±4 days) / Month 2 – interim visit
- Visit 4 / Day 84 (±4 days) / Month 3 – interim visit
- Visit 5 / Day 168 (±7 days) / Month 6 – End of Study (EOS) Visit. All subjects will undergo the consent procedure for the open-label retreatment protocol.

Telephone contacts for safety follow-up will occur at:

- Day 3 (±2 days) - Safety follow-up telephone call
- Day 14 (±2 days) – Safety follow-up telephone call
- Day 33 (±2 days) – Safety follow-up telephone call (for subjects with touch-up treatment)
- Day 44 (±2 days) – Safety follow-up telephone call (for subjects with touch-up treatment)
- Day 112 (±4 days) / Month 4 – Safety follow-up telephone call
- Day 140 (±4 days) / Month 5 – Safety follow-up telephone call

Evaluations include:

- Lip Fullness Grading Scale (LFGS) (Overall lip fullness considering both lips together, fullness of the upper lip and fullness of the lower lip)

- Perioral lines at rest severity scale (POL) (Overall perioral lines at rest severity considering both lips together, perioral lines at rest severity of the upper lip and perioral lines at rest severity of the lower lip)
- Patient Global Aesthetic Improvement (pGAI)
- Investigator Global Aesthetic Improvement (iGAI)
- Swelling Assessment
- Subject Satisfaction with Lips Assessment (using VAS)

Safety will be assessed by monitoring adverse events (AEs) and concomitant medications at all study visits. Other Safety evaluations include lip function, lip sensation, lip texture, lip firmness, lip symmetry and lip movement/function. Other evaluations include Investigator Ease of Use Assessment.

At Visit 5, subjects and blinded evaluating investigators will be asked which treatment they thought was administered as a way of evaluating the blinding.

3.2 Sample Size Determination

For the PRO 2018-02 study, the primary variable is change from baseline to Month 3 in LFGS. The sample size was determined based on: (1) both PN40082 and Restylane Silk having an equal mean value with a common standard deviation of 0.85 for change from baseline in LFGS, and (2) the non-inferiority limit of -0.50. The test:control ratio of 1:1 results in 126 (63:63) per-protocol (PP) subjects at power of 90%. A total of 158 subjects will be randomized to obtain 126 (63:63) PP subjects assuming that 80% of randomized subjects meet the PP criteria.

4 Populations To Be Analyzed

Three subject populations are defined as follows:

(1) As-treated (AT) (safety population): All randomized subjects who received study device. AT subjects will be included in the safety analysis for the treatment they actually received.

(2) Modified intent-to-treat (mITT): All randomized subjects who met the inclusion/exclusion criteria, and received study device.

(3) Per-protocol (PP): All randomized subjects who met all inclusion/exclusion criteria; received study device; completed Visit 5/Month 6 within the specified window; had overall LFGS score by the Blinded Evaluating Investigator at Visit 3/Month 2 within the specified visit window; and had no significant protocol violations that would affect the treatment evaluation.

For the purpose of determining the PP status of the subject, "significant protocol violations" are any unforeseen events that occurred during the conduct of the trial that result in noteworthy study protocol violations that could have possibly interfered with the therapeutic administration of the treatment or the precise evaluation of treatment efficacy.

Efficacy analyses will be performed on the mITT and PP populations, with PP as the primary population and mITT supportive. Analyses of safety and other evaluations will be performed on the AT population.

5 Planned Analyses

5.1 Methodological Considerations

SAS software (version 9.4 or higher) will be used for all data analyses and tabulations.

Two-sided hypothesis testing will be conducted for all inferential analyses. Resulting p-values less than 0.05 will be considered statistically significant. To control the overall error rate, a hierarchical approach will be applied. Upon the significance of the primary efficacy outcome, secondary endpoints will be analyzed and no adjustment to the p-values will be applied to multiple comparisons. For this non-inferiority study, the null hypothesis to be tested for all the secondary endpoints is that there is no difference between the two products, and all statistical comparisons for these endpoints will be considered descriptive (non-inferential).

No interim analyses are planned.

All the data points will be presented in subject data listings.

5.2 Handling of Dropouts or Missing Data

For demographics, baseline characteristics, safety profile and other evaluations, each variable will be analyzed using the existing data. Subjects with missing data will be excluded only from the analyses for which data are not available.

No missing values will be replaced in the PP analyses. There will not be missing data for the primary efficacy endpoint for the PP population based on the PP definition in Section 4.

Only for the overall LFGS and its derivatives for the mITT analysis, missing scores will be replaced using the multiple imputation (MI) approach for the mITT analysis only. Depending on the pattern of missingness, a two-step process may be employed. If missing data occur for an intermediate visit, they will be imputed first via a Markov Chain Monte Carlo (MCMC) method. As a result, a monotone missingness pattern will be obtained for the data to be fully imputed. The subsequent imputation will use Monotone Regression to produce 5 imputed datasets where the remaining missing data are filled in.

When missing overall LFGS score at a given visit is imputed, the values from all its previous visits will be included as predictor in the imputation model. For example, for a subject with missing overall LFGS at Visit 4, the overall LFGS scores from Visits 1 through 3 for the subjects will be included in the imputation model. Other variables that go into the imputation models include treatment, site, and key baseline characteristics of age, gender, race and Fitzpatrick skin type.

To prepare for MI, for subjects who are early discontinued from the study, their efficacy data captured at the termination visit will be assigned to the nearest corresponding scheduled visit.

The SAS code for MI is as follows, using the random number 69833 as the seed for the first Step and 192185 as the seed for the second step. Where notation of main variables:

- Trt = treatment: 1 for Test product, 2 for competitor product
- Invid = site number
- Age = subject's age

- Sexn = gender: 1 for female, 2 for male
- Nrace = race: 1 for White, 2 for Asian, 3 for Native Hawaiian or Other Pacific-Islander, 4 for Black or African American, 5 for American Indian or Alaska Native, 6 for Other, 7 for Mixed
- Fstn = Fitzpatrick skin type in numeric value
- v1 - v5: LFGS at Visits 1-5 accordingly

```
*Step 1: MCMC fills interim missingness to make monotone;
 PROC MI data=eff out=step1 seed=69833 nimpute=1;
   mcmc impute=monotone;
   var trt invid age sexn nrace fstn  v1 v2 v3 v4 v5;
 run;

*Step 2: MI regression;
PROC MI data=step1 out=step2  seed=192185 nimpute=5;
  var trt invid age sexn nrace fstn v1 v2 v3 v4 v5;
  monotone reg(v2 = trt invid age sexn nrace fstn v1); *for  missing at v2;
  monotone reg(v3 = trt invid age sexn nrace fstn v1 v2); *for  missing at v3;
  monotone reg(v4 = trt invid age sexn nrace fstn v1 v2 v3); *for missing at v4;
  monotone reg(v5 = trt invid age sexn nrace fstn v1 v2 v3 v4); *for missing at v5;
run;
```

The imputed values will be round to integer and within the range of 0 to 4.

5.3 Demographics and Baseline Characteristics

Baseline and demographic characteristic variables (including age, sex, race, ethnicity, and Fitzpatrick skin type) will be tabulated using descriptive statistics. For each continuous variable, the summary will include the mean, standard deviation (SD), median, minimum and maximum. For each categorical variable, the summary will include frequencies and percentages.

Poolability of the data across study sites for key demographic and baseline characteristics (age, sex, Fitzpatrick skin type, race, Body Mass Index) will be assessed for the AT population. For age and Body Mass Index, one-way analysis of variance (ANOVA) will be performed with study site as the main factor. For Fitzpatrick Skin Type Classification (I-VI), nonparametric Kruskal Wallis test will be conducted with study site as the class variable. For sex, Pearson's Chi-square test, or exact test if more appropriate, will be performed.

Demographic and baseline characteristics will be summarized and compared for PP subjects versus non-PP subjects. For categorical variables, comparison will be performed using the Cochran-Mantel-Haenszel (CMH) test for general association adjusted for site. For continuous variables, comparison will be conducted using two-way analysis of variance model (ANOVA) with fixed factors of group and site, with respect to the original values if normality assumption is satisfied, or with respect to ranked values if otherwise.

Descriptive summary of racial distribution within Fitzpatrick Skin Type will provided for the AT subjects.

5.4 Subject Accountability

A summary of subject disposition will be provided for all subjects descriptively, including reason for discontinuation and analysis populations. Disposition of analysis populations will also be tabulated by study site.

5.5 Efficacy Variables

Key efficacy assessments include the following:

- LFGS: 0 = very thin, 1 = thin, 2 = moderately thick, 3 = thick, 4 = full
- POL: 0 = None (a mouth with no perioral lines), 1 = Mild (a mouth with a few shallow perioral lines), 2 = Moderate (a mouth with some moderate lines), 3 = Severe (a mouth with many deep lines or crevices)
- Subject Satisfaction with Lips using a visual analog scale (VAS) on a 100-mm scale from 0 = Very Unsatisfied to 100 = Very Satisfied
- Patient Global Aesthetic Improvement (pGAI) Score: 1=Worse, 2=No change, 3=Improved, 4=Much improved, 5=Very much improved
- Investigator Global Aesthetic Improvement (iGAI) Score: 1=Worse, 2=No change, 3=Improved, 4=Much improved, 5=Very much improved
- Swelling Assessment: 0 = None, 1 = Minimal, 2 = Mild, 3 = Moderate, 4 = Severe

All efficacy analyses will be performed for both the PP and mITT populations.

5.5.1 Primary Efficacy Analysis

The primary efficacy endpoint is change from baseline to Visit 3/Month 2 in overall LFGS. The null hypothesis to be tested is that the Test device is inferior to the Control device. The results for PP are considered as definitive and those for mITT as supportive.

Summary statistics (mean, SD, minimum, median, maximum) and 95% confidence interval (CI) for mean will be presented for the changes scores for each treatment.

Due to the fact that the change scores would only contain 5 possible values (0, 1, 2, 3, and 4), the normal distribution assumption is hardly attainable, and therefore, the nonparametric Hodges-Lehmann (HL) estimators will be employed to test the study hypothesis. The 95% confidence limits for the median differences between the two treatment groups (PN40082 minus Restylane Silk) will be derived using PROC NPAR1WAY with the option for the HL estimators. If the lower limit is on or above -1.0, the null hypothesis will be rejected to support the claim that PN40082 is non-inferior to Restylane Silk.

For the mITT analysis, the above analysis will be carried out for each copy of the MI data sets. Then PROC MIANALYZE will be performed to account for the between and within variation in the multiply imputed data sets.

To assist an assessment for the consistency of the treatment effect among sites, summary of the primary endpoint will be presented by site for the primary population (i.e., the PP subjects).

The primary endpoint will also be analyzed for the following two subsets of the PP subjects: (1) subjects that have injection on one lip only, and (2) subjects that have injections on both lips.

5.5.2 Secondary Efficacy Analysis

The secondary efficacy endpoints include the following:

- percent of subjects with treatment success (responder on overall LFGS) at Visit 3/Month 2, where responder is defined as a subject with at least a 1-grade increase from baseline on the overall LFGS
- percent of responders on the overall POL severity scale at Visit 4/Month 3 (defined as a subject demonstrating ≥ 1-point improvement, i.e., decrease in severity, from baseline)
- change from baseline to Visit 4/Month 3 in overall LFGS
- change from baseline to Visit 5/Month 6 in overall LFGS

The supporting importance of the secondary endpoints is ordered by [1] percent of subject with treatment success (responder on overall LFGS) at Visit 3/Month 2, [2] percent of responders on the overall POL severity scale at Visit 4/Month 3, [3] change from baseline to Visit 4/Month 3 in overall LFGS, and [4] change from baseline to Visit 5/Month 6 in overall LFGS.

These secondary variables will be summarized with descriptive statistics for each treatment arm and a 95% CI for the difference between treatments. For the proportion variables, the 95% CI for treatment difference will be calculated using the Wald's method, with subjects pooled from all study sites. For the change variables, the 95% CI for the median differences between treatments will be derived using PROC NPAR1WAY with the option for the HL estimators.

For the mITT analysis, the LFGS-related secondary endpoints will be analyzed for each copy of the MI data sets. PROC MIANALYZE will then be performed to account for the between and within variation in the multiply imputed data sets.

5.5.3 Other Efficacy Analysis

Other efficacy variables include:

- pGAI, iGAI, and Swelling Assessment at each scheduled visit,
- percent of subjects with treatment success (upper lips, lower lips) at Visit 3/Month 2 where responder is defined as a subject with at least a 1-grade increase from baseline on the LFGS post augmentation,
- percent of responders (upper lips, lower lips) on the POL severity scale at Visit 4/Month 3 (defined as a subject demonstrating ≥ 1-point improvement, i.e., decrease in severity, from baseline),
- Subject Satisfaction with Lips VAS at each scheduled visit,
- change from baseline to Visit 4/Month 3 and Visit 5/Month 6 in upper lips, lower lips LFGS.

These other efficacy variables will be summarized for each treatment using descriptive statistics based on the observed data.

5.6 Safety Variables

Key safety variables include incidence rate of treatment-emergent adverse events (TEAEs) and the exposure to the study product, as well as Investigator Ease of Use Assessment, lip function,

lip sensation, lip texture, lip firmness, lip symmetry, and lip movement/function. They will be summarized using the AT population.

5.6.1 Adverse Events

All adverse events (AEs) occurring during the study will be recorded and coded in the Medical Dictionary for Regulatory Activities (MedDRA), version 20 or higher. TEAEs are defined as events that appear subsequent to the first injection or that were present prior to the first injection but worsened in intensity after the first injection.

Frequency and percent of subjects reporting TEAEs will be tabulated for each treatment by system organ class and preferred terms, and further by severity and relationship to study device. In summaries of severity and relationship, subjects who reported more than one event in a treatment arm that are mapped to the same preferred term will be counted only once in that treatment arm under the strongest severity and relationship, respectively.

TEAEs related to vascular injections/Visual events will also be tabulated by subject Fitzpatrick Skin Type (I-III vs. IV-VI), each Fitzpatrick Skin Type individually and by number of injections subjects received. Most frequently occurring TEAEs related to vascular injections/Visual events (those reported by 5% or more subjects of either treatment group) will be tabulated by preferred term. These TEAEs will also be summarized by event's severity and duration.

Treatment-Emergent Serious Adverse Events (TESAEs) and TEAEs that led to treatment interruption or discontinuation will be presented in data listings.

5.6.2 Exposure to Study Product

Amount of syringe used will be summarized using descriptive statistics (mean, SD, minimum, median, maximum) at Visit 1 for all the AT subjects and at Visit 2/Month 1 for those who received a touch-up treatment.

5.6.3 Other Variables

Investigator Ease of Use Assessment

Overall ease of use of the device will be evaluated by the Treating Investigator using the numerical rating scale (NRS) from 0 being not easy to 10 being most easy at Visit 1/Day 1 and for subjects who have touch-up treatment at Visit 2/Month 1. It will be summarized for the AT subjects descriptively with mean, SD, minimum, median, and maximum.

Lip Evaluations

Lip function, lip sensation, lip texture, lip firmness, lip symmetry, and lip movement/function will be evaluated by the Blinded Evaluating Investigator at each visit. These variables will be summarized using frequency and percent of subjects by categories of incidence.

Concomitant Medications

Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary, Version March 2013 or later, and will be presented in data listings.

5.7 Other Analysis

Blinding of subjects and evaluators will be assessed at Visit 5/Month 6, end of study or early termination. Both subjects and blinded evaluating investigators will be asked to identify which treatment they thought had been administered. The results of subject guesses and results of blinded evaluator guesses will be compared to the actual treatment assignment separately. The null hypothesis to be tested is that the proportion of correct guesses is 50%, using p-values and 95% confidence intervals from the exact binomial distribution. A correct guess is defined as guessing PN40082 when the subject was randomized to PN40082 or guessing Restylane Silk when the subject was randomized to Restylane Silk. The proportion of correct guesses is defined to be the number of subjects who guessed correctly divided by the number of subjects who responded.

6 Tables and Listings

The following is an example of tables and listings that will be included in the clinical study report. Tables and listings may be modified as needed during the data analyses.

7 Appendices

7.1 Handling of Missing or Incomplete Dates for Adverse Events and Concomitant Medications

Adverse Events

Handling of partial dates is only considered for the start date. An adverse event with a partial start date is considered treatment emergent if:

- only the day is missing and the start month/year is the same or after the month/year of the first injection
- the day and month are missing and the start year is the same or greater than the year of the first injection date
- the start date is completely missing

Concomitant Medications

Handling of partial dates is only considered for the stop date. A medication with a partial stop date is considered concomitant if:

- only the day is missing and the stop month/year is the same or after the month/year of the first injection
- the day and month are missing and the stop year is the same or greater than the year of the first injection date
- the stop date is completely missing or the medication is ongoing.

7.2 Summary of Assessments

Visit Number (Month)	**Visit 1 (Week 0)**	**Phone Contacts**	**Visit 2 (Mo 1)**	**Phone Contacts [a]**	**Visit 3 (Mo 2)**	**Visit 4 (Mo 3)**	**Phone Contacts**	**Visit 5 (Mo 6) End of Study/Early Termination**	**Unsched Visit**
Scheduled Day(s)	**Day 1**	**Day 3 & Day 14**	**Day 28**	**Day 33 & Day 44**	**Day 56**	**Day 84**	**Day 112 & Day 140**	**Day 168 [b]**	
Scheduling Window	**none**	**± 2 days**	**± 2 days**	**± 2 days**	**± 4 days**	**± 4 days**	**± 4 days**	**± 7 days**	
Informed consent	X								
Medical history/ demographics	X								
Abbreviated Physical examination (including vital signs)	X								
Vision evaluations (Snellen visual acuity, confrontational visual fields, ocular motility)[d]	X		X		X	X	X	X	X[c]
Prior/Concomitant Medication/ Treatment	X	X	X	X	X	X	X	X	X
Inclusion/exclusion criteria review	X								
Urine pregnancy test[e]	X								
Fitzpatrick Skin Type	X								
Lip Fullness Grading Scale (LFGS) (Overall, upper lip and lower lip)	X		X		X	X		X	X[c]
Perioral lines at rest severity scale (POL) (Overall, upper lip and lower lip)	X		X		X	X		X	X[c]
Randomization	X								
Treatment with study device	X		X[a]						
Investigator Ease of Use Assessment	X		X[a]						
Evaluation for touch-up			X						
Patient GAI (pGAI)			X		X	X		X	X[c]
Swelling Assessment			X		X	X		X	X[c]
Investigator GAI (iGAI)			X		X	X		X	X[c]
Subject Satisfaction with Lips			X		X	X		X	X[c]
Lip Function (prior to injections)	X		X		X	X		X	X[c]
Lip Sensation (prior to injections)	X		X		X	X		X	X[c]
Lip Texture (prior to injections)	X		X		X	X		X	X[c]
Lip Firmness (prior to injections)	X		X		X	X		X	X[c]
Lip Symmetry (prior to injections)	X		X		X	X		X	X[c]

Lip Movement/Function	X		X		X	X		X	X[e]
Adverse event assessment	X	X	X	X	X	X	X	X	X
Treatment question								X	
Subject Diary	Dispense		Collect/ dispense[f]		Collect[f]				

Note: The timing of each visit is relative to Day 1, which is defined as the day the subject is randomized and first treated.

a. For subjects who have touch-up treatment at Visit 2
b. All subjects will receive a follow-up phone call at 12 months after first treatment.
c. If/as needed
d. performed prior to any treatment and repeated 30 minutes following any treatment and all follow-up visits.
e. For women of childbearing potential, to be completed prior to enrollment.
f. Dispense/collect diary only if touch up is performed

Summary Tables

Table 14.1.1 – Analysis Population

	PN40082	Restylane Silk	Total
Subjects Randomized	0	0	0
Subjects Included in the As-Treated (AT) Population	0 (0%)	0 (0%)	0 (0%)
Subjects Included in the Modified Intent-to-Treat (mITT) Population	0 (0%)	0 (0%)	0 (0%)
Subjects Included in the Per-Protocol (PP) Population	0 (0%)	0 (0%)	0 (0%)

Source: Listings 16.2.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.1.2 – Subject Discontinuations by Reason for All Randomized Subjects

	PN40082	Restylane Silk	Total
Subjects Randomized	0	0	0
Number Completed Study	0 (0%)	0 (0%)	0 (0%)
Total Discontinued	0 (0%)	0 (0%)	0 (0%)
Reason Discontinued			
-- Subject or legal representative withdrew consent	0 (0%)	0 (0%)	0 (0%)
-- Subject's study device assignment was unblinded	0 (0%)	0 (0%)	0 (0%)
-- Significant protocol violation	0 (0%)	0 (0%)	0 (0%)
-- Subject became pregnant			
-- An AE occurs for which the subject or the investigator determines that it is in the subject's best interest to be discontinued	0 (0%)	0 (0%)	0 (0%)
-- Lost to follow-up	0 (0%)	0 (0%)	0 (0%)
-- Investigator discretion	0 (0%)	0 (0%)	0 (0%)
-- Other	0 (0%)	0 (0%)	0 (0%)

Source: Listing 16.2.1.2
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.1.3 – Subject Enrollment by Study Site

Site Number	Randomized	AT	mITT	PP	Completed	Discontinued
1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2						
3						
4						
5						
6						
Total	XX	XX	XX	XX	XX	XX

AT: As-Treated, mITT: Modified Intent-to-Treat, PP: Per-Protocol
Percentages are based on the total number of subjects in each column.
Source: Listing 16.2.1.1, 16.2.1.2
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Table 14.1.4 – Significant Protocol Violations

Significant Protocol Violation	PN40082	Restylane Silk	Total
Did not use any study product	0 (0%)	0 (0%)	0 (0%)
Violation of inclusion/exclusion criteria	0 (0%)	0 (0%)	0 (0%)
Did not complete Visit 5 within the specified window	0 (0%)	0 (0%)	0 (0%)
Use of prohibited medications	0 (0%)	0 (0%)	0 (0%)
...			

Significant protocol violations (SPVs) are those events that exclude subjects from any of the analysis populations.
Subjects with multiple SPVs are presented under each category as appropriate (e.g., Subjects who had no post-baseline visit are not counted under SPVs related to Visit 5).
Source: Listing 16.2.1.1, 16.2.2.1, 16.2.2.2, 16.2.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.1.5.1 – Demographic and Baseline Characteristics for As-Treated Population

Parameter	Category	PN40082 (N=xx)	Restylane Silk (N=xx)	Total (N=xx)
Gender	Female	0 (0%)	0 (0%)	0 (0%)
	Male	0 (0%)	0 (0%)	0 (0%)
Ethnicity	Hispanic or Latino	0 (0%)	0 (0%)	0 (0%)
	Not Hispanic or Latino	0 (0%)	0 (0%)	0 (0%)
	Not Willing to Provide	0 (0%)	0 (0%)	0 (0%)
Race	White	0 (0%)	0 (0%)	0 (0%)
	Asian	0 (0%)	0 (0%)	0 (0%)
	Native Hawaiian or Other Pacific-Islander	0 (0%)	0 (0%)	0 (0%)
	Black or African American	0 (0%)	0 (0%)	0 (0%)
	American Indian or Alaska Native	0 (0%)	0 (0%)	0 (0%)
	Other	0 (0%)	0 (0%)	0 (0%)
	Mixed*	0 (0%)	0 (0%)	0 (0%)
Age (years)	N	0	0	0
	Mean ± SD	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00
	Median	0.0	0.0	0.0
	Min, Max	0, 0	0, 0	0, 0
Age Groups	18 to < 40	0 (0%)	0 (0%)	0 (0%)
	40 to < 64	0 (0%)	0 (0%)	0 (0%)
	64 to <75	0 (0%)	0 (0%)	0 (0%)
	>= 75	0 (0%)	0 (0%)	0 (0%)
Body Mass Index (BMI)**	N	0	0	0
	Mean ± SD	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00
	Median	0.0	0.0	0.0
	Min, Max	0.0, 0.0	0.0, 0.0	0.0, 0.0

Parameter	Category	PN40082 (N=xx)	Restylane Silk (N=xx)	Total (N=xx)
Fitzpatrick Skin Type	I	0 (0%)	0 (0%)	0 (0%)
	II	0 (0%)	0 (0%)	0 (0%)
	III	0 (0%)	0 (0%)	0 (0%)
	IV	0 (0%)	0 (0%)	0 (0%)
	V	0 (0%)	0 (0%)	0 (0%)
	VI	0 (0%)	0 (0%)	0 (0%)
Lip Fullness Grading Scale - Overall	n (%) with 0=Very Thin	0 (0%)	0 (0%)	0 (0%)
	n (%) with 1=Thin	0 (0%)	0 (0%)	0 (0%)
	n (%) with 2=Moderately Thick	0 (0%)	0 (0%)	0 (0%)
	n (%) with 3= Thick	0 (0%)	0 (0%)	0 (0%)
	n (%) with 4= Full	0 (0%)	0 (0%)	0 (0%)
Lip Fullness Grading Scale – Upper Lips	n (%) with 0=Very Thin	0 (0%)	0 (0%)	0 (0%)
	n (%) with 1=Thin	0 (0%)	0 (0%)	0 (0%)
	n (%) with 2=Moderately Thick	0 (0%)	0 (0%)	0 (0%)
	n (%) with 3= Thick	0 (0%)	0 (0%)	0 (0%)
	n (%) with 4= Full	0 (0%)	0 (0%)	0 (0%)
Lip Fullness Grading Scale – Lower Lips	n (%) with 0=Very Thin	0 (0%)	0 (0%)	0 (0%)
	n (%) with 1=Thin	0 (0%)	0 (0%)	0 (0%)
	n (%) with 2=Moderately Thick	0 (0%)	0 (0%)	0 (0%)
	n (%) with 3= Thick	0 (0%)	0 (0%)	0 (0%)
	n (%) with 4= Full	0 (0%)	0 (0%)	0 (0%)
Perioral Lines at Rest Severity Scale - Overall	n (%) with 0=None	0 (0%)	0 (0%)	0 (0%)
	n (%) with 1=Mild	0 (0%)	0 (0%)	0 (0%)
	n (%) with 2=Moderate	0 (0%)	0 (0%)	0 (0%)
	n (%) with 3= Severe	0 (0%)	0 (0%)	0 (0%)

Parameter	Category	PN40082 (N=xx)	Restylane Silk (N=xx)	Total (N=xx)
Perioral Lines at Rest Severity Scale – Upper Lips	n (%) with 0=None	0 (0%)	0 (0%)	0 (0%)
	n (%) with 1=Mild	0 (0%)	0 (0%)	0 (0%)
	n (%) with 2=Moderate	0 (0%)	0 (0%)	0 (0%)
	n (%) with 3= Severe	0 (0%)	0 (0%)	0 (0%)
Perioral Lines at Rest Severity Scale – Lower Lips	n (%) with 0=None	0 (0%)	0 (0%)	0 (0%)
	n (%) with 1=Mild	0 (0%)	0 (0%)	0 (0%)
	n (%) with 2=Moderate	0 (0%)	0 (0%)	0 (0%)
	n (%) with 3= Severe	0 (0%)	0 (0%)	0 (0%)

*Subjects who reported more than one race are categorized as Mixed race.
** BMI = weight (lbs) / height² (in) x 703
Source: Listing 16.2.4.1, 16.2.4.2, 16.2.6.1.1, 16.2.6.1.2
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Note:

Table 14.1.5.1 will be used as the shell for the following tables:

Table 14.1.5.2 - Demographic and Baseline Characteristics for Modified Intent-to-Treat Population

Table 14.1.5.3 - Demographic and Baseline Characteristics for Per-Protocol Population

Table 14.1.5.4 – Key Demographic and Baseline Characteristics by Site for As-Treated Population

Parameter	Category	Site 1 (N=xx)	Site 2 (N=xx)	Site 3 (N=xx)	Site 4 (N=xx)	Site 5 (N=xx)	Site 6 (N=xx)	p-value
Gender	Female	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.xxx[1]
	Male	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Age (years)	N	0	0	0	0	0	0	
	Mean ± SD	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	0.xxx[2]
	Median	0.0	0.0	0.0	0.0	0.0	0.0	
	Min, Max	0, 0	0, 0	0, 0	0, 0	0, 0	0, 0	
Body Mass Index (BMI)	N	0	0	0	0	0	0	
	Mean ± SD	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	00.0 ± 00.00	0.xxx[2]
	Median	0.0	0.0	0.0	0.0	0.0	0.0	
	Min, Max	0, 0	0, 0	0, 0	0, 0	0, 0	0, 0	
Fitzpatrick Skin Type	I	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.xxx[3]
	II	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	III	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	IV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	V	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	VI	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

[1]P-value from Pearson's Chi-square test or exact test if appropriate.
[2]P-value from one-way analysis of variance (ANOVA) with study site as the main factor.
[3]P-value from nonparametric Kruskal Wallis test with study site as the class variable.
Source: Listing 16.2.4.1, 16.2.4.2
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.1.5.5 – Summary of Racial Distribution within Fitzpatrick Skin Type for As-Treated Population

	Skin Type			Total	Skin Type			Total	Overall
Race	I (N=xx)	II (N=xx)	III (N=xx)	I-III (N=xx)	IV (N=xx)	V (N=xx)	VI (N=xx)	IV-VI (N=xx)	Total (N=xx)
White	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Asian	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Black or African American	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
American Indian or Alaska Native	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Native Hawaiian or Other Pacific Islander	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Source: Listing 16.2.4.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh mm on data from Month Day, Year.

Table 14.1.5.6 – Demographic and Baseline Characteristics for Per-Protocol (PP) Subjects and Subjects Excluded from the PP Population

Parameter	Category	PP Subjects (N=xx)	Non-PP Subjects (N=xx)	p-value
Gender	Female	0 (0%)	0 (0%)	0.xxx[1]
	Male	0 (0%)	0 (0%)	
Ethnicity	Hispanic or Latino	0 (0%)	0 (0%)	0.xxx[1]
	Not Hispanic or Latino	0 (0%)	0 (0%)	
	Not Willing to Provide	0 (0%)	0 (0%)	
Race	White	0 (0%)	0 (0%)	NA
	Asian	0 (0%)	0 (0%)	
	Native Hawaiian or Other Pacific-Islander	0 (0%)	0 (0%)	
	Black or African American	0 (0%)	0 (0%)	
	American Indian or Alaska Native	0 (0%)	0 (0%)	
	Other	0 (0%)	0 (0%)	
Age (years)	N	0	0	
	Mean ± SD	00.0 ± 00.00	00.0 ± 00.00	0.xxx[2]
	Median	0.0	0.0	
	Min, Max	0, 0	0, 0	
-- Age Groups	18 to <40	0 (0%)	0 (0%)	
	40 to <64	0 (0%)	0 (0%)	
	64 to <75	0 (0%)	0 (0%)	
	>=75	0 (0%)	0 (0%)	
Body Mass Index (BMI)	N	0	0	
	Mean ± SD	00.0 ± 00.00	00.0 ± 00.00	0.xxx[2]
	Median	0.0	0.0	
	Min, Max	0, 0	0, 0	
Fitzpatrick Skin Type	I	0 (0%)	0 (0%)	0.xxx[1]
	II	0 (0%)	0 (0%)	
	III	0 (0%)	0 (0%)	
	IV	0 (0%)	0 (0%)	
	V	0 (0%)	0 (0%)	
	VI	0 (0%)	0 (0%)	

BMI = weight (lbs) / height^2 (in) x 703

[1] P-values for group comparisons from Cochran-Mantel-Haenszel test for general association, adjusted for site.
[2] P-value for group comparisons from nonparametric ranked two-way analysis of variance with fixed factors of group and site.
Source: Listing 16.2.4.1, 16.2.4.2
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.2.1.1 – Primary Analysis of Primary Efficacy Endpoint for Per-Protocol Population: Change from Baseline to Visit 3/Month 2 in Overall Lip Fullness Grading Scale (LFGS)

Population	Statistics	PN40082	Restylane Silk
Per-Protocol (PP)	N	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	

LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
[1]Median differences and 95% confidence limits are derived using Hodges-Lehmann estimators from PROC NPAR1WAY.
Source: Listing 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.1.2 – Supportive Analysis of Primary Efficacy Endpoint for Modified Intent-to-Treat Population: Change from Baseline to Visit 3/Month 2 in Overall Lip Fullness Grading Scale (LFGS)

Imputation Date Set	Statistics	PN40082	Restylane Silk
Data Set #1	N	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
Data Set #2			
...			
Data Set #5	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
Combined Analysis	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[2]	

LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
For the mITT analysis, missing overall LFGS scores will be replaced using the multiple imputation (MI) approach.
[1]Median differences and 95% confidence limits are derived using Hodges-Lehmann estimators from PROC NPAR1WAY.
[2]Median differences and 95% confidence limits for combined analysis are derived from PROC MIANALYZE.
Source: Listing 16.2.6.2.2
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.1.3 – Supportive Analysis of Primary Efficacy by Study Site for Per-Protocol Population: Change from Baseline to Visit 3/Month 2 in Overall Lip Fullness Grading Scale (LFGS)

Site Number	Statistics	PN40082	Restylane Silk
1	N	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
2			
...			
6	N	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	

LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
For the mITT analysis, missing overall LFGS scores will be replaced using the multiple imputation (MI) approach.
[1]Median differences and 95% confidence limits are derived using Hodges-Lehmann estimators from PROC NPAR1WAY.
Source: Listing 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.1.4 –Supportive Analysis of Primary Efficacy Endpoint by Subject Subset for Per-Protocol Population: Change from Baseline to Visit 3/Month 2 in Overall Lip Fullness Grading Scale (LFGS) for Who Had Injection on One Lip Only Versus Who Had Injections on Both Lips

Subset	Statistics	PN40082	Restylane Silk
Subjects Who Had Injection on One Lip Only	N	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
Subjects Who Had Injections on Both Lips	N	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
	95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
	Median	0.0	0.0
	Min, Max	0, 0	0, 0
	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	

LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
For the mITT analysis, missing overall LFGS scores will be replaced using the multiple imputation (MI) approach.
[1]Median differences and 95% confidence limits are derived using Hodges-Lehmann estimators from PROC NPAR1WAY.
Source: Listing 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.2.1 – Secondary Efficacy: Percent of Subjects with Treatment Success on Overall Lip Fullness Grading Scale (LFGS) at Visit 3/Month 2

Population	Imputation Data Set	Statistics	PN40082	Restylane Silk	95% CI for PN40082 minus Restylane Silk
Per-Protocol (PP)		N	0	0	
		n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
Modified Intent-to-Treat (mITT)		N	0	0	
	Data Set #1	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
	Data Set #2	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
	Data Set #3	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
	Data Set #4	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
	Data Set #5	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
	Combined Analysis	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[2]

For the mITT analysis, missing overall LFGS scores will be replaced using the multiple imputation (MI) approach.
Treatment success is defined as an achievement of at least a 1-grade increase from baseline on the overall LFGS, where LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
[1]The 95% confidence intervals are constructed using Wald's method.
[2]The 95% confidence interval for combined analysis is derived from PROC MIANALYZE.
Source: Listing 16.2.6.2.2, 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.2.2 – Secondary Efficacy: Percent of Responders on Overall Perioral Lines at Rest (POL) Severity Scale at Visit 4/Month 3

Population	Statistics	PN40082	Restylane Silk	95% CI for PN40082 minus Restylane Silk
Per-Protocol (PP)	N	0	0	
	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]
Modified Intent-to-Treat (mITT)	N	0	0	
	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	(0.0%, 0.0%)[1]

Responder is defined as a subject demonstrating at least 1-point improvement, i.e., decrease in severity, from baseline POL severity, where POL severity: 0=None, 1=Mild, 2=Moderate, 3=Severe.
[1]The 95% confidence intervals are constructed using Wald's method.
Source: Listing 16.2.6.2.2, 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.2.3 – Secondary Efficacy: Change from Baseline to Visit 4/Month 3 in Overall Lip Fullness Grading Scale (LFGS)

Population	Imputation Date Set	Statistics	PN40082	Restylane Silk
Per-Protocol		N	0	0
		Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
		95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
		Median	0.0	0.0
		Min, Max	0, 0	0, 0
		Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
Modified Intent-to-Treat	Data Set #1	N	0	0
		Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
		95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
		Median	0.0	0.0
		Min, Max	0, 0	0, 0
		Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
	Data Set #2			
	…			
	Data Set #5	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00
		95% CI of Mean	(0.00, 0.00)	(0.00, 0.00)
		Median	0.0	0.0
		Min, Max	0, 0	0, 0
		Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[1]	
	Combined Analysis	Median Differences and 95% Confidence Limits for PN40082 minus Restylane Silk	0.0 (0.0, 0.0)[2]	

LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
For the mITT analysis, missing overall LFGS scores will be replaced using the multiple imputation (MI) approach.
[1]Median differences and 95% confidence limits are derived using Hodges-Lehmann estimators from PROC NPAR1WAY.
[2]Median differences and 95% confidence limits for combined analysis are derived from PROC MIANALYZE.
Source: Listing 16.2.6.2.2, 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Note:

Table 14.2.2.3 will be used as the shell for the following tables:

Table 14.2.2.4 – Secondary Efficacy: Change from Baseline to Visit 5/Month 6 in Overall Lip Fullness Grading Scale (LFGS)

Table 14.2.3.1 – Other Efficacy: Patient Global Aesthetic Improvement (pGAI) by Visit Based on Observed Data

		Modified Intent-to-Treat		Per-Protocol	
Study Visit	Category	PN40082	Restylane Silk	PN40082	Restylane Silk
Visit 2/Month 1	N	0	0	0	0
	1 = Worse	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	2 = No Change	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	3 = Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	4 = Much Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	5 = Very Much Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Visit 3/Month 2					
...					
Visit 5/Month 6	N	0	0	0	0
	1 = Worse	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	2 = No Change	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	3 = Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	4 = Much Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	5 = Very Much Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Source: Listing 16.2.6.1.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Note:

Table 14.2.3.1 will be used as the shell for the following table:

Table 14.2.3.2 – Other Efficacy: Investigator Global Aesthetic Improvement (iGAI) by Visit Based on Observed Data

Table 14.2.3.3 – Other Efficacy: Swelling Assessment by Visit Based on Observed Data

		Modified Intent-to-Treat		Per-Protocol	
Study Visit	Category	PN40082	Restylane Silk	PN40082	Restylane Silk
Visit 2/Month 1	N	0	0	0	0
	0 = None	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	1 = Minimal	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	2 = Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	3 = Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	4 = Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Visit 3/Month 2					
...					
Visit 5/Month 6	N	0	0	0	0
	0 = None	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	1 = Minimal	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	2 = Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	3 = Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	4 = Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Source: Listing 16.2.6.1.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.3.4 – Other Efficacy: Percent of Subjects with Treatment Success on Lip Fullness Grading Scale (LFGS) at Visit 3/Month 2 for Upper Lips and Lower Lips Based on Observed Data

		Upper Lips		Lower Lips	
Population	Category	PN40082	Restylane Silk	PN40082	Restylane Silk
Per-Protocol	N	0	0	0	0
	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Modified Intent-to-Treat	N	0	0	0	0
	n (%) of Treatment Success	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Treatment success is defined as an achievement of at least a 1-grade increase from baseline on the overall LFGS, where LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
Source: Listing 16.2.6.2.2, 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Note:

Table 14.2.3.4 will be used as the shell for the following table:

Table 14.2.3.5 – Other Efficacy: Percent of Responders on Perioral Lines at Rest (POL) Severity Scale at Visit 4/Month 3 for Upper Lips and Lower Lips Based on Observed Data

With first footnote changed to the following:

Responder is defined as a subject demonstrating at least 1-point improvement, i.e., decrease in severity, from baseline POL severity, where POL severity: 0=None, 1=Mild, 2=Moderate, 3=Severe.
Source: Listing 16.2.6.2.2, 16.2.6.2.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.2.3.6 – Other Efficacy: Subject Satisfaction with Lips VAS by Visit Based on Observed Data

		Modified Intent-to-Treat		Per-Protocol	
Study Visit	Category	PN40082	Restylane Silk	PN40082	Restylane Silk
Visit 2/Month 1	N	0	0	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
	Median	0.0	0.0	0.0	0.0
	Min, Max	0, 0	0, 0	0, 0	0, 0
Visit 3/Month 2					
...					
Visit 5/Month 6	N	0	0	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
	Median	0.0	0.0	0.0	0.0
	Min, Max	0, 0	0, 0	0, 0	0, 0

Source: Listing 16.2.6.1.3
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh mm on data from Month, Day, Year.

Table 14.2.3.7 – Other Efficacy: Change from Baseline to Visit 4/Month 3 and Visit 5/Month 6 in Lip Fullness Grading Scale (LFGS) for Upper Lips and Lower Lips Based on Observed Data

			Upper Lips		Lower Lip	
Population	Visit	Category	PN40082	Restylane Silk	PN40082	Restylane Silk
Per-Protocol	Visit 4/Month 3	N	0	0	0	0
		Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
		Median	0.0	0.0	0.0	0.0
		Min, Max	0, 0	0, 0	0, 0	0, 0
	Visit 5/Month 6	N	0	0	0	0
		Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
		Median	0.0	0.0	0.0	0.0
		Min, Max	0, 0	0, 0	0, 0	0, 0
Modified Intent-to-Treat	Visit 4/Month 3	N	0	0	0	0
		Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
		Median	0.0	0.0	0.0	0.0
		Min, Max	0, 0	0, 0	0, 0	0, 0
	Visit 5/Month 6	N	0	0	0	0
		Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
		Median	0.0	0.0	0.0	0.0
		Min, Max	0, 0	0, 0	0, 0	0, 0

Source: Listing 16.2.6.2.4
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh mm on data from Month, Day, Year.

Table 14.3.1.1 – Exposure to Study Product and Investigator Ease of Use Assessment (Upper Lips) at Visit 1/Day 1 and Visit 2/Month 1 for As-Treated Population

		Visit 1/Day 1		Visit 2/Month 1	
	Statistics	PN40082	Restylane Silk	PN40082	Restylane Silk
Amount of Syringe Used (ml)	N	0	0	0	0
	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
	Median	0.0	0.0	0.0	0.0
	Min, Max	0, 0	0, 0	0, 0	0, 0
Injection Techniques Used	N (%) Serial Puncture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Antegrade Linear Threading	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Retrograde Linear Threading	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Depth of Injection	N (%) Submucosa	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Intramuscular	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Superficial Dermis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Mid Dermis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Deep Dermis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	N (%) Subcutaneous Fat	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Investigator Ease of Use Assessment	Mean ± SD	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
	Median	0.0	0.0	0.0	0.0
	Min, Max	0, 0	0, 0	0, 0	0, 0

Investigator Ease of Use Assessment based on the Numerical Rating Scale (NRS): 0 (Not Easy) to 10 (Most Easy).
Source: Listing 16.2.5.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh mm on data from Month, Day, Year.

Note:

Table 14.3.1.1 will be used as the shell for the following table:

Table 14.3.1.2 – Exposure to Study Product and Investigator Ease of Use Assessment (Lower Lips) at Visit 1/Day 1 and Visit 2/Month 1 for As-Treated Population

Table 14.3.1.3 – Exposure to Study Product and Investigator Ease of Use Assessment (Perioral Areas) at Visit 1/Day 1 and Visit 2/Month 1 for As-Treated Population

Table 14.3.2.1 – Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA System Organ Class and Preferred Term for As-Treated Population

	All TEAEs		Reported by Subject		Reported by Investigator	
System Organ Class Preferred Term	PN40082 (N=xx)	Restylane Silk (N=xx)	PN40082 (N=xx)	Restylane Silk (N=xx)	PN40082 (N=xx)	Restylane Silk (N=xx)
Subjects with at Least One Injection-Site or Visual TEAE	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

…

Counts reflect numbers of subjects reporting one or more TEAE related to vascular injections/visual event that map to the MedDRA (version x x) system organ class/preferred term. At each level of summarization (system organ class or preferred term), subjects reporting more than one event are counted only once.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.2 – Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Severity for As-Treated Population

System Organ Class Preferred Term	PN40082 (N=xx)			Restylane Silk (N=xx)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Subjects with at Least One Injection-Site or Visual TEAE	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

…

Counts reflect numbers of subjects reporting one or more TEAE related to vascular injections/visual event that map to the MedDRA (version x x) system organ class/preferred term. At each level of summarization (system organ class or preferred term), subjects reporting more than one event are counted only once (under the greatest reported severity).
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.3 – Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Causality for As-Treated Population

System Organ Class Preferred Term	PN40082 (N=xx)		Restylane Silk (N=xx)	
	Unlikely	Related*	Unlikely	Related*
Class 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)

…

*Related category includes Possibly and Probably Related.
Counts reflect numbers of subjects reporting one or more TEAE related to vascular injections/visual event that map to the MedDRA (version x x) system organ class/preferred term. At each level of summarization (system organ class or preferred term) subjects reporting more than one event are only counted once (under the most likely relationship to study medication).
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.4 – Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Number of Injections for As-Treated Population

	PN40082		Restylane Silk	
System Organ Class Preferred Term	1 Injection (N=xx)	2 Injections (N=xx)	1 Injection (N=xx)	2 Injections (N=xx)
Class 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)

…

TEAEs are grouped by number of injection(s) a subject received up to when the events started. 1 Injection = ON or AFTER the injection on Day 1 AND BEFORE the touch up. 2 Injections = ON or AFTER the touch up.
Note: The denominator for a grouping includes all the subjects who went through the indicated period regardless if they reported any TEAEs during the period.
Counts reflect numbers of subjects reporting one or more TEAE related to vascular injections/visual event that map to the MedDRA (version x x) system organ class/preferred term. At each level of summarization (system organ class or preferred term), subjects reporting more than one event are counted only once.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.5 – Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Fitzpatrick Skin Type (FST) for As-Treated Population

System Organ Class Preferred Term	Treatment Group	FST I (N=xx)	FST II (N=xx)	FST III (N=xx)	Pooled FST I-III (N=xx)	FST IV (N=xx)	FST V (N=xx)	FST VI (N=xx)	Pooled FST IV-VI (N=xx)
Subjects with at Least One Injection-Site or Visual TEAE	PN40082	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Restylane Silk	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Class 1	PN40082	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Restylane Silk	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Term 1	PN40082	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	Restylane Silk	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
…									
…									
…									

Counts reflect numbers of subjects reporting one or more TEAE related to vascular injections/visual event that map to the MedDRA (version x x) system organ class/preferred term. At each level of summarization (system organ class or preferred term), subjects reporting more than one event are counted only once.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.6 – Most Frequently Occurring Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA Preferred Term for As-Treated Population

System Organ Class Preferred Term	PN40082 (N=xx)	Restylane Silk (N=xx)
Class 1		
Term 1	0 (0%)	0 (0%)
Term 2	0 (0%)	0 (0%)
Class 2		
Term 1	0 (0%)	0 (0%)
…		

Most frequently occurring TEAEs related to vascular injections/visual event are those that were reported by 5% or more subjects of either treatment group.
Counts reflect numbers of subjects reporting one or more TEAE related to vascular injections/visual event that map to the MedDRA (version x x) system organ class/preferred term. At each level of summarization (preferred term) subjects reporting more than one event are only counted once.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.7 – Severity of Most Frequently Occurring Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events by MedDRA Preferred Term for As-Treated Population

	PN40082				Restylane Silk			
Adverse Event	Events % (n/N)[1]	Mild % (n/N)[2]	Moderate % (n/N)[2]	Severe % (n/N)[2]	Events % (n/N)[1]	Mild % (n/N)[2]	Moderate % (n/N)[2]	Severe % (n/N)[2]
Preferred Term 1	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)
Preferred Term 2	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)

Most frequently occurring TEAEs related to vascular injections/visual event are those that were reported by 5% or more subjects of either treatment group.
[1] Denominator is the number of TEAEs related to vascular injections/visual event reported by all subjects who received the corresponding treatment.
[2] Denominator for percentages by severity is the number of subjects with respective TEAEs after receiving the corresponding treatment. Numerator (count of subjects) is based on the rule that subjects reporting more than one same incidence associated with a treatment arm are counted only once for the treatment arm under the greatest reported severity.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.8 – Duration of Most Frequently Occurring Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injection/Visual Events by MedDRA Preferred Term for As-Treated Population

	PN40082				Restylane Silk			
Adverse Event	Events % (n/N)[1]	<7 Days % (n/N)[2]	7-30 Days % (n/N)[2]	>30 Days % (n/N)[2]	Events % (n/N)[1]	<7 Days % (n/N)[2]	7-30 Days % (n/N)[2]	>30 Days % (n/N)[2]
Preferred Term 1	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)
Preferred Term 2	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)	0% (0/0)

Most frequently occurring TEAEs related to vascular injections/visual event are those that were reported by 5% or more subjects of either treatment group.
[1] Denominator is the number of TEAEs related to vascular injections/visual event reported by all subjects who received the corresponding treatment.
[2] Denominator for percentages by duration is the number of subjects with respective TEAEs after receiving the corresponding treatment. Numerator (count of subjects) is based on the rule that subjects reporting more than one same incidence associated with a treatment arm are counted only once for the treatment arm under the longest duration.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month Day, Year.

Table 14.3.2.9 – Overall Summary of Treatment-Emergent Adverse Events (TEAEs) Related to Vascular Injections/Visual Events for As-Treated Population

	PN40082		Restylane Silk	
	Subjects[1] (N=xx)	Events[2] (N=xx)	Subjects[1] (N=xx)	Events[2] (N=xx)
Overall	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Duration				
Less than 1 week	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Between 1 week and 1 month (30 days)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
More than 1 month (30 days)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severity				
Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Causality				
Treatment-related*	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not treatment-related	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Outcome				
Resolved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Improved	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Stabilized	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Worsened	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Unchanged	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Treatment Required (Action Taken)				
None	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Study treatment interrupted/discontinued	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Non-drug therapy	0 (0%)	0 (0%)	0 (0%)	0 (0%)
New OTC or Rx drug added	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hospitalized (includes ER visits)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

[1] Denominator is the number of subjects who received the corresponding treatment.
[2] Denominator is the number of adverse events reported by subjects who received the corresponding treatment.
*Treatment-related includes Possibly and Probably Related.
For Severity and Causality, subjects reporting more than one TEAE related to vascular injections/visual event associated with a treatment arm are counted only once for the treatment arm under the greatest reported severity and most likely causality, respectively.

For Duration, Outcome and Treatment Required (Action Taken), at each level of the categories, subjects reporting more than one TEAE related to vascular injections/visual event associated with a treatment arm are counted only once for the treatment arm at that category level.
Source: Listing 16.2.7.1.1
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh mm on data from Month Day, Year.

Note:

Tables 14.3.2.1, 14.3.2.2, 14.3.2.3, 14.3.2.4 will be used as the shell for the following tables:

Table 14.3.3.1 – Treatment-Emergent Adverse Events (TEAEs) Excluding Vascular Injections/Visual Events by MedDRA System Organ Class and Preferred Term for As-Treated Population

Table 14.3.3.2 – Treatment-Emergent Adverse Events (TEAEs) Excluding Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Severity for As-Treated Population

Table 14.3.3.3 – Treatment-Emergent Adverse Events (TEAEs) Excluding Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Causality for As-Treated Population

Table 14.3.3.4 – Treatment-Emergent Adverse Events (TEAEs) Excluding Vascular Injections/Visual Events by MedDRA System Organ Class, Preferred Term, and Number of Injection for As-Treated Population

With footnote regarding data source change to "Source: Listing 16.2.7.1.2".

Table 14.3.4.1 – Lip Function by Visit for As-Treated Population

Study Visit	Category	PN40082	Restylane Silk
Visit 1/Day 1 (Prior to injection)	N	0	0
	n (%) subjects able to sip liquid through a straw	0 (0%)	0 (0%)
Visit 2/Month 1 (Prior to touch-up)	N	0	0
	n (%) subjects able to sip liquid through a straw	0 (0%)	0 (0%)
Visit 3/Month 2	N	0	0
	n (%) subjects able to sip liquid through a straw	0 (0%)	0 (0%)
Visit 4/Month 3	N	0	0
	n (%) subjects able to sip liquid through a straw	0 (0%)	0 (0%)
Visit 5/Month 6	N	0	0
	n (%) subjects able to sip liquid through a straw	0 (0%)	0 (0%)

Source: Listing 16.2.4.8
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Note:

Table 14.3.4.1 will be used as the shell for the following table:

Table 14.3.4.2 – Lip Sensation Test (Cotton Wisp) by Visit for As-Treated Population

Table 14.3.4.3 – Lip Sensation Test (0.4G Monofilament) by Visit for As-Treated Population

Table 14.3.4.4 – Lip Texture Evaluation by Visit for As-Treated Population

Study Visit	Category	PN40082	Restylane Silk
Visit 1/Day 1 (Prior to injection)	N	0	0
	n (%) Normal	0 (0%)	0 (0%)
	n (%) Abnormal	0 (0%)	0 (0%)
	- n (%) Abnormal: Mild	0 (0%)	0 (0%)
	- n (%) Abnormal: Moderate	0 (0%)	0 (0%)
	- n (%) Abnormal: Severe	0 (0%)	0 (0%)
Visit 2/Month 1 (Prior to touch-up)	...		
	...		
Visit 3/Month 2			
Visit 4/Month 3			
Visit 5/Month 6			

Source: Listing 16.2.4.9
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Note:

Table 14.3.4.4 will be used as the shell for the following table:

Table 14.3.4.5 – Lip Firmness Evaluation by Visit for As-Treated Population

Table 14.3.4.6 – Lip Symmetry Evaluation by Visit for As-Treated Population

Table 14.3.4.7 – Lip Movement/Function Evaluation by Visit for As-Treated Population

Study Visit	Category	PN40082	Restylane Silk
Visit 1/Day 1 (Prior to injection)	N	0	0
	n (%) Normal – Subject's ability to pucker lips	0 (0%)	0 (0%)
	n (%) Normal – Subject's ability to blow with lips	0 (0%)	0 (0%)
	n (%) Normal – Subject's ability to pronounce words that begin with "W"	0 (0%)	0 (0%)
Visit 2/Month 1 (Prior to touch-up)	...		
	...		
Visit 3/Month 2			
Visit 4/Month 3			
Visit 5/Month 6			

Source: Listing 16.2.4.8
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Table 14.3.5 – Other Analysis: Assessment of Blinding to Subjects and Evaluators at End of Study

Assessed by Subject or Evaluator	Treatment Subject Received	Treatment Guessed	n/N[1] (%)	P-value and 90% Confidence Interval[2]
By Subject	PN40082	PN40082	0/0 (0%)	
		Restylane Silk	0/0 (0%)	
		Unsure	0/0 (0%)	
	Restylane Silk	PN40082	0/0 (0%)	
		Restylane Silk	0/0 (0%)	
		Unsure	0/0 (0%)	
	Overall Correct Guesses		0/0 (0%)	(0.0%, 0.0%)
By Evaluator	PN40082	PN40082	0/0 (0%)	
		Restylane Silk	0/0 (0%)	
		Unsure	0/0 (0%)	
	Restylane Silk	PN40082	0/0 (0%)	
		Restylane Silk	0/0 (0%)	
		Unsure	0/0 (0%)	
	Overall Correct Guesses		0/0 (0%)	(0.0%, 0.0%)

[1] N = Total number of responses, n = number of responses associated with a given combination (e.g. number of subjects who received PN40082 and guessed Restylane Silk).
[2] P-values and 95% confidence intervals from the exact binomial distribution to test the null hypothesis that the proportion of correct guesses is 50%.
Source: Listing 16.2.1.2
O:\Studies\Prollenium\SYM 2018-02\Biometrics\Programs\Tables\xxx.sas ran on Month Day, Year at hh:mm on data from Month, Day, Year.

Subject Listings

Listing 16.2.1.1 – Subject Analysis Status

	As-Treated (AT)		Modified Intent-to-Treat (mITT)		Per-Protocol (PP)	
Site-Subject	Included?	Reason for Not Included	Included?	Reason for Not Included	Included?	Reason for Not Included
Treatment:						

O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.1.2 – Subject Disposition and Assessment of Blinding at End of Study

Site-Subject	Analy	Subject Disposition	Date Completed or Discontinued	Reason, if discontinued	Evaluation of Subject for Participation in PRO 2018-03 study: Subject underwent consent?	Subject agreed to participate?	Evaluator	Subject was asked to identify treatment he received? If Yes, response	Blinded evaluating investigator was asked to identify treatment subject received? If Yes, response
Treatment:									

Analy (Analyses): A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.1.3 – Dates of Visits

Site-Subject	Analyses	Visit 1/ Day 1 (Baseline)	Visit 2/ Month 1 Day 28 (±2 days) [Day #]	Visit 3/ Month 2 Day 56 (±4 days) [Day #]	Visit 4/ Month 3 Day 84 (±4 days) [Day #]	Visit 5/ Month 6 Day 168 (±7 days) [Day #]	No. of UVs: Unscheduled Visit(s) [Day #]
Treatment:							

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Day # (Study Days) = Visit Date - Baseline (Visit 1) Date +1.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.2.1 – Violation of Inclusion Criteria

Site-Subject	Analyses	1	2	3	4
Treatment:					

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
*Please see section 7.3.1 of study protocol for description of the inclusion criteria.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.2.2 – Violation of Exclusion Criteria

Site-Subject	Analy.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Treatment:																										

Analy. (Analyses): A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
*Please see section 7.3.2 of study protocol for description of the exclusion criteria.
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Listing 16.2.2.3 – Significant Protocol Violations

Site-Subject	Analyses	Significant Protocol Violation
Treatment:		

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Significant protocol violations are those events that exclude subjects from any analysis population.
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Listing 16.2.2.4 – Comments

Site-Subject	Analyses	Date of Comments	CRF Page Number	Comment(s)	Initials
Treatment:					

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
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Listing 16.2.4.1 – Demographics

Site-Subject	Subject Initials	Analyses	Age (yrs)	Sex	Race	Ethnicity	Fitzpatrick Skin Type	Informed Consent	
								Signed?	Date
Treatment:									

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
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Listing 16.2.4.2 – Brief Physical Examination at Baseline

				Physical Examination		
Site-Subject	Analyses	Height (inches)	Weight (lbs)	Heart	Lungs	Abdomen
Treatment:						

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
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Listing 16.2.4.3 – Medical History Findings

Site-Subject	Analyses	Medical System	Diagnosis/Procedure	Onset Date	Stop Date	Concomitant Medication?
Treatment:						
		xxxxxxx	xxxxxxxxxxx	-----1997	Ongoing	No

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
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Listing 16.2.4.4 – Prior and Concomitant Medications/Treatments

Site-Subject	Analy	If Used on Face	WHO Class // WHO Name //Medication	Indication	Start Date [Day #]	Stop Date [Day #]	Dosage	Freq.	Route
Treatment:									
		QD1	XXXXXXXXX // XXXXXXXXXX XXX // XXXXXXXX	XXXXXXX	01JAN05 [3]	Ongoing	xxxxx	xxxx	xxx

Analy (Analyses): A = As-Treated (AT) Analyses only, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Note: Medications coded using the WHO Drug Dictionary, version xxx.
Day # is calculated from baseline (Visit 1) date. Day 1 is the baseline date while Day -1 is the day prior to the baseline visit. L=Left side of the face, R=Right side of the face.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh:mm on data from Month Day, Year.

Listing 16.2.4.5 – Non-Pharmacological Interventions (NPIs)

Site-Subject	Analy	If Used on Face	Non-Pharmacological Intervention	Indication	Start Date [Day #]	Stop Date [Day #]	Dosage	Freq.	Route
Treatment:									
		QD1,QD2	XXXXXXXXX XXX XXXXXXXX	XXXXXXX	01JAN05 [3]	Ongoing	xxxxx	xxxx	xxx

Analy (Analyses): A = As-Treated (AT) Analyses only, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Day # is calculated from baseline (Visit 1) date. Day 1 is the baseline date while Day -1 is the day prior to the baseline visit. L=Left side of the face, R=Right side of the face.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh:mm on data from Month Day, Year.

Listing 16.2.4.6 – Vital Signs and Urine Pregnancy Test at Baseline

Site-Subject	Analyses	Sitting Systolic BP (mmHg)	Sitting Diastolic BP (mmHg)	Heart Rate (bpm)	Oral Temperature (°F)	Respiratory Rate (breath/min)	Urine Pregnancy Test	
							Test Results	Test Date
Treatment:								

Analyses: A = As-Treated (AT) Analyses only, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh:mm on data from Month Day, Year.

Listing 16.2.4.7 – Vision Evaluation

Site-Subject	Analyses	Study Visit (Time Point)	Confrontational Visnal Field Results (Specify if abnormal)	Ocular Visual Field Results (Specify if abnormal)	Subject wearing corrective lenses?	Snellen Visual Acuity Score		Initials of Assessor	Vision at Post-Baseline Visit	
						Left Eye	Right Eye		Changed significantly from baseline?	If yes, the study ophthalmologist contacted?
Treatment:										

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.4.8 – Lip Function, Lip Sensation and Lip Movement/Function Tests

Site-Subject	Analyses	Study Visit (Time Point)	Able to sip liquid through a straw?	Assessor of Lip Function	Able to feel sensation of a cotton wisp?	Able to feel sensation of a 0.4G monofilament	Assessor of Lip Sensation	Ability to pucker lips	Ability to blow with lips	Ability to pronounce words that begin with "W"	Assessor of Lip Movement /Function
Treatment:											

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
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Listing 16.2.4.9 – Lip Texture, Lip Firmness and Lip Symmetry Evaluations

			Lip Texture		Lip Firmness		Lip Symmetry	
Site-Subject	Analyses	Study Visit (Time Point)	Normal or Abnormal (severity)	Evaluator	Normal or Abnormal (severity)	Evaluator	Normal or Abnormal (severity)	Evaluator
Treatment:								

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.5.1 – Treatment Administration at Visit 1/Day 1 and Visit 2/Month 1

Site-Subject	Analy	Random Number	Visit Number	Injection placed successfully?	Site of Injection	Time of Injection	Amount of Syringe Used (ml)	Injection Techniques Used	Depth of Injection	Initials Who Performed Injection	Investigator Ease of Use Assessment	Evaluator
Treatment:												

Analy (Analyses): A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Investigator Ease of Use Assessment assess on the Numerical Rating Scale (NRS): 0 (Not Easy) to 10 (Most Easy).
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.1.1 – Efficacy Evaluations of Lip Fullness Grading Scale (LFGS)

Site-Subject	Analyses	Study Visit	By Treating Investigator or Blinded Evaluating Investigator	Overall Rating	Upper Lip Rating	Lower Lip Rating	Initials of Who Performed Assessment
Treatment:							

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.1.2 – Efficacy Evaluations of Perioral Lines at Rest Severity Scale (POL)

Site-Subject	Analyses	Study Visit	By Treating Investigator or Blinded Evaluating Investigator	Overall Rating	Upper Lip Rating	Lower Lip Rating	Assessment Performed By
Treatment:							

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.1.3 – Efficacy Evaluations of Subject Satisfaction with Lips, Swelling and Global Aesthetic Improvement

Site-Subject	Analyses	Study Visit	Subject Satisfaction with Lips VAS	Swelling Assessment		Patient Global Aesthetic Improvement (pGAI)	Investigator Global Aesthetic Improvement (iGAI)	
				Grade	Performed By		Score	Performed By
Treatment:								

Analyses: A = As-Treated (AT) Analyses, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.2.1 – Derived Overall Lip Fullness Grading Scale (LFGS) for Modified Intent-to-Treat Population

Site-Subject	Fitzpatrick skin type	Lips Treated	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Treatment:							
xx-xxx	II	Both	1	2	3	2	2, 3, 2, 2, 3

LFGS: 0=Very Thin Lips, 1=Thin Lips, 2=Moderately Thick Lips, 3=Thick Lips, 4=Full Lips.
Note: The 5 entries contained under a visit for a subject are the 5 imputed LFGS scores for the missing value through multiple imputations.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.2.2 – Derived Primary and Secondary Efficacy Responses on Overall LFGS and Overall POL for Modified Intent-to-Treat Population

		Lip Fullness Grading Scale (LFGS)			Perioral Lines at Rest Severity Scale (POL)		
Site-Subject	Study Visit	Overall LFGS Rating	Change from Baseline	Treatment Success*	Overall POL Rating	Change from Baseline	Responder**
Treatment:							
xx-xxx	4	2	-1	Y			
	5	2, 3, 2, 2, 3	-1, -2, -1, -1, -2	Y, Y, Y, Y, Y			

Change from Baseline for Visit x = Baseline – Visit x, where x=2, 3, 4, 5.
*Treatment success is defined as an achievement of at least a 1-grade increase from baseline on the overall LFGS.
**Responder is defined as a subject demonstrating at least 1-point improvement, i.e., decrease in severity, from baseline POL severity.
Note: The 5 entries contained under a visit for a subject are associated the 5 imputed LFGS scores for the missing value through multiple imputations.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.2.3 – Derived Primary and Secondary Efficacy Responses on Overall LFGS and Overall POL for Per-Protocol Population

		Lip Fullness Grading Scale (LFGS)			Perioral Lines at Rest Severity Scale (POL)		
Site-Subject	Study Visit	Overall LFGS Rating	Change from Baseline	Treatment Success*	Overall POL Rating	Change from Baseline	Responder**
Treatment:							

Change from Baseline for Visit x = Baseline – Visit x, where x=2, 3, 4, 5.
*Treatment success is defined as an achievement of at least a 1-grade increase from baseline on the overall LFGS.
**Responder is defined as a subject demonstrating at least 1-point improvement, i.e., decrease in severity, from baseline POL severity.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.6.2.4 – Derived Other Efficacy Responses Based on Observed Data: LFGS and POL for Upper/Lower Lip

Site-Subject	Analyses	Study Visit	Upper or Lower Lip	Lip Fullness Grading Scale (LFGS)			Perioral Lines at Rest Severity Scale (POL)		
				LFGS Rating	Change from Baseline	Treatment Success*	POL Rating	Change from Baseline	Responder**
Treatment:									

Change from Baseline for Visit x = Baseline – Visit x, where x=2, 3, 4, 5.
*Treatment success is defined as an achievement of at least a 1-grade increase from baseline on the overall LFGS.
**Responder is defined as a subject demonstrating at least 1-point improvement, i.e., decrease in severity, from baseline POL severity.
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.7.1.1 – Adverse Events (Related to Vascular Injections/Visual Events)

Site-Subject	Analy	FST	Reported by	System Organ Class// Preferred Term// Verbatim Term	Start Date Time [Day #]	Stop Date Time [Day #]	Severity Causality Outcome	Where on face Rel. to injection? Vision related?	Action Taken[1]	SAE
Treatment:										
xx-xxx	A	III	Subj/Diary	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS//	01JAN2019	04JAN2019	MILD	QD1, QD3	3,4	N
				INJECTION SITE SWELLING//	13:25	08:30	PROBABLY	Y		
				SWELLING ON FACE	2	5	STABLIZED	N		

Analy (Analyses): A = As-Treated (AT) Analyses only, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Day # is calculated from baseline (Visit 1) date. Day 1 is the baseline date while Day -1 is the day prior to the baseline visit.
[1] Action Taken: 1=None, 2=Study treatment interrupted/discontinued, 3=Non-drug therapy, 4=New OTC or Rx drug added, 4=Hospitalized
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Listing 16.2.7.1.2 – Adverse Events (Excluding Vascular Injections/Visual Events)

Site-Subject	Analy	FST	Reported by	System Organ Class// Preferred Term// Verbatim Term	Start Date [Day #]	Stop Date [Day #]	Severity Causality Outcome	Where on face	Action Taken[1]	SAE
xx-xxx	M	III	Subj/Diary	NERVOUS SYSTEM DISORDERS// HEADACHE // HEADACHE	01JAN2019 2	04JAN2019 5	MILD UNLIKELY STABLIZED	QD1,QD3	1	N

Analy (Analyses): A = As-Treated (AT) Analyses only, M = Modified Intent-to-Treat (MITT) Analyses, P = Per-Protocol Analyses
Day # is calculated from baseline (Visit 1) date. Day 1 is the baseline date while Day -1 is the day prior to the baseline visit.
[1] Action Taken: 1=None, 2=Study treatment interrupted/discontinued, 3=Non-drug therapy, 4=New OTC or Rx drug added, 4=Hospitalized
O:\Studies\ Prollenium\SYM 2018-02\Biometrics\Programs\Listing\xxx.sas ran on Month Day Year at hh mm on data from Month Day, Year.

Note:

Repeat Listings 16.2.7.1.1 and 16.2.7.1.2 for AEs that led to study treatment interrupted/Discontinued and Serious AEs –

Listing 16.2.7.2.1 – Adverse Events (Related to Vascular Injections/Visual Events) Leading to Study Treatment Interrupted/Discontinued

Listing 16.2.7.2.2 – Adverse Events (Excluding Vascular Injections/Visual Events) Leading to Study Treatment Interrupted/Discontinued

Listing 16.2.7.3.1 – Serious Adverse Events (Related to Vascular Injections/Visual Events)

Listing 16.2.7.3.2 – Serious Adverse Events (Excluding Vascular Injections/Visual Events)

Listing 16.2.7.4 – Adverse Events (Related to Vascular Injections/Visual Events) Lasted more than 30 Days