A Single-Arm Study to Evaluate and Demonstrate Safety and Performance of a Novel Ocular Lubricant in Adult Subjects with Dry Eye Disease

STUDY ID

DEP918-C001

STATISTICAL ANALYSIS PLAN v.4

21 Feb 2025

NCT06444516

Alcon

Statistical Analysis Plan for DEP918-C001
Title: A Single-Arm Study to Evaluate and Demonstrate Safety and Performance of a Novel Ocular Lubricant in Adult Subjects with Dry Eye Disease

[redacted]

This version of the Statistical Analysis Plan is based on Version 4.0 of the study protocol.

Executive Summary:

Key Objectives:

The primary objective of this study is to demonstrate efficacy of a novel lubricant eye drop.

Decision Criteria for Study Success:

Success of this study will be based on the demonstration of a reduction in the Impact of Dry Eye on Everyday Life - Symptom Bother (IDEEL-SB) questionnaire score at Day 30 from baseline).

Table of Contents

List of Tables

List of Figures

1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

The primary objective of this study is to demonstrate efficacy of a novel lubricant eye drop.

The safety objective of this study is to evaluate safety of a novel lubricant eye drop.

1.2 Study Description

Key components of the study are summarized in Table 1-1.

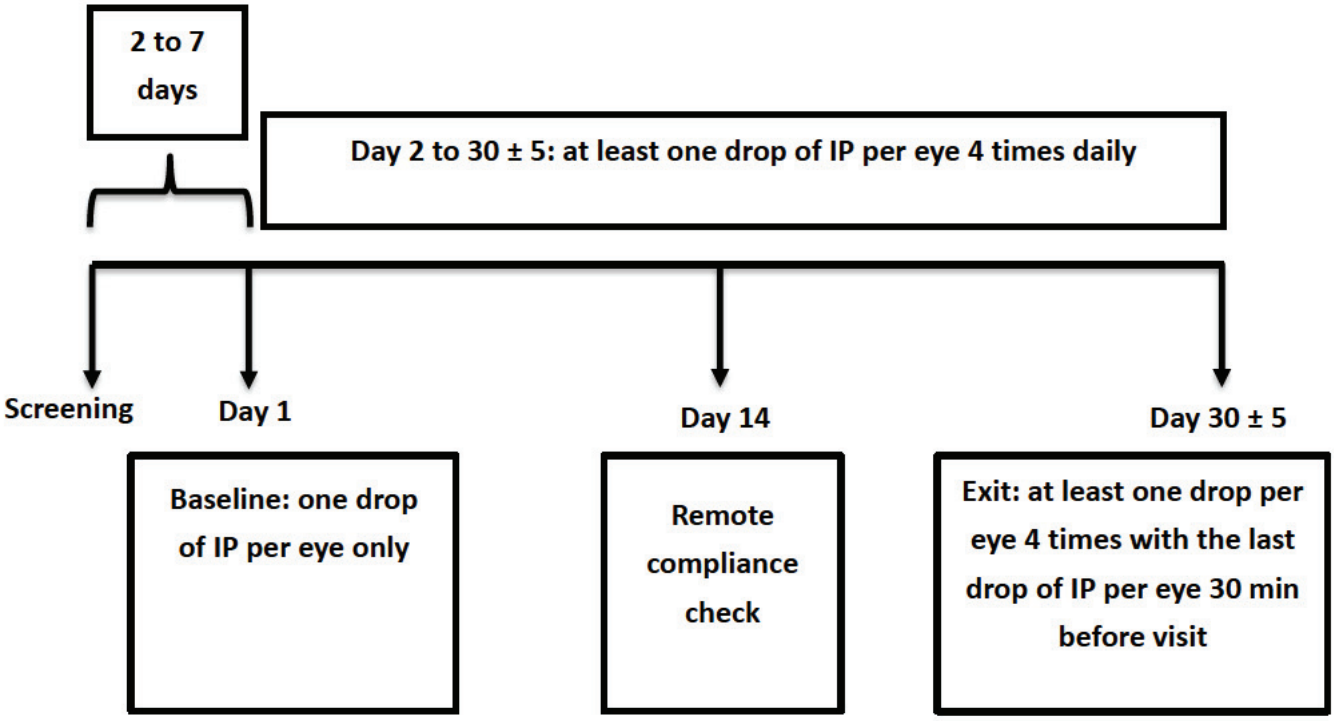
Table 1–1 Study Description Summary

Study Design	Phase 3, multicenter, single-arm, open label, nonrandomized
Study Population	Mild to moderate dry eye disease (DED) subjects ≥18 years of age with an IDEEL-SB score ≥16 and ≤65, best corrected visual acuity (BCVA) equal to or better than 20/80 in each eye, noninvasive tear break-up time (NITBUT) >5 and <10 seconds in each eye [redacted] will be included in this study. Target to complete: 143 Planned to enroll: ~185
Number of Sites	~ 20 United States
Investigational Product	FID123300
Planned Duration of Exposure	~ 30 days At Visit 2/Day 1, subjects will receive one drop of investigational product (IP) per eye in the morning. On Days 2 to 30 ± 5 (including day of) subjects will self-administer at least one drop per eye 4 times daily. On Visit 4/Day 30 ± 5, subjects will self-administer the last drop per eye 30 minutes prior to visit.
Visits	Visit 1 – Screening Visit 2 – Baseline/Day 1 (occurs 2-7 days after Visit 1) Visit 3 – Remote Compliance Check (Day 14 ± 3 days)

	Visit 4 – Day 30/Exit (Day 30 ± 5 days)

A study design schematic is depicted in Figure 1–1.

Figure 1–1 Study Design



1.3 Randomization

Randomization is not applicable for this single-arm study.

1.4 Masking

All members associated with the study (at the site and the study sponsor) are unmasked to the assigned IP.

[redacted]

2 ANALYSIS SETS

2.1 Safety Analysis Set

Safety analyses will be conducted using the Safety Analysis Set on a treatment-emergent basis. As such, the Safety Analysis Set will include all subjects/eyes exposed to at least one dose of study IP evaluated in this study.

Adverse events occurring from the time of informed consent but prior to first exposure to study IP will be summarized in subject listings.

2.2 Per Protocol Analysis Set

The Per Protocol (PP) Analysis Set is a subset of Safety Analysis Set and excludes all data/subjects that have met any of the critical deviation or evaluability criteria identified in the Data Evaluability Plan (DEP).

3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

The following tables will be presented:

- Subject Disposition
- Analysis Sets
- Subject Accounting
- Demographics
- Baseline Characteristics (dry eye subgroup; subjects with multi-symptoms)

[redacted]

[redacted]

Subject accounting, demographics and baseline characteristics will be summarized on the safety and PP analysis sets. In addition, the following subject listings will be provided:

- Listing of Analysis Sets Exclusions
- Listing of IP Assignment
- Listing of Subjects Discontinued from Study
- Listing of Subjects That Discontinued Treatment
- Listing of Ocular Concomitant Medications
- Listing of Nonocular Concomitant Medications
- Listing of Ocular Medical History
- Listing of Nonocular Medical History

4 EFFICACY ANALYSIS STRATEGY

This study defines 1 primary efficacy endpoint and [redacted] will use the Safety Analysis Set as the primary analysis set. [redacted]

Continuous variables will be summarized using the number of observations, mean, standard deviation (SD), median, minimum, and maximum, as well as confidence intervals (CIs) or confidence limits where applicable. Categorical variables will be summarized with frequencies and percentages from each category.

Unless otherwise specified, baseline will be defined as the last available measurement prior to IP exposure. Change from baseline will be calculated as postbaseline timepoint/visit value minus baseline value.

All data obtained in evaluable subjects/eyes will be included in the analysis. [redacted]

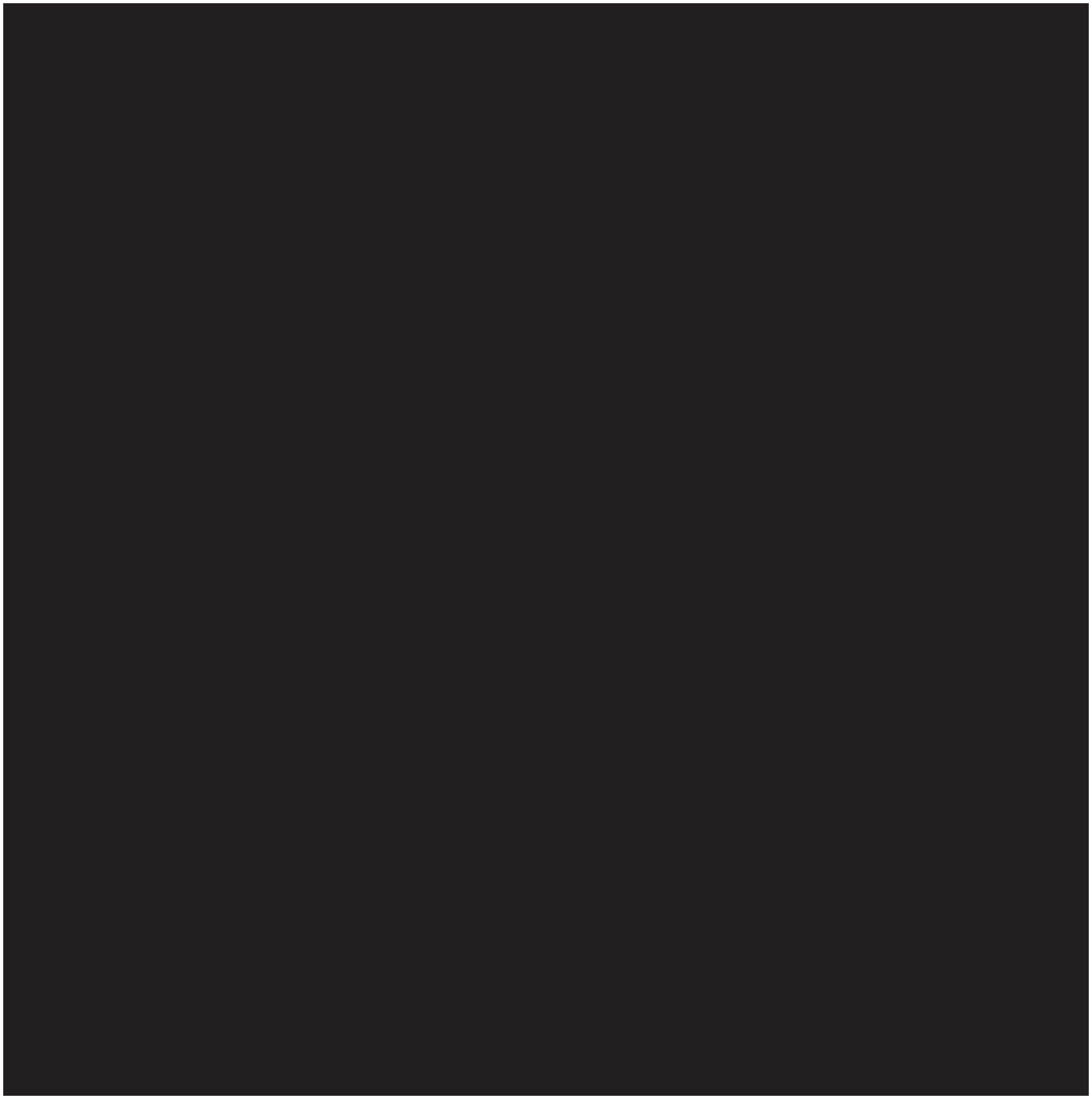
[redacted].

A listing of select efficacy data will also be provided.

4.1 Efficacy Endpoints

Primary Endpoint

The primary efficacy endpoint is change from baseline in IDEEL-SB questionnaire score at Day 30.



4.2 Efficacy Hypotheses

Primary Endpoint

The null and alternative hypotheses for the analysis of the primary efficacy endpoint are:

H_0: $\mu_{(T)} \geq 0$

H_a: $\mu_{(T)} < 0$

where $\mu_{(T)}$ denotes the mean change from baseline in total IDEEL-SB score at Day 30.

4.3 Statistical Methods for Efficacy Analyses

4.3.1 Primary Efficacy Analysis

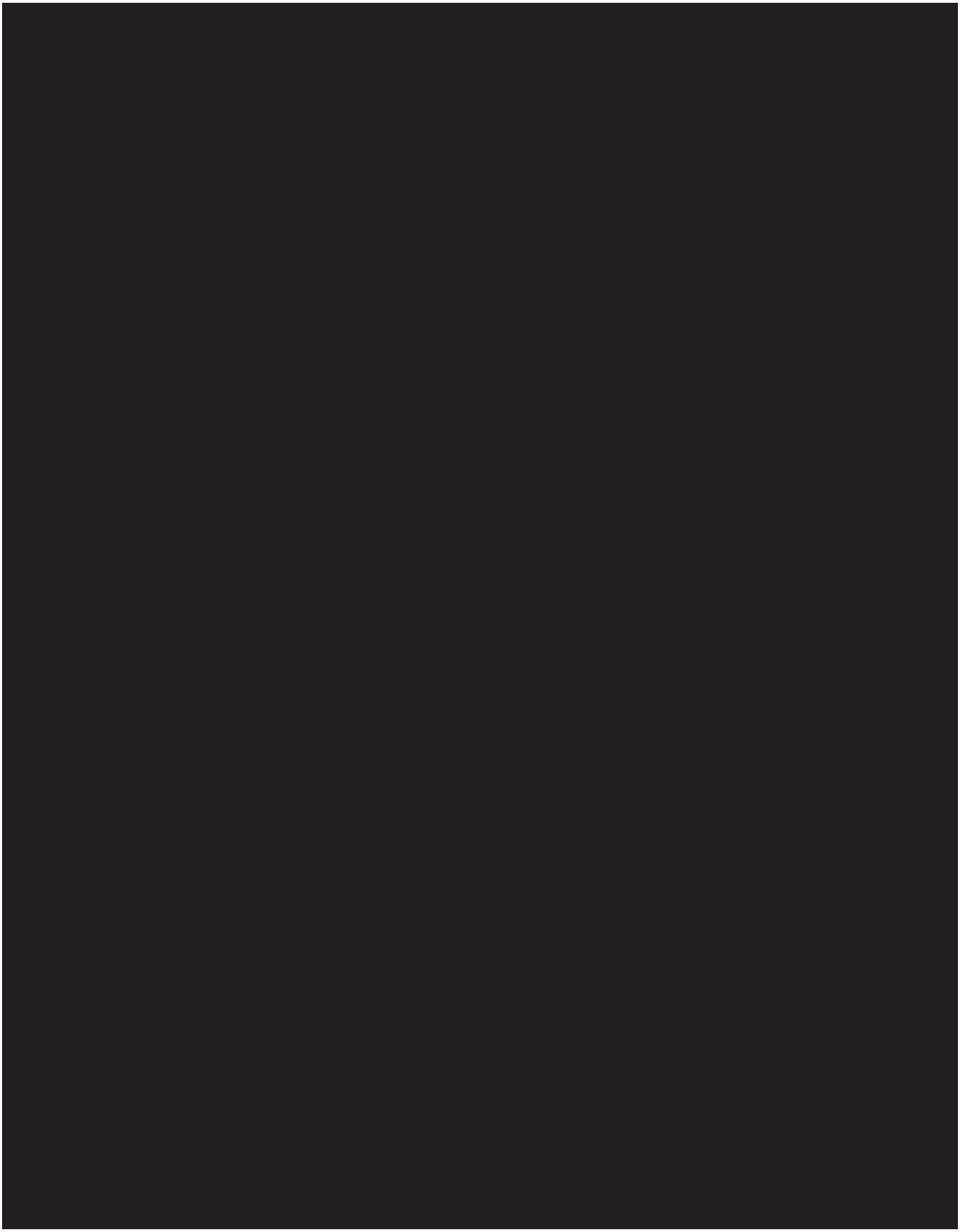
A paired (one-sample) t-test will be used on the change from baseline value at Day 30 to test the primary hypothesis. One-sided p-value will be calculated, and null hypothesis will be rejected if p-value < 0.05.

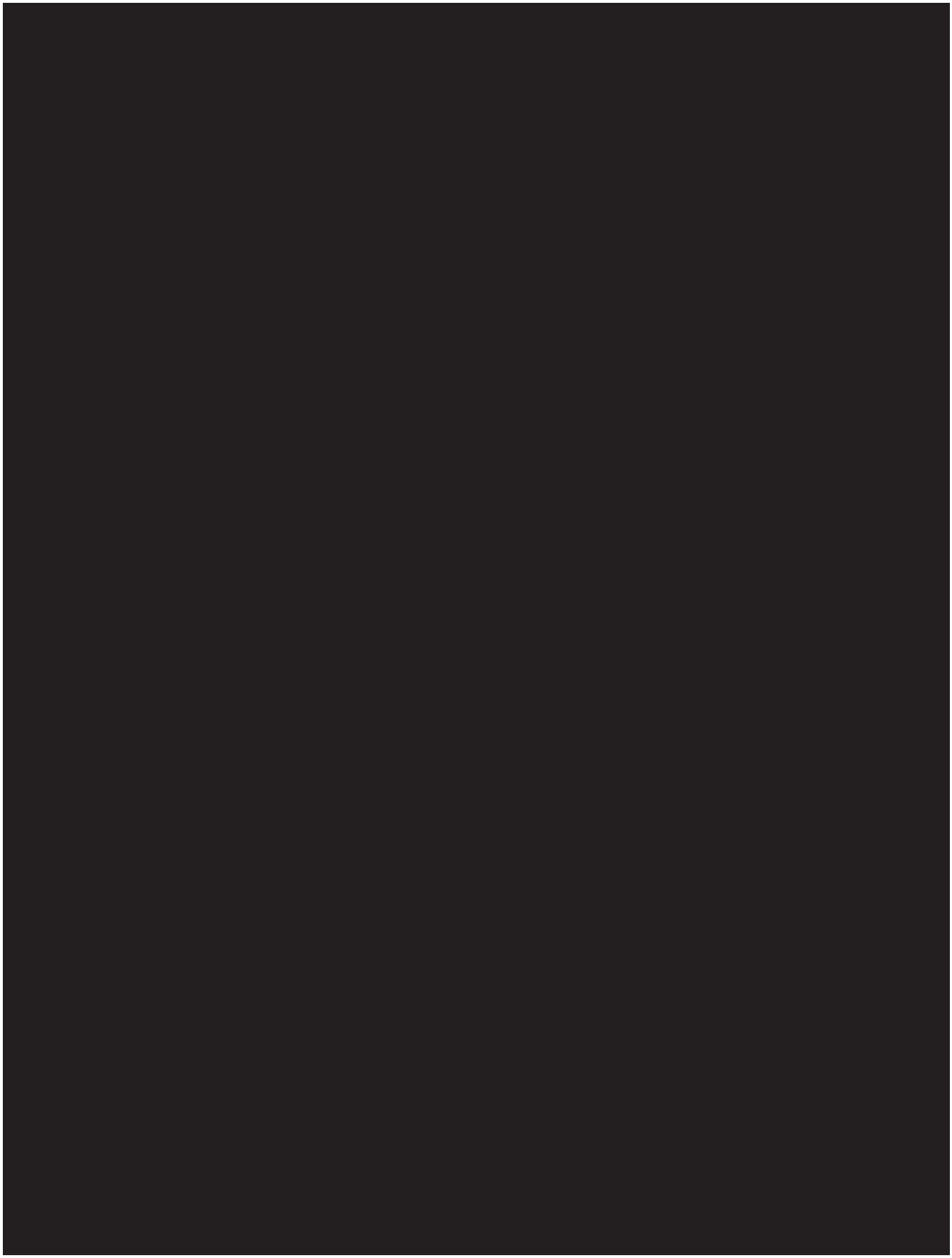
Table 4-2 Summary of Analytical Strategy for Primary Endpoint

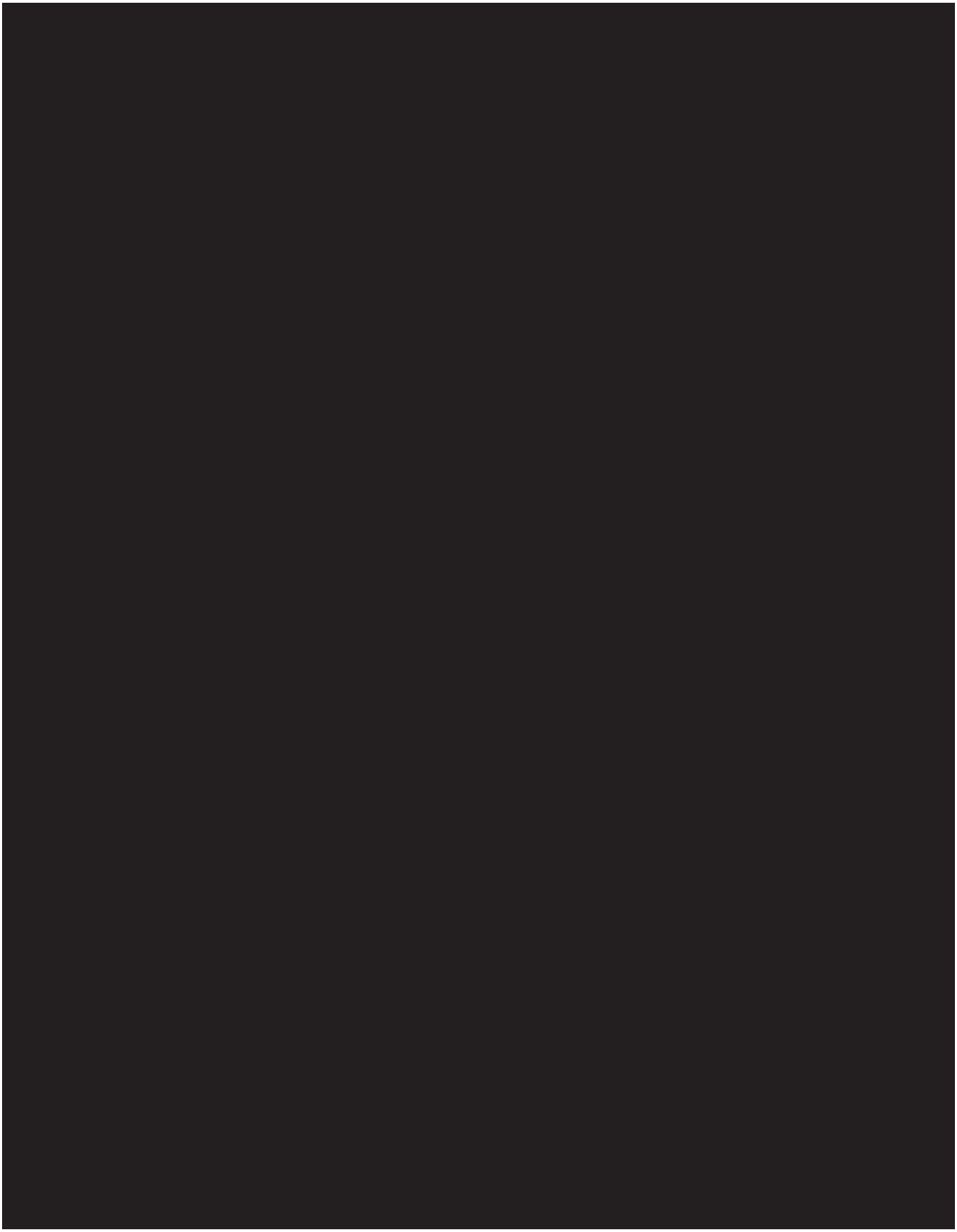
Endpoint	Estimand Designation (Primary/Supplementary/Sensitivity)	Analysis Set	Intercurrent Event	Intercurrent Event Strategy and Estimator (efficacy analysis)	Handling of Missing Data Unrelated to Intercurrent Events and Summary Measure
Change from baseline in IDEEL-SB questionnaire score at Day 30	Primary	Safety Analysis Set	Use of prohibited medication	Use data as collected	No imputation
			IP discontinuation	Use data as collected	No imputation

[redacted]

[redacted]







[redacted]

5 SAFETY ANALYSIS STRATEGY

The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of adverse events as well as the other listed parameters. Therefore, no inferential testing will be done for the safety analysis.

5.1 Safety Endpoints

The safety endpoints are

- Adverse events (AE)
- BCVA
- Biomicroscopy Findings
    - Bulbar Hyperemia
    - Limbal Hyperemia
    - Palpebral Conjunctiva - Upper Eyelids Hyperemia
    - Palpebral Conjunctiva - Upper Eyelids Papillae
    - Palpebral Conjunctiva - Lower Eyelids Hyperemia
    - Palpebral Conjunctiva - Lower Eyelids Papillae
    - Total Ocular Staining Score (TOSS)
        - Nasal Interpalpebral Conjunctiva
        - Cornea
        - Temporal Interpalpebral Conjunctiva
    - Corneal infiltrates
    - Anterior Segment Health
        - Aqueous Flare Grading
        - Aqueous Inflammatory Cell Grading

        - Lens
        - Status of lens
    - Other findings

- Device deficiencies

5.2 Safety Hypotheses

There are no formal safety hypotheses in this study. The focus of the safety analysis will be a comprehensive descriptive assessment of safety endpoints listed in Section 5.1.

5.3 Statistical Methods for Safety Analyses

The analysis set for all safety analyses is defined in Section 2.1. Baseline will be defined as the last measurement prior to exposure to study IP. For BCVA and biomicroscopy data, baseline will be defined as Visit 2. Safety variables will be summarized descriptively.

5.3.1 Adverse Events

The applicable definition of an AE is in the study protocol. All AEs occurring from when a subject signs informed consent to the time of their study exit will be accounted for in the reporting.

Presentation of AEs will be separated into pretreatment AEs and treatment-emergent AEs as defined below:

- Pretreatment: an event that occurs after signing informed consent but prior to day of first exposure to study IP

- Treatment-emergent: an event that occurs from the day of first exposure to study IP until subject exits from the study

The following tables and supportive listings will be provided:

- Overall Summary of Treatment-Emergent Adverse Events
- Incidence of All Ocular Treatment-Emergent Adverse Events
- Incidence of Ocular Serious Treatment-Emergent Adverse Events
- Incidence of All Nonocular Treatment-Emergent Adverse Events
- Incidence of Nonocular Serious Treatment-Emergent Adverse Events

- Summary of Ocular Treatment-Emergent Adverse Events by Maximum Severity and Outcome
- Listing of All Ocular Treatment-Emergent Adverse Events
- Listing of All Nonocular Treatment-Emergent Adverse Events
- Listing of All Ocular Pretreatment Adverse Events
- Listing of All Nonocular Pretreatment Adverse Events

5.3.2 BCVA

BCVA in logMAR will be summarized as continuous by visit and change from baseline will be summarized as categorical (increase or no change, less than 2 lines decrease, 2 or more lines decrease).

5.3.3 Biomicroscopy Findings/Slit Lamp Examination

Increased severity is defined as 1 grade increase in Lens and Status of lens and 2 grade increase in other biomicroscopy findings, including each of the individual regions used in TOSS.
The following tables and supportive listings will be provided:

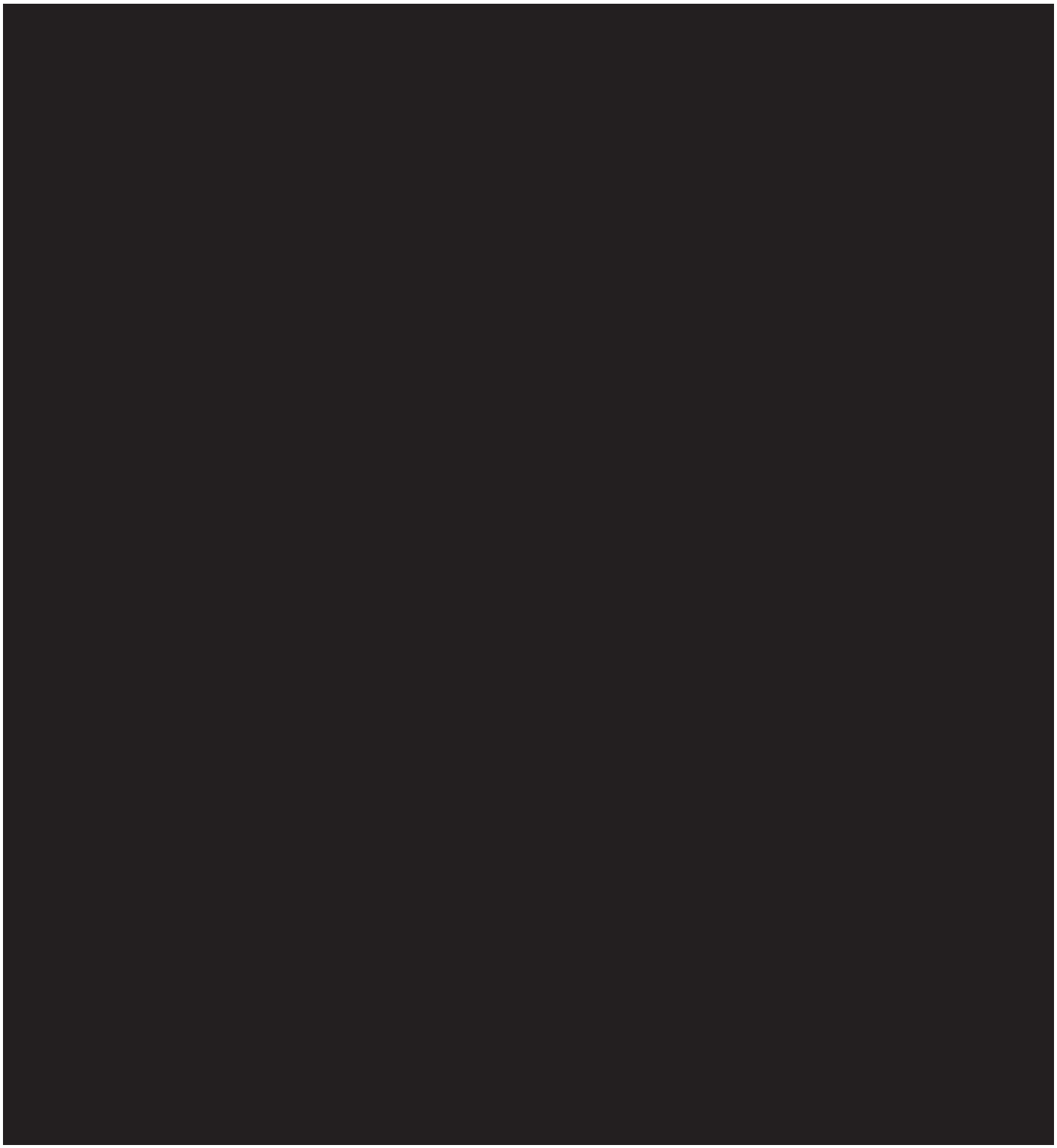
- Summary Statistics for Biomicroscopy Findings by Visit
- Incidence of Increased Severity in Biomicroscopy Findings
- Summary Statistics for Total Ocular Staining Score by Visit
- Listing of Eyes With Other Biomicroscopy Findings
- Listing of Eyes With Increased Severity in Biomicroscopy Findings
- Listings of Eyes with Infiltrates

5.3.4 Device Deficiencies

The following table and supportive listings will be provided:

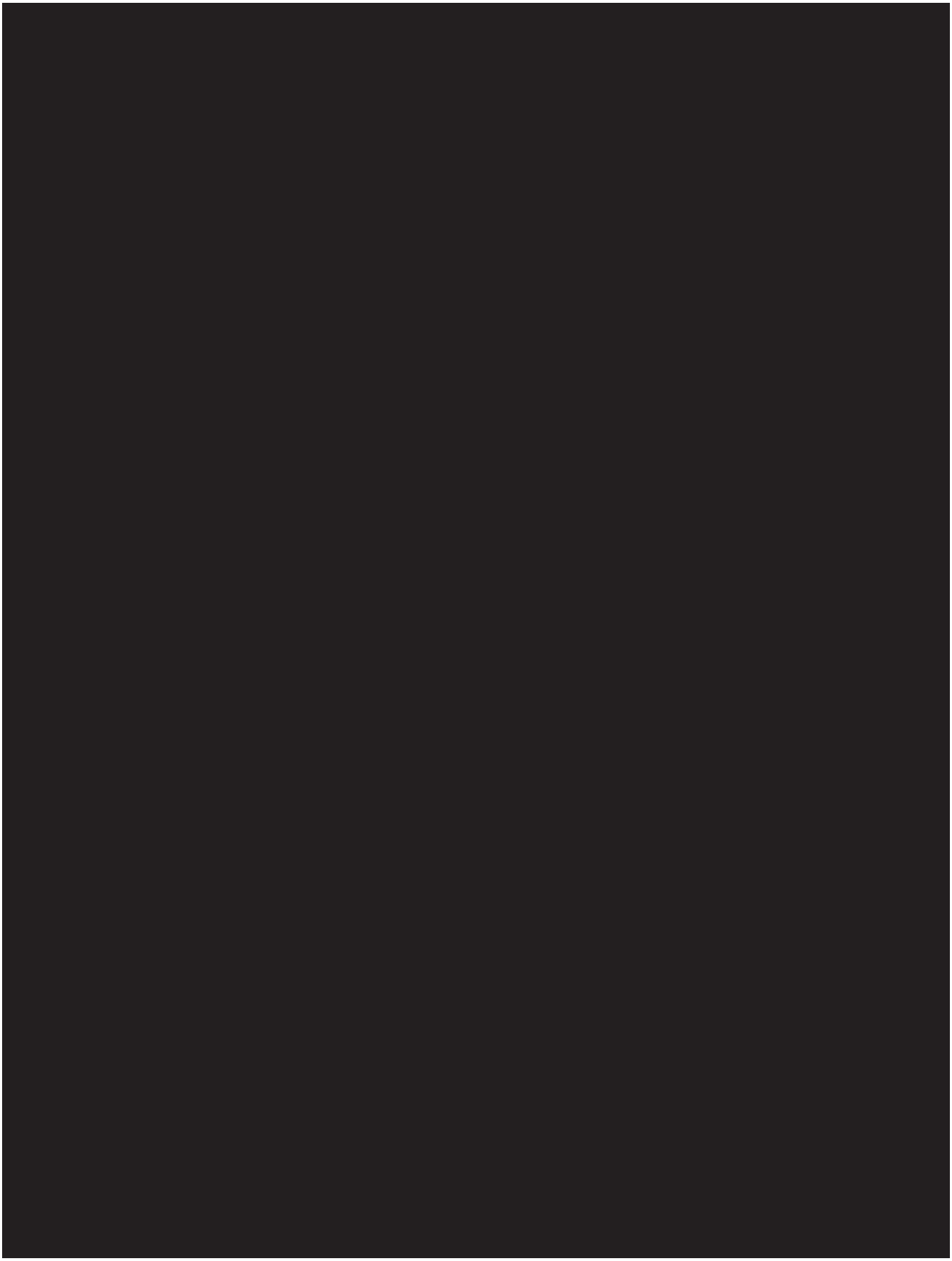
- Frequency of Treatment-Emergent Device Deficiencies
- Listing of Treatment-Emergent Device Deficiencies
- Listing of Device Deficiencies Prior To Treatment Exposure

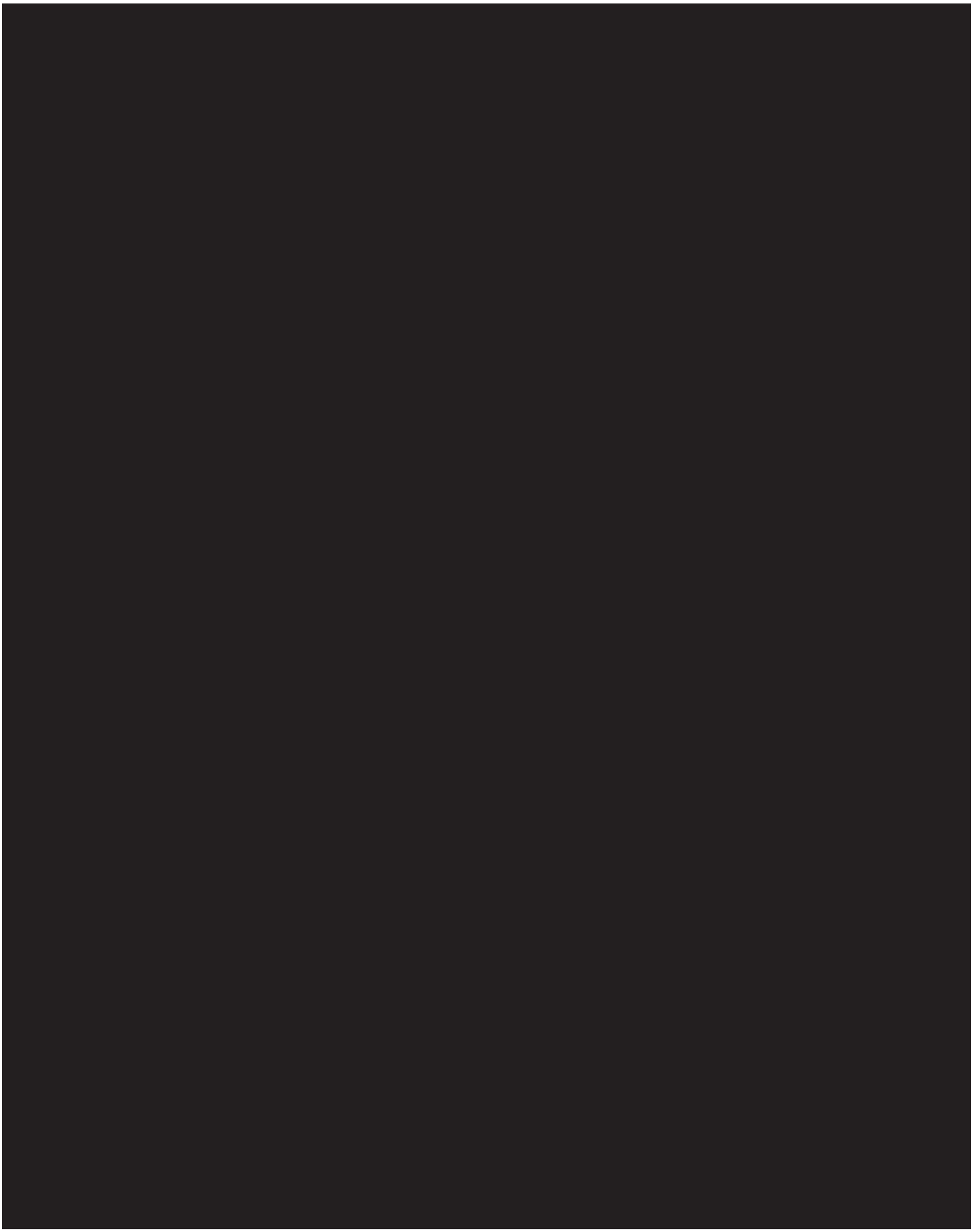
[redacted]

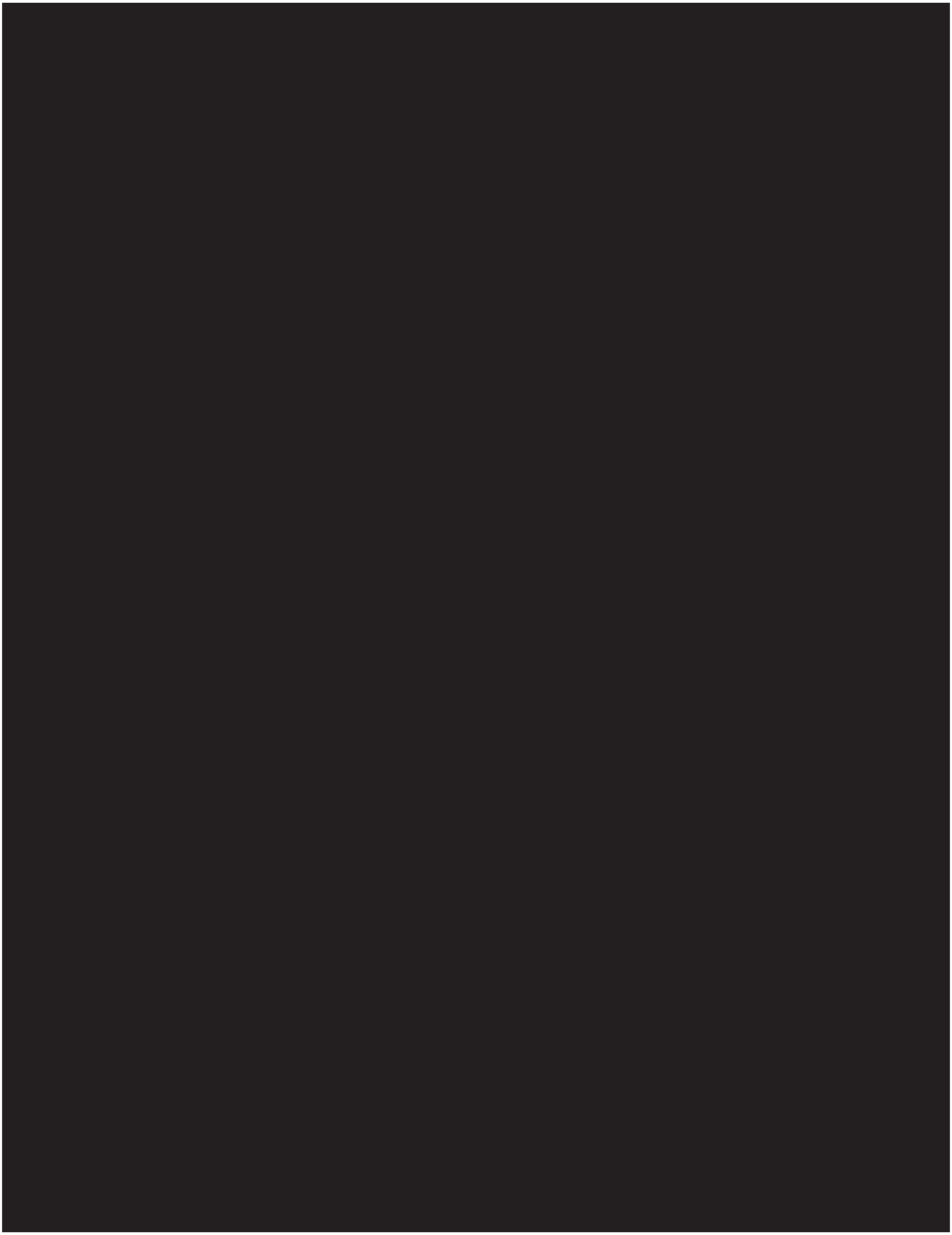


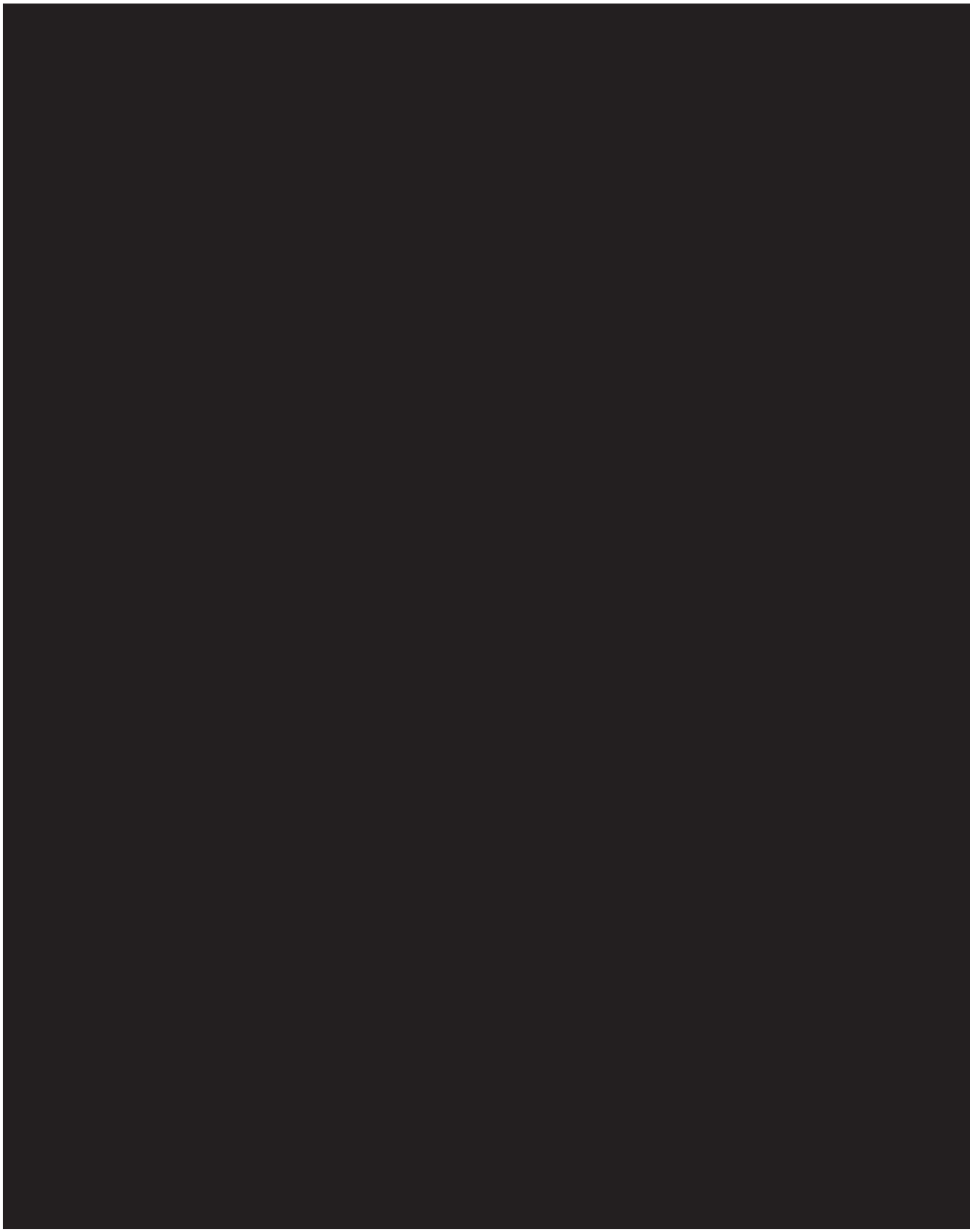
8 REFERENCES

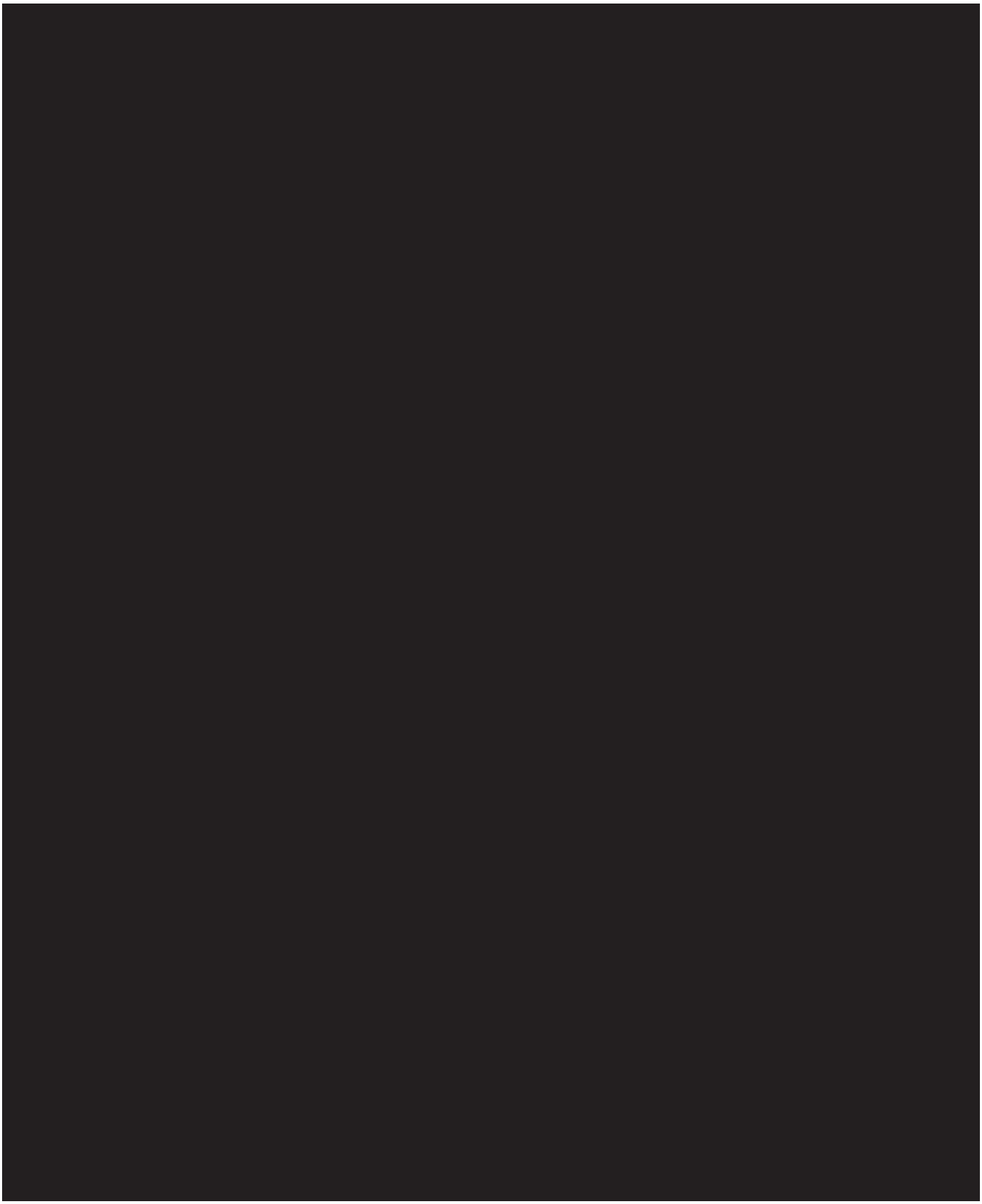
Not applicable.











10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

Visit	Visit 1 Screening	Visit 2 Baseline	Visit 3 Remote Compliance Check	Visit 4 Exit	Unscheduled Visit	Early Exit
Study Day and Visit Window	**2 to 7 days prior to Visit 2**	**Day 1**	**Day 14 ± 3 days**	**Day 30 ± 5 days**		
Informed consent	X					
Connect to electronic patient reported outcomes	X[9]	X		X	(X)	X
Demographics	X					
Medical history	X					
Concomitant medications	X					
Changes to concomitant medications or medical history		X	X	X	X	X
Urine pregnancy test[1]	X			X	(X)	X
Inclusion/exclusion	X					
Meibomian gland functionality test[1]	X					
BCVA (OD, OS; logMAR; distance)	X	X		X	(X)	X
IDEEL-SB Questionnaire[8]	X			X		X
[redacted]						
Slit lamp biomicroscopy examination (with corneal staining)	X	X		X	X[7]	X
Administer IP (IP instillation on site)		X				
[redacted]						
Adverse events	X	X	X	X	X	X
Device deficiencies	X	X	X	X	X	X

Visit	Visit 1 Screening	Visit 2 Baseline	Visit 3 Remote Compliance Check	Visit 4 Exit	Unscheduled Visit	Early Exit
Study Day and Visit Window	**2 to 7 days prior to Visit 2**	**Day 1**	**Day 14 ± 3 days**	**Day 30 ± 5 days**		
[redacted]						
Distribute subject instructions		X			(X)	
Dispense IP		X			(X)	
Collect used and unused IP				X	(X)	X
Remote compliance check			X			

(X) Assessments performed as necessary

[1] Source Only

[redacted]

[7] Assessment performed as necessary for unplanned IP replacement

[8] Electronic patient reported outcomes unless otherwise specified by sponsor

[9]Screening may be rescheduled within 7 days/1 week if connection cannot be established. All remaining criteria will be verified after completing connection.

Signature Page for V-CLN-0196386 v4.0

Signature Page for V-CLN-0196386 v4.0