Alcon

Statistical Analysis Plan for CLY935-C022 / NCT05050578
Title: Clinical Assessment of Two Reusable Silicone Hydrogel Contact Lenses

[redacted]

This version of the Statistical Analysis Plan is based on Version 2.0 of the study protocol.

Executive Summary:

Key Objectives:

The primary objective of this study is to demonstrate noninferiority (NI) in visual acuity (VA) at distance when wearing [redacted] soft contact lenses [redacted] compared to ACUVUE OASYS® with HYDRACLEAR® PLUS soft contact lenses (AOHP).

Decision Criteria for Study Success:

Success of this study will be based on demonstration of NI in distance VA with [redacted] contact lenses when compared to AOHP contact lenses at Day 30, using a margin of 0.05.

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[redacted]

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1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective of this study is to demonstrate NI in distance VA when wearing [redacted] compared to AOHP.

[redacted]

1.2 Study Description

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

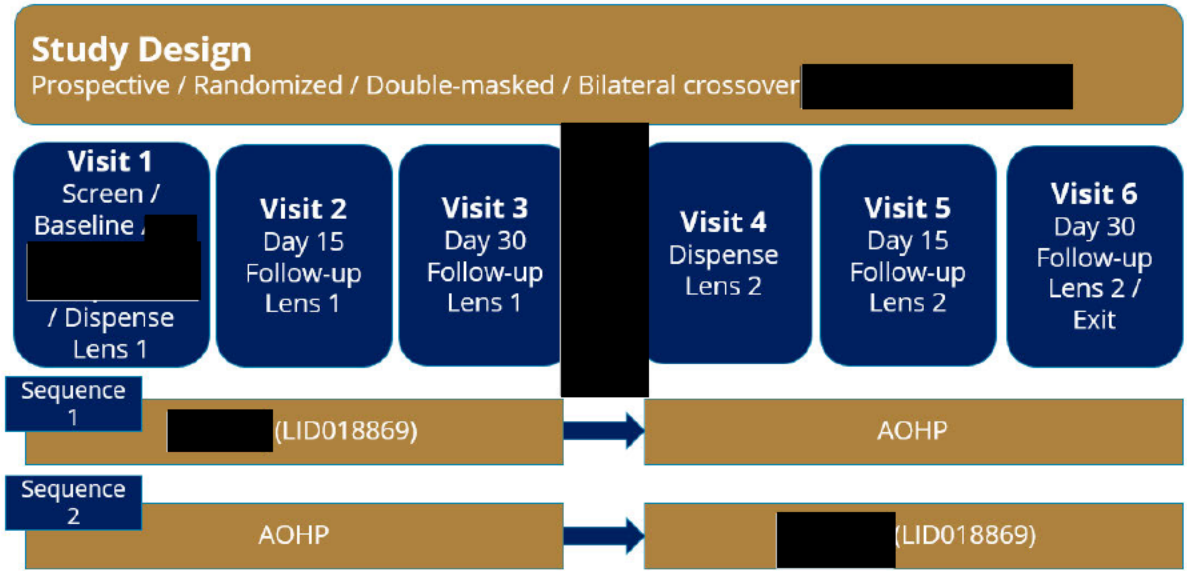
Table 1-1 Study Description Summary

Study Design	Prospective, randomized, controlled, double-masked, bilateral crossover
Study Population	Volunteer subjects aged 18 or older who are habitual spherical weekly/monthly soft contact lens wearers, have at least 3 months of contact lens wearing experience, who wear their habitual lenses at least 5 days per week and at least 10 hours per day, [redacted] Target to complete: 144; Planned to enroll: ~160
Number of Sites	~10 US
Test Product(s)	[redacted] soft contact lenses [redacted] lehifilcon A; LID018869)
Comparator Product(s)	ACUVUE OASYS® with HYDRACLEAR® PLUS soft contact lenses (AOHP; senofilcon A)
Planned Duration of Exposure	~60 days total (test and comparator): Test Product: 30 (±2) days Comparator Product: 30 (±2) days

Visits	Prescreening Visit 1 – Screening/Baseline/[redacted]/Dispense Lens 1 (Day 1) Visit 2 – Day 15 Follow-up Lens 1 [Day 15 ±2 days] Visit 3 – Day 30 Follow-up Lens 1 [Day 30 ±2 days] Visit 4 – Dispense Lens 2[redacted] Visit 5 – Day 15 Follow-up Lens 2 [Day 15 ±2 days] Visit 6 – Day 30 Follow-up Lens 2/Exit [Day 30 ±2 days] [redacted]

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

Figure 1–1 Flowchart of Study Visits



1.3 Randomization

A member of the Randomization Programming group at Alcon who is not part of the study team will generate the randomized allocation schedule(s) for treatment (lens) sequence assignment. Randomization will be implemented in the Electronic Data Capture (EDC)/randomization integration system.

Subjects will be randomized in a 1:1 manner to receive one of 2 lens sequences:

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	LID018869/AOHP	[redacted]/AOHP
Sequence 2	AOHP/LID018869	AOHP/[redacted]

1.4 Masking

This study is double-masked.

[redacted]

2 ANALYSIS SETS

2.1 Safety Analysis Sets

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 any study lenses evaluated in this study. [redacted] For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding lens sequence.

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

2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study, [redacted]

2.3 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that have met any of the critical deviation or evaluability criteria identified in the Deviation and Evaluability Plan.

3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

The following tables will be presented:

- Subject Disposition by Lens Sequence
- Analysis Sets by Lens
- Analysis Sets by Lens Sequence
- Subject Accounting by Lens Sequence
- Demographics Characteristics by Lens Sequence
- Baseline Characteristics by Lens Sequence [lens brand; lens solution]

Subject accounting and demographics characteristics tables will be summarized on the safety, full, and PP analysis sets. Baseline characteristics will be summarized on the full and PP analysis sets.

In addition, the following subject listings will be provided:

- Listing of Subjects Excluded from Protocol Defined Analysis Sets
- Listing of Lens Sequence Assignment by Investigator
- Listing of Subjects Discontinued from Study

4 EFFECTIVENESS ANALYSIS STRATEGY

This study defines 1 primary, [redacted] effectiveness endpoint [redacted] FAS as the primary analysis set. [redacted]

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum, as well as confidence intervals (CI) or

confidence limits (CL) where applicable. Categorical variables will be summarized with frequencies and percentages from each category.

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out [redacted]

[redacted]

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary endpoint is distance VA with study lenses at Day 30, collected for each eye in logMAR.

[redacted]

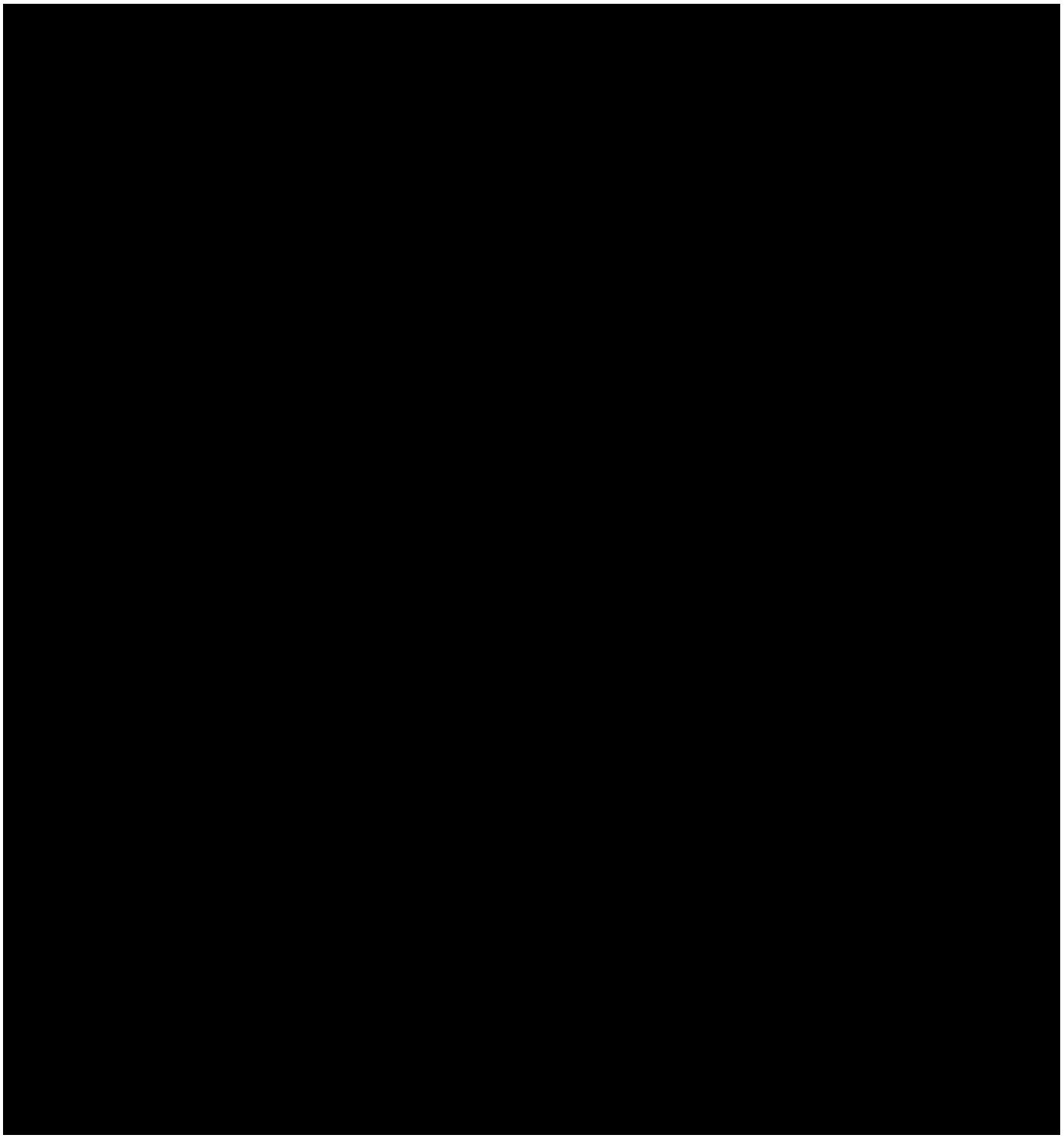
4.2 Effectiveness Hypotheses

Primary Effectiveness

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.05 for NI:

H_0: $\mu_{(T)} - \mu_{(C)} \geq 0.05$
H_a: $\mu_{(T)} - \mu_{(C)} < 0.05$

where $\mu_{(T)}$ and $\mu_{(C)}$ denote the mean distance VA for [redacted] and AOHP, respectively, on the logMAR scale.

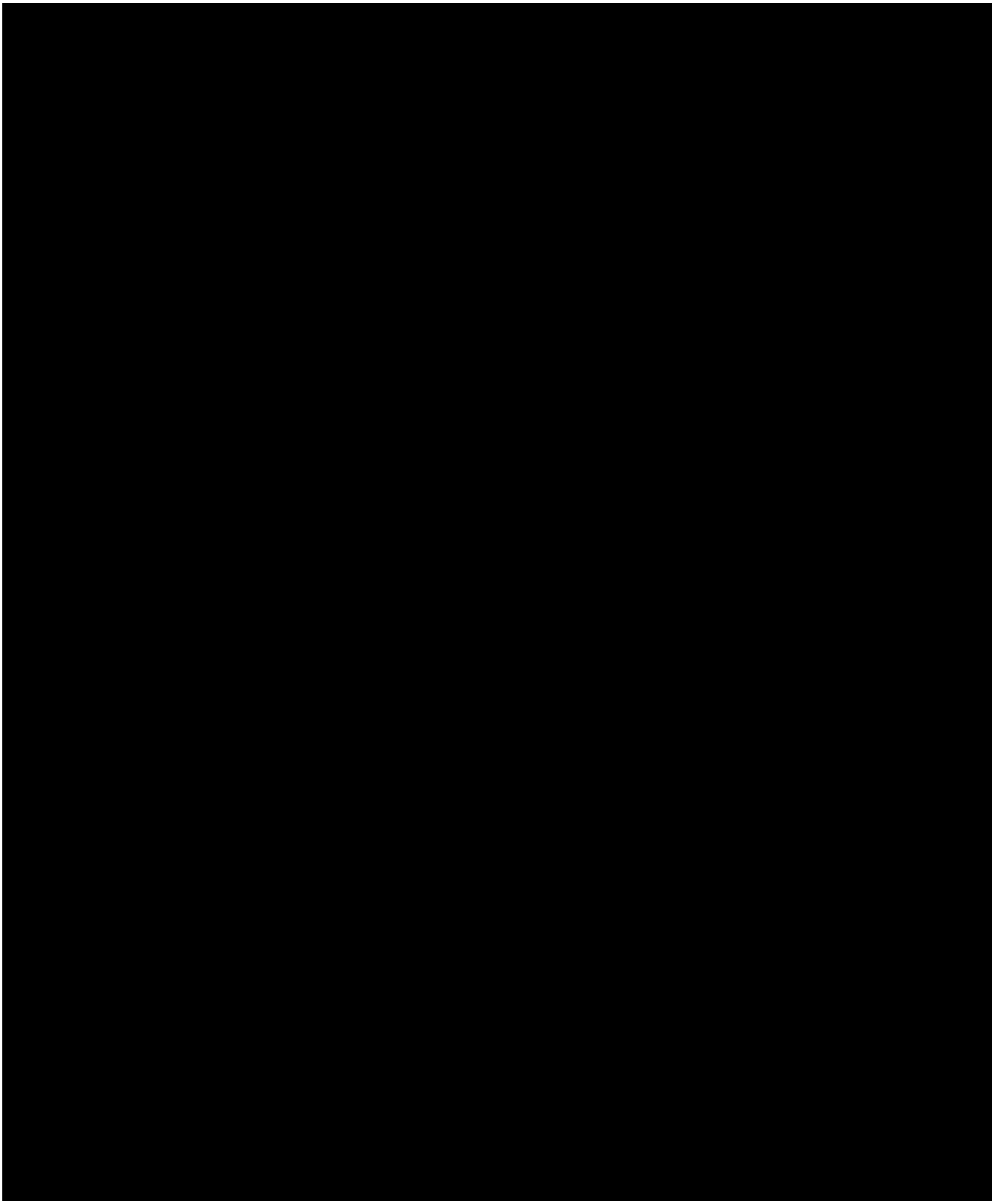


4.3 Statistical Methods for Effectiveness Analyses

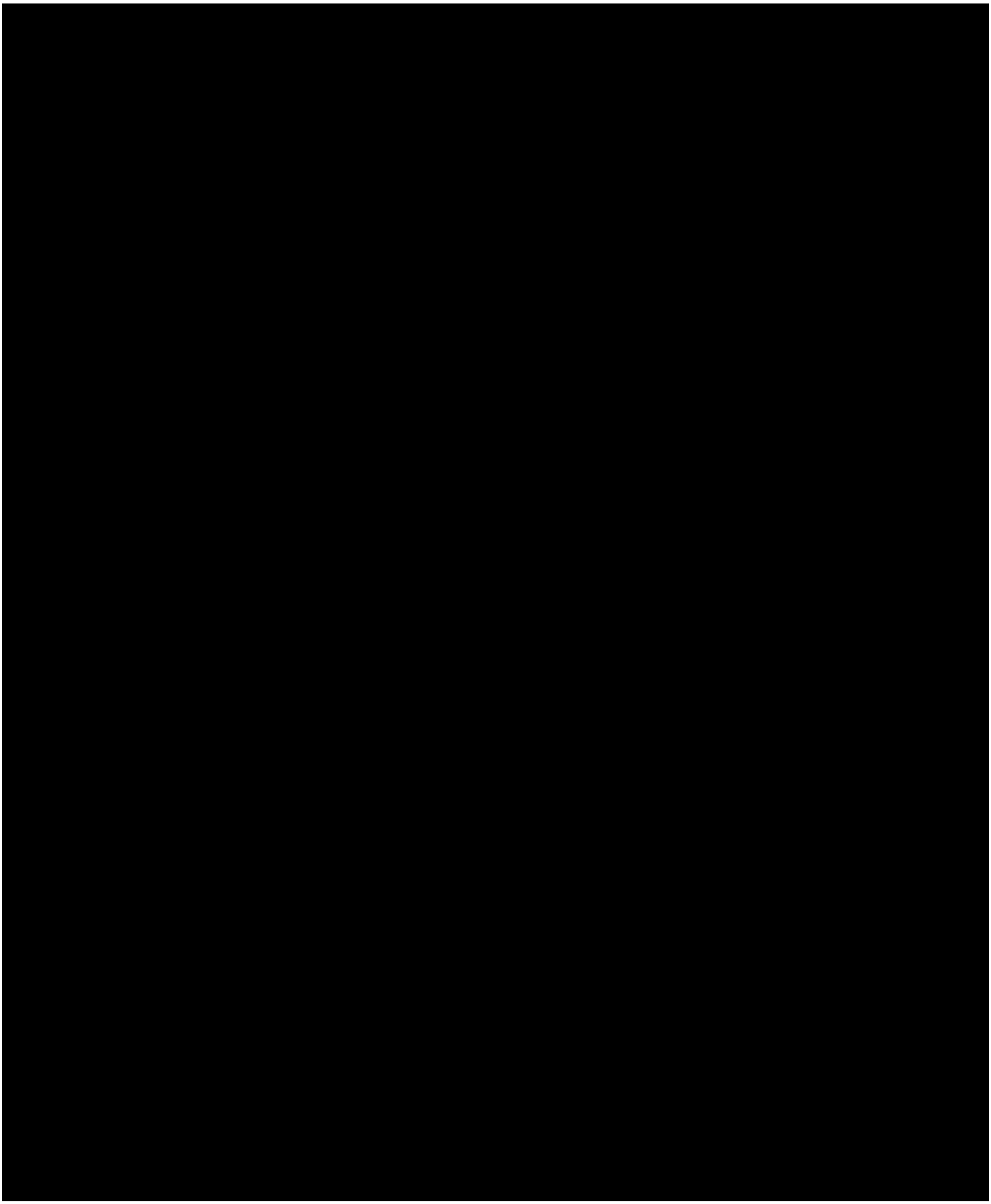
4.3.1 Primary Effectiveness Analysis

A mixed effects repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, visit, lens by visit interaction, period, and sequence. Within-

subject correlation due to eye and the crossover design will also be accounted for in the model. Lens difference [redacted] and the corresponding one-sided 95% upper confidence limit will be computed at Day 30. NI in distance VA will be declared if upper confidence limit is less than 0.05.



[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

- AE
- Biomicroscopy Findings/Slit Lamp Examinations
    - Limbal hyperemia
    - Bulbar hyperemia
    - Corneal staining
    - Conjunctival staining
    - Palpebral conjunctival observations
    - Corneal epithelial edema
    - Corneal stromal edema
    - Corneal vascularization
    - Conjunctival compression/indention

  - Chemosis
  - Corneal infiltrates
  - 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 lenses. For biomicroscopy data, baseline will be defined as Visit 1 for Period 1 and Visit 4 for Period 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.

Pre-treatment AEs and between-treatment AEs will be separated from treatment-emergent AEs occurring during the study period. A pre-treatment AE is an event that occurs after signing informed consent but prior to exposure to study lens. A between-treatment AE is an event that occurs after last exposure to Period 1 lenses but prior to exposure to Period 2 lenses. The period for treatment-emergent AE analysis starts from exposure to study lenses for Period 1 or Period 2 until the subject completes the respective period or is discontinued from the study. Each AE will be summarized under the exposed lens based upon the event onset date/time up until the start of the next lens in the crossover sequence.

The following tables and supportive listings will be provided:

- 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
- Listing of All Ocular Treatment-Emergent Adverse Events
- Listing of All Nonocular Treatment-Emergent Adverse Events

- Listing of All Ocular Pre-Treatment Adverse Events
- Listing of All Nonocular Pre-Treatment Adverse Events
- Listing of All Ocular Between-Treatment Adverse Events
- Listing of All Nonocular Between-Treatment Adverse Events

5.3.2 Biomicroscopy Findings/Slit Lamp Examination

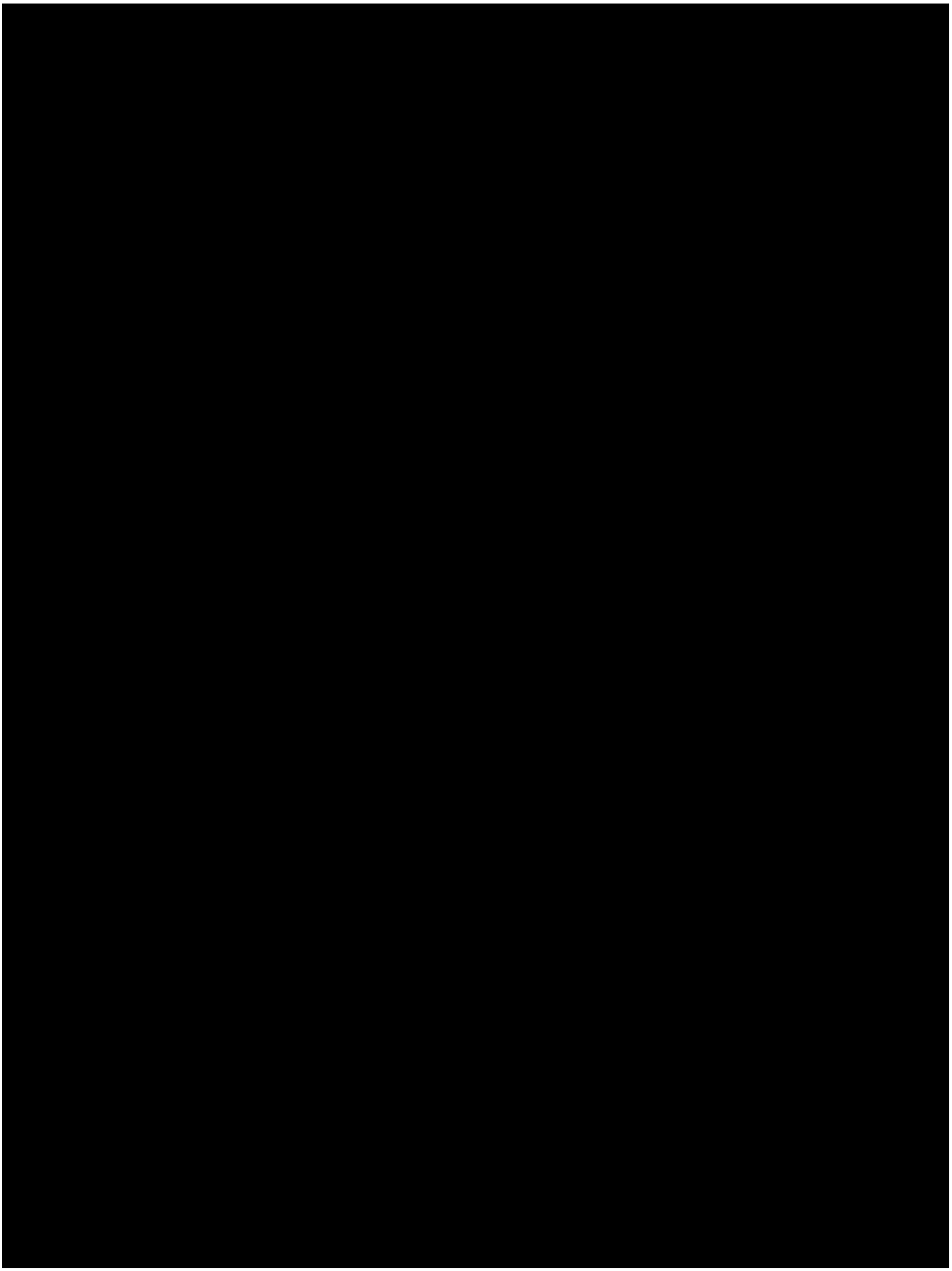
The following tables and supportive listings will be provided:

- Frequency and Percentage for Biomicroscopy Findings by Visit
- Incidence of Increased Severity by 2 or More Grades in Biomicroscopy Findings
- Listing of Subjects With Other Biomicroscopy Findings
- Listing of Subjects With Conjunctival Compression/Indentation or Chemosis
- Listing of Subjects With Increased Severity by 2 or More Grades in Biomicroscopy Findings [This listing will include all relevant visit within the crossover period]
- Listing of Subjects with Infiltrates

5.3.3 Device Deficiencies

The following tables 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



8 REFERENCES

Not Applicable.

10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Prescreening	Lens 1 (Period 1)			[redacted]	Lens 2 (Period 2)			Early Exit	USV
		Visit 1 Screen/ Baseline[redacted] / Dispense Lens 1 [Day 1]	Visit 2 Day 15 Follow-up Lens 1 [Day 15 ± 2 days]	Visit 3 Day 30 Follow-up Lens 1 [Day 30 ± 2 days]		Visit 4 Dispense Lens 2 [Day 1]	Visit 5 Day 15 Follow-up Lens 2 [Day 15 ± 2 days]	Visit 6 Day 30 Follow-up Lens 2 / Exit [Day 30 ± 2 days]		
Informed Consent		X								
Demographics		X								
Medical History[¥]		X	X	X		X	X	X	X	X
Concomitant Medications[¥]		X	X	X		X	X	X	X	X
Pregnancy Form		X	X	X		X	X	X	X	X
Inclusion/ Exclusion		X								
Habitual (lens brand, lens power*, lens care)		X								
VA w/ habitual correction* (OD, OS, Snellen distance)		X						X	X	(X)
Manifest Refraction and BCVA with manifest refraction* (OD, OS, Snellen distance)		X	(X)	(X)		(X)	(X)	(X)	(X)	(X)
Biomicroscopy		X	(X)	X		X	(X)	X	X	X[Ω]
[redacted]	[redacted]	[redacted]								
[redacted]		[redacted]	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Randomization and record lens power*		X								
Dispense study lenses*		X				X				
Planned lens replacement*			(X)[α]				(X)[α]			

Procedure/ Assessment	Prescreening	Lens 1 (Period 1)			[redacted]	Lens 2 (Period 2)			Early Exit	USV
		Visit 1 **Screen/ Baseline[redacted] / Dispense Lens 1** [Day 1]	**Visit 2** **Day 15 Follow-up Lens 1** [Day 15 ± 2 days]	**Visit 3** **Day 30 Follow-up Lens 1** [Day 30 ± 2 days]		**Visit 4** **Dispense Lens 2** [Day 1]	**Visit 5** **Day 15 Follow-up Lens 2** [Day 15 ± 2 days]	**Visit 6** **Day 30 Follow-up Lens 2 / Exit** [Day 30 ± 2 days]		
VA w/ study lenses (OD, OS, logMAR distance)		X	X	X		X	X	X	X	(X)
[redacted]										

Procedure/ Assessment	Prescreening	Lens 1 (Period 1)			[redacted]	Lens 2 (Period 2)			Early Exit	USV
		Visit 1 Screen/ Baseline[redacted] Dispense Lens 1	**Visit 2** Day 15 Follow-up Lens 1 [Day 15 ± 2 days]	**Visit 3** Day 30 Follow-up Lens 1 [Day 30 ± 2 days]		**Visit 4** Dispense Lens 2 [Day 1]	**Visit 5** Day 15 Follow-up Lens 2 [Day 15 ± 2 days]	**Visit 6** Day 30 Follow-up Lens 2 / Exit [Day 30 ± 2 days]		
[redacted]										
AEs§		X	X	X		X	X	X	X	X
Device deficiencies		X	X	X		X	X	X	X	X
Exit Form								X	X	

USV = Unscheduled visit; [redacted] AE = Adverse Event; OD = Right Eye; OS = Left Eye

* Source only

[redacted]

§ Limited details will be collected in the eCRF if the AE is not related, not serious, nonocular, and the subject did not withdraw due to the AE. If the event is related, serious, ocular and/or the subject withdrew due to the AE, the all details will be collected in the eCRFs.

[redacted]