Alcon

Statistical Analysis Plan for CLE383-P005 / NCT04865354
Title: Clinical Comparison of Two Daily Disposable Contact Lenses

[redacted]

This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

Executive Summary:

Key Objectives:

The primary objective of this study is to demonstrate noninferiority (NI) in the visual acuity (VA) at distance when wearing PRECISION1™ (verofilcon A) Soft Contact Lenses (PRECISION1) compared to CooperVision® Clariti® 1 day (Clariti 1-Day).

Decision Criteria for Study Success:

Success of this study will be based on demonstration of NI of PRECISION1 compared to Clariti 1-Day in distance VA, using a margin of 0.05 on the logMAR scale.

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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 the VA at distance when wearing PRECISION1 contact lenses compared to Clariti 1-Day contact lenses.

[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, daily wear, multicenter
Study Population	Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous PRECISION1, Clariti 1-Day and DAILIES TOTAL1® habitual lens wearers), have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and at least 10 hours per day. [redacted] Target to complete: 150; Planned to enroll: ~173
Number of Sites	~ 10 (US)
Test Product	PRECISION1™ (verofilcon A) soft contact lenses (PRECISION1) [redacted]
Control Product	CooperVision® Clariti® 1 day soft contact lenses (Clariti 1-Day) [redacted]

Planned Duration of Exposure	16 days total duration (test and control) • Test Product: 8 [redacted] days • Control Product: 8 [redacted] days
Visits	Visit 1: Screening/Baseline/Dispense Lens 1 Visit 2: Week 1 Follow-up Lens 1/Dispense Lens 2 [8 [redacted] days after Visit 1] Visit 3: Week 1 Follow-up Lens 2/Exit [8 [redacted] days after Visit 2] [redacted]

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 study lens sequence assignment. Randomization will be implemented in the Electronic Data Capture (EDC)/randomization integration system.

Subjects will be randomized in a 1:1 ratio to receive treatment (lens) in crossover sequence as follows:

Sequence	**EDC/randomization integration system**	**Lens Name**
Sequence 1	[redacted]	PRECISION1/Clariti 1-Day
Sequence 2	[redacted]	Clariti 1-Day/PRECISION1

1.4 Masking

This study is double-masked.

[redacted]

1.5 Interim Analysis

There are no plans to conduct an interim analysis and no criteria by which the study would be terminated early based upon statistical determination.

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 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.

[redacted]

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].

[redacted]

[redacted] 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 [habitual lens brand, and habitual lens power: sphere]

[redacted]

4 EFFECTIVENESS ANALYSIS STRATEGY

This study defines 1 primary, [redacted] All effectiveness evaluations will use the FAS as the primary analysis set.

[redacted]

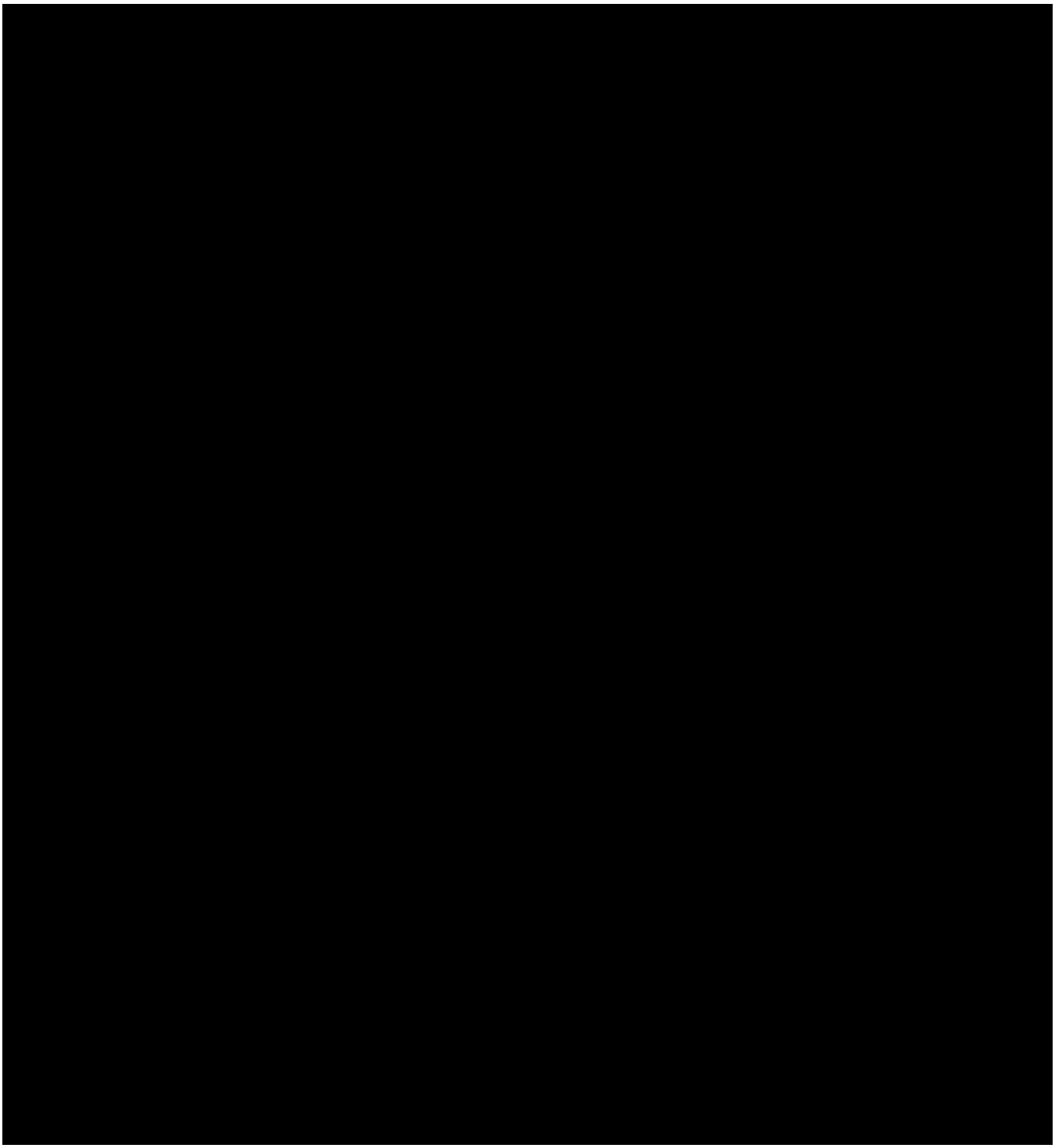
All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out.

[redacted]

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

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



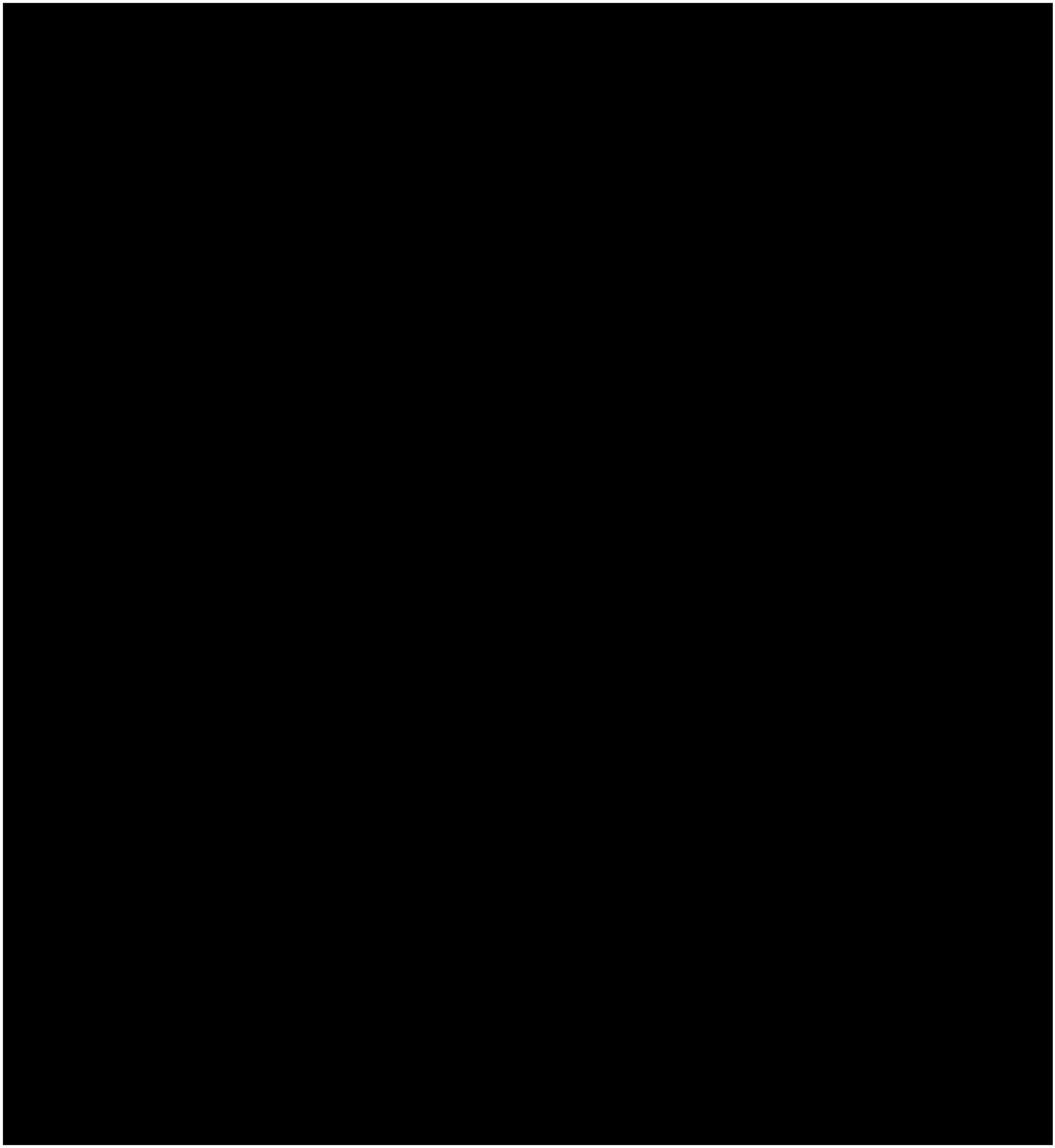
4.2 Effectiveness Hypotheses

Primary Effectiveness

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

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 PRECISION1 and Clariti 1-Day, respectively, on the logMAR scale.



[redacted]

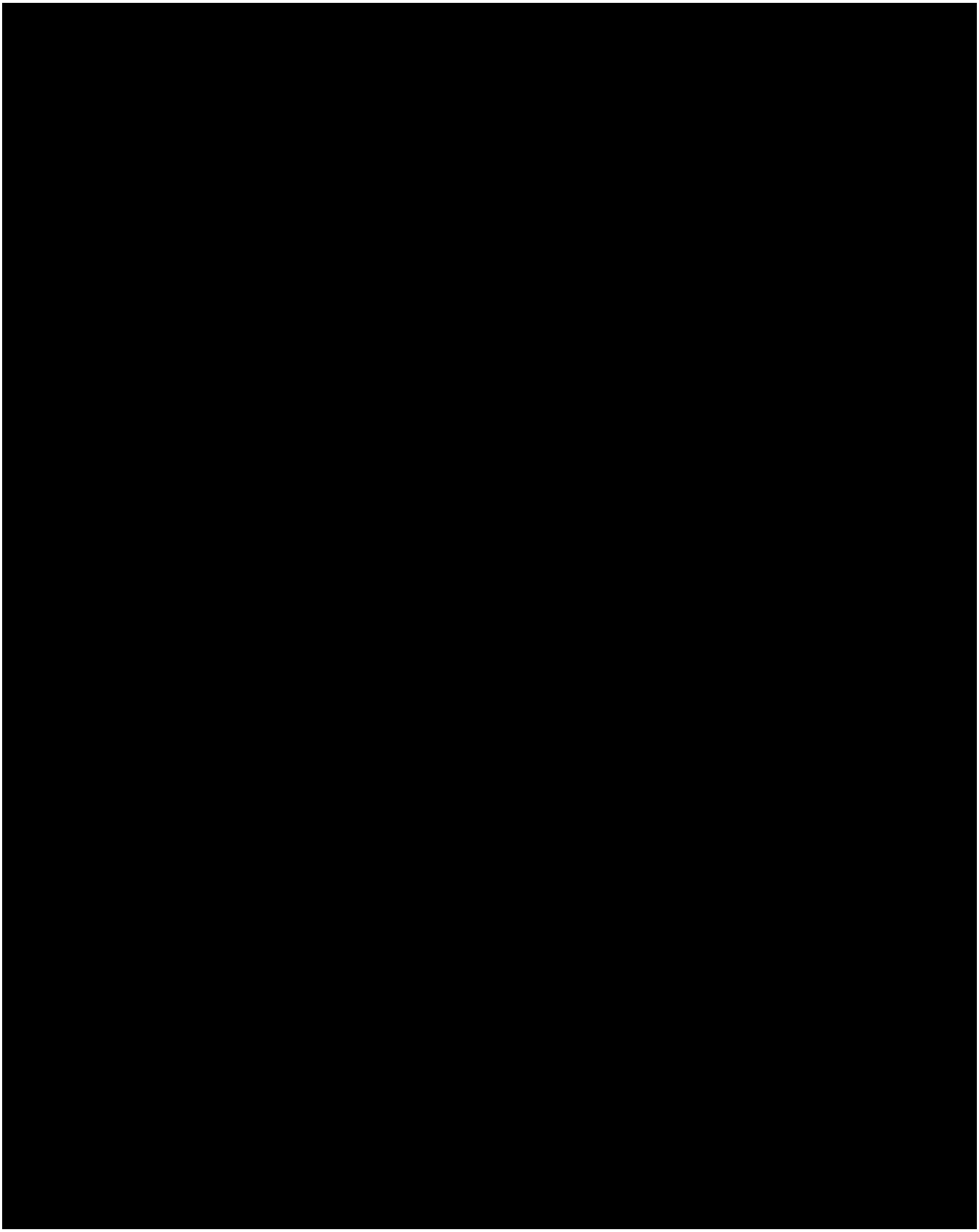
4.3 Statistical Methods for Effectiveness Analyses

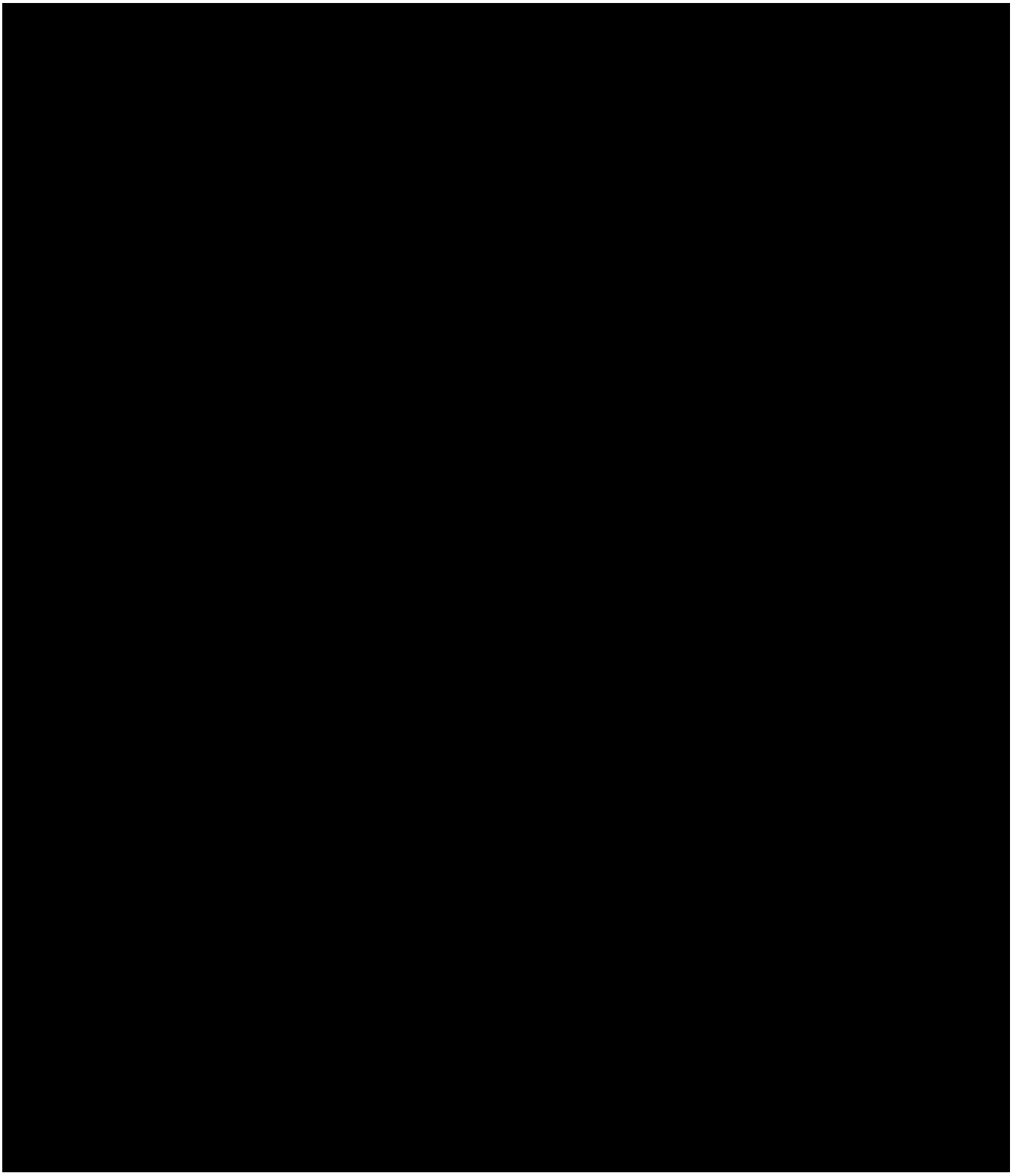
4.3.1 Primary Effectiveness Analyses

A mixed effects repeated measures model will be utilized to test the hypotheses. The model will include terms for lens, period, and sequence as fixed effect. Within-subject correlation due to eye and the crossover design will also be accounted for in the model. Lens difference (PRECISION1 minus Clariti 1-Day) and the corresponding one-sided 95% upper confidence limit will be computed. Noninferiority in distance VA will be declared if upper confidence limit is less than 0.05.

[redacted]

[redacted]





4.6 Interim Analysis for Effectiveness

No interim analysis is planned for the effectiveness endpoints.

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)
- Biomicroscopy Findings/Slit Lamp Examinations

- 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 2 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 when a subject exits the study 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 periods. A pre-treatment AE is an event that occurs after signing informed consent but prior to exposure to study lenses. 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

[redacted]

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.

[redacted]

9 REVISION HISTORY

This is the original (Version 1.0) Statistical Analysis Plan for this study. This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

Procedure / Assessment	**Prescreening (optional)**	**Visit 1** Screening/Baseline/ Dispense Lens 1 [redacted]	**Visit 2** Week 1 Follow-up Lens 1 / Dispense Lens 2	**Visit 3** Week 1 Follow-up Lens 2 / Exit	**Unscheduled Visit / Early Exit**
		[redacted]	8 [redacted] days after Visit 1 [redacted]	8 [redacted] days after Visit 2	**N/A**
Informed Consent	-	✓	-	-	-
Demographics	-	✓	-	-	-
Medical History ‡	-	✓	✓	✓	✓
Concomitant Medications ‡	-	✓	✓	✓	✓
Inclusion/Exclusion	-	✓	-	-	-
Habitual lens information (brand, power)	-	✓	-	-	-
VA with habitual contact lens correction (OD, OS, LogMAR distance)*	-	✓	-	✓ (Exit procedure)	(✓)
BCVA with manifest refraction (OD, OS, logMAR distance)	-	✓	(✓)	(✓)	(✓)
Biomicroscopy	-	✓	✓	✓	✓
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Randomize	-	✓	-	-	-
Dispense (provide) study lenses	-	✓	✓	-	(✓)

Procedure / Assessment	**Prescreening (optional)**	**Visit 1** Screening/Baseline/ Dispense Lens 1 (Lens 1 to be worn after washout period)	**Visit 2** Week 1 Follow-up Lens 1 / Dispense Lens 2	**Visit 3** Week 1 Follow-up Lens 2 / Exit	**Unscheduled Visit / Early Exit**
		[redacted]	8[redacted] days after Visit 1 [redacted]	8[redacted] days after Visit 2	**N/A**
VA (logMAR distance) with study lenses, OD, OS	-	-	✓	✓	-
[redacted]					
AEs	-	✓	✓	✓	✓
Device Deficiencies	-	✓	✓	✓	✓
Exit Form	-	(✓)	(✓)	(✓)	(✓)

(✓) assessment performed as necessary, [redacted]

* source only

[redacted]

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