Clinical Performance of Two Reusable

Silicone Hydrogel Contact Lenses

STUDY ID

CLL949-C024
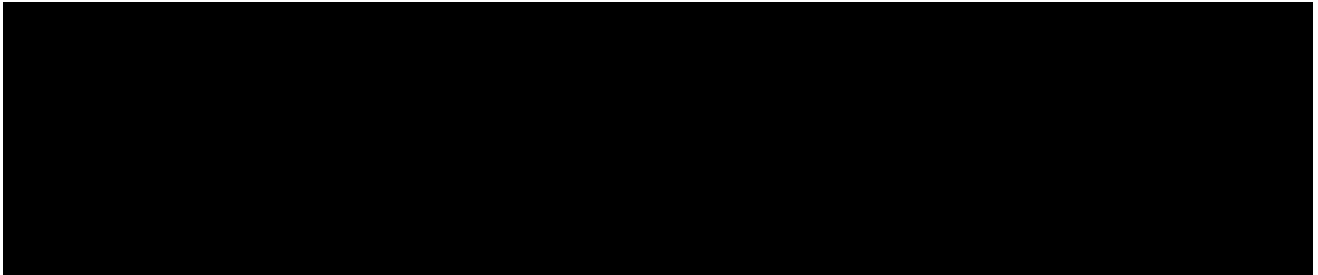

STATISTICAL ANALYSIS PLAN

NCT05766787

Alcon

Statistical Analysis Plan for CLL949-C024
Title: Clinical Performance of Two Reusable Silicone Hydrogel Contact Lenses

Executive Summary:

Key Objectives:

The primary objective of this study is to demonstrate noninferiority (NI) in the visual acuity (VA) at distance when wearing Alcon serafilcon A contact lenses compared to ACUVUE® OASYS with HYDRACLEAR® PLUS Technology (AOHP) contact lenses when worn in a daily wear modality.

Decision Criteria for Study Success:

Success of this study will be based on demonstration of NI in distance VA with Alcon serafilcon A contact lenses when compared to AOHP contact lenses at Week 1, using a margin of 0.05 on the logMAR scale.

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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 Alcon serafilcon A contact lenses compared to AOHP contact lenses when worn in a daily wear modality.

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, double masked, bilateral, crossover
Study Population	Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous AOHP habitual lens wearers and daily disposable 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 8 hours per day. Target to complete: 168 Planned to enroll: ~ 185
Number of Sites	~ 14 US
Test Product	Alcon serafilcon A contact lenses (serafilcon A; LID 022821)
Comparator Product	ACUVUE® OASYS with HYDRACLEAR® PLUS Technology contact lenses (AOHP; senofilcon A)
Planned Duration of Exposure	~ 28 days total duration (test and comparator): Test product: 14 (-0/+2) days Comparator Product: 14 (-0/+2) days
Visits	Visit 1: Screening/Baseline

	Visit 2: Dispense Lens 1 [2 (at least 48 hours) – 4* days after Visit 1] Visit 3: Week 1 Follow-up Lens 1 [7 -0/+ 1 days after Visit 2] Visit 4: Week 2 Follow-up Lens 1 [7 -0/+ 1 days after Visit 3] Visit 5: Dispense Lens 2 [2 (at least 48 hours) – 4* days after Visit 4] Visit 6: Week 1 Follow-up Lens 2 [7 -0/+ 1 days after Visit 5] Visit 7: Week 2 Follow-up Lens 2/ Exit [7 -0/+ 1 days after Visit 6] * Washout period with habitual spectacles only after Visit 1 and Visit 4

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

Figure 1–1   Study Design
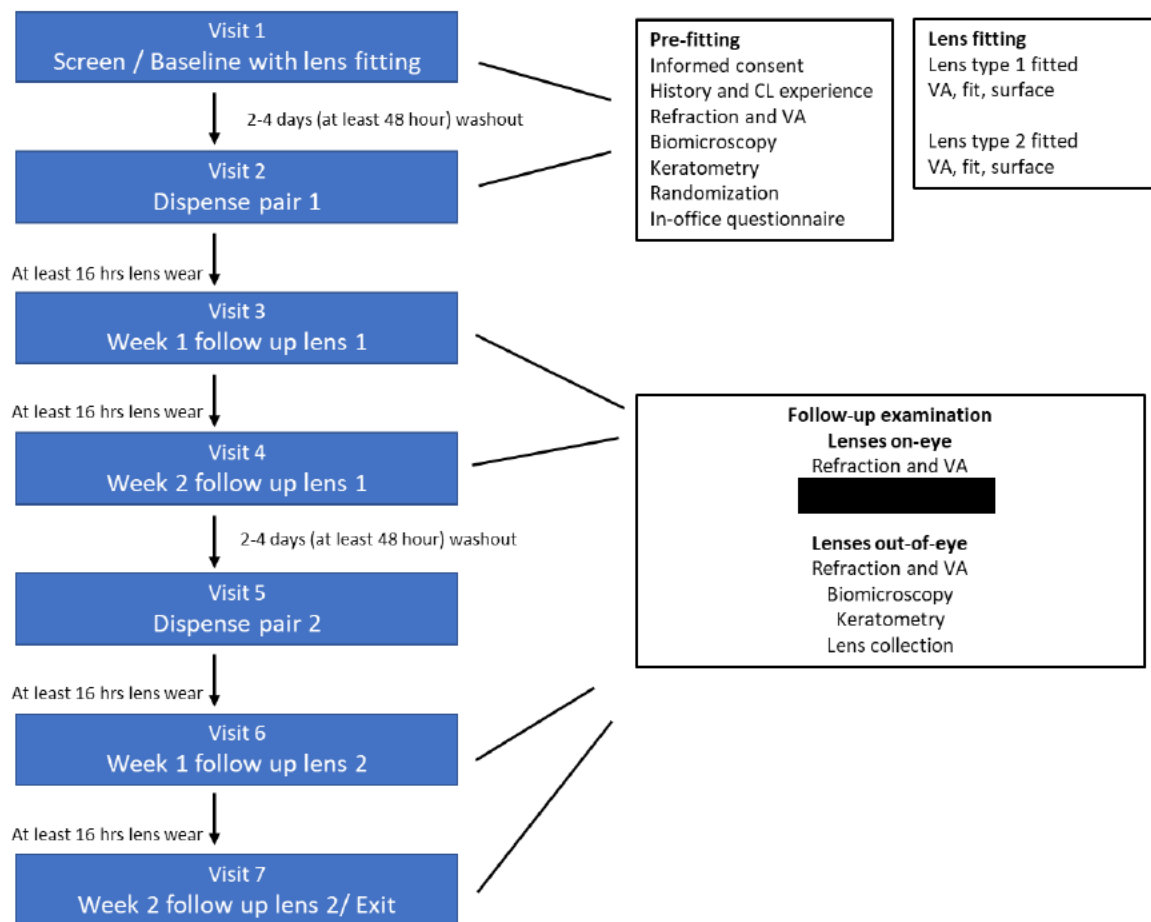
1.3 Randomization

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.

Qualifying subjects will be randomized in a 1:1 manner to receive treatment (lens) in crossover sequence: test product then comparator product or comparator product then test product, respectively.

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	LID022821/AOHP	Alcon serafilcon A/AOHP
Sequence 2	AOHP/LID022821	AOHP/Alcon serafilcon A

1.4 Masking

This study is double-masked.

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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 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. ███████████████████████████████ 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.

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 Deviations and Evaluability Plan (DEP).

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 by Lens Sequence

- Baseline Characteristics by Lens Sequence [lens brand; lens power; lens care; ████████████████████████████████████ keratometry readings; Best Corrected Visual Acuity (BCVA); habitual lens wear and rewetting drops usage]

Subject accounting and demographics tables will be summarized on the safety, full and per protocol analysis datasets. Baseline characteristics will be summarized on the full and per protocol analysis datasets.

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

All effectiveness analyses will be carried based on the randomization assignment.

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.

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for the primary and key exploratory effectiveness analyses.

For all planned inferential analyses, alternative models/methods may be considered if convergence cannot be achieved. Furthermore, if significant carryover effects are noted (confounded with sequence effect), results will be examined by period to ensure the overall conclusion is valid.
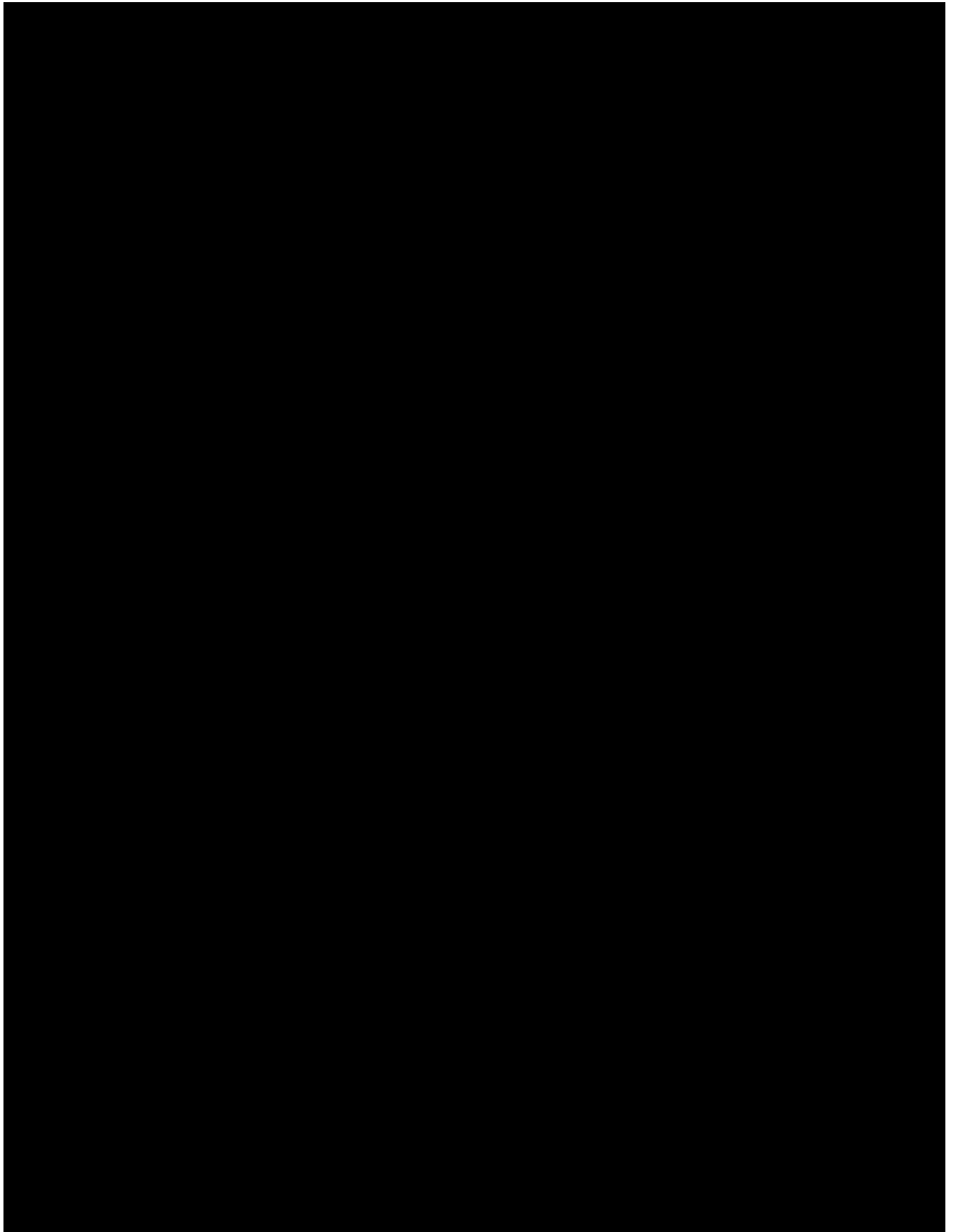
A listing of select effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary endpoint is distance VA with study lenses at Week 1, collected for each eye in logMAR.
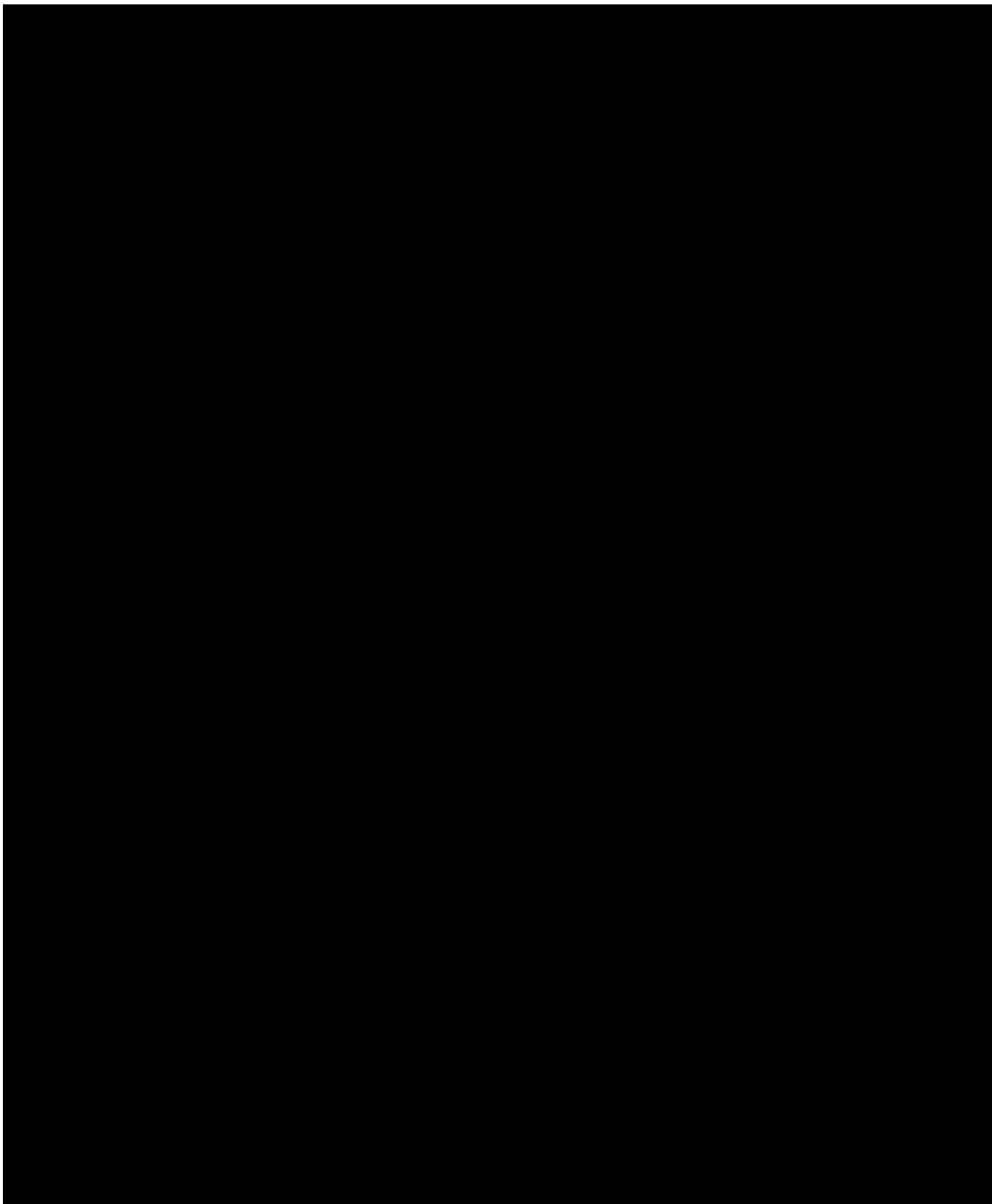
- Time to questionnaire completion (hours or minutes, as applicable)
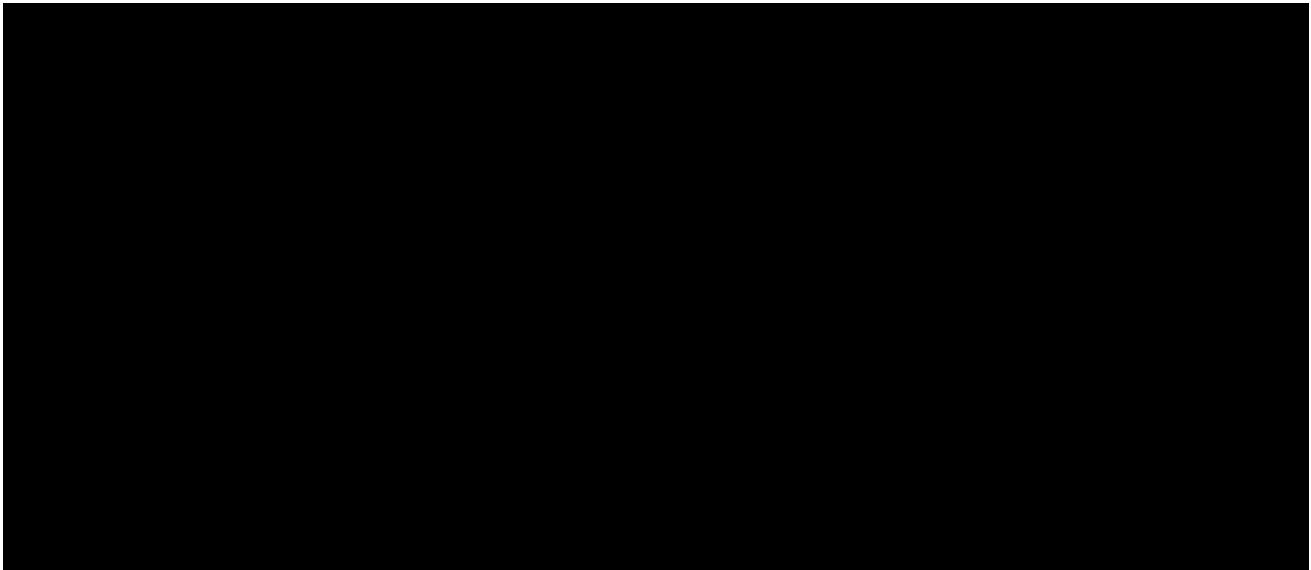

4.2   Effectiveness Hypotheses

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 at Week 1 for Alcon serafilcon A and AOHP, respectively, on the logMAR scale.

4.3   Statistical Methods for Effectiveness Analyses

4.3.1   Primary Effectiveness Analyses

A mixed effects repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, period, sequence, visit (Dispense, Week 1, Week 2), and lens by visit interaction. Within subject correlation due to eye and crossover will also be accounted for in the model. Lens difference (Alcon serafilcon A minus AOHP) and the corresponding one-sided 95% upper confidence limit (UCL) will be computed at Week 1. Noninferiority will be declared if the UCL is less than 0.05.
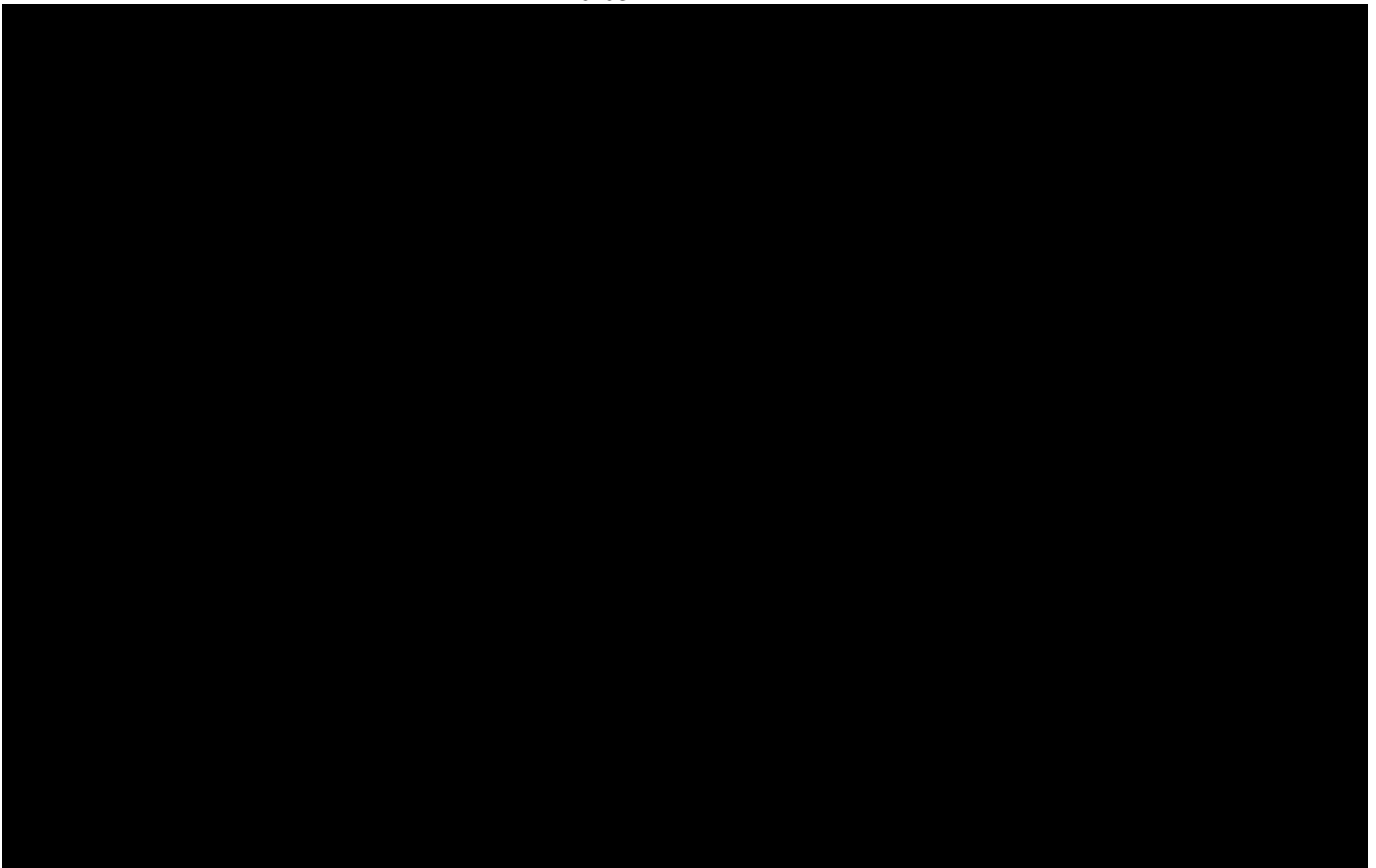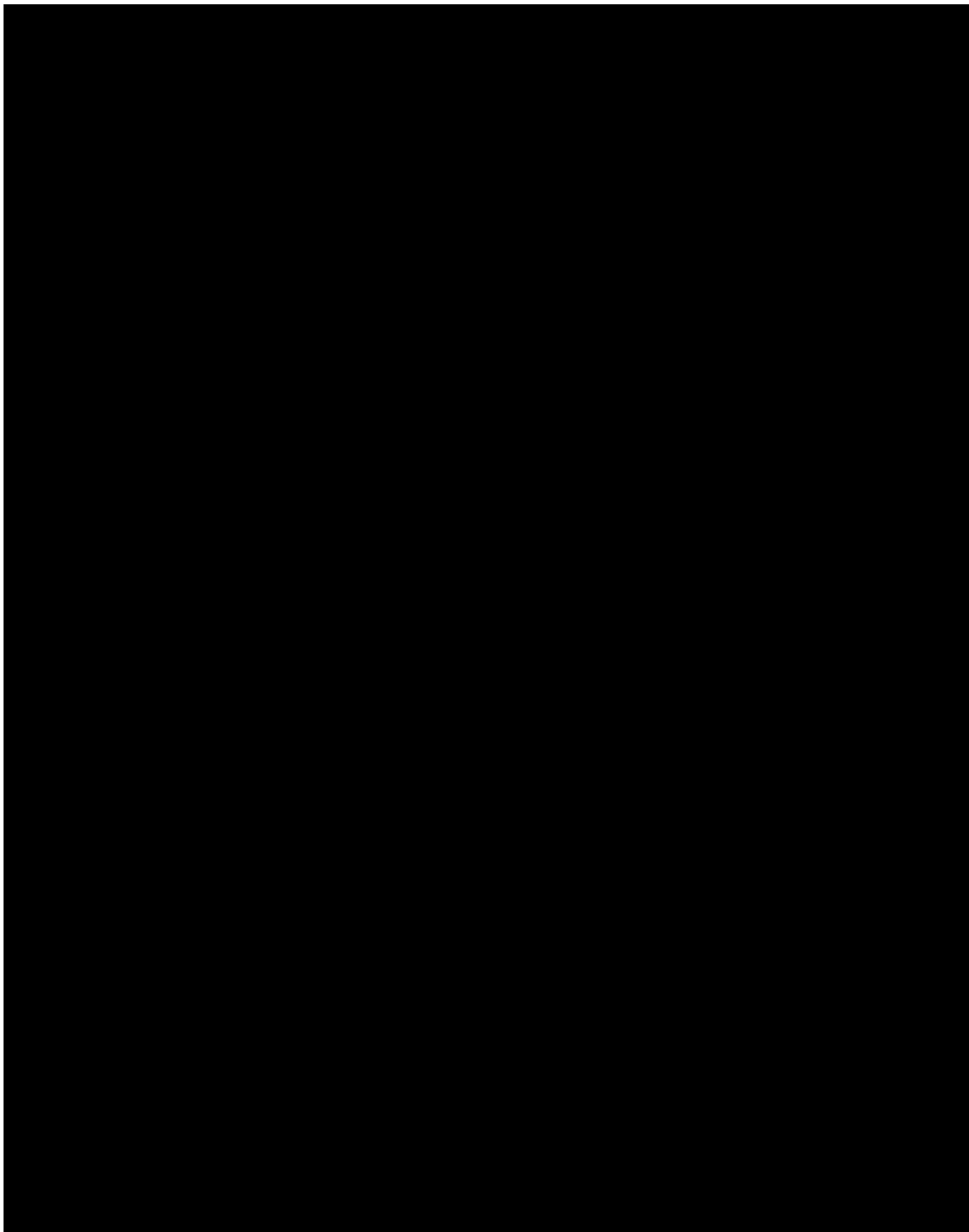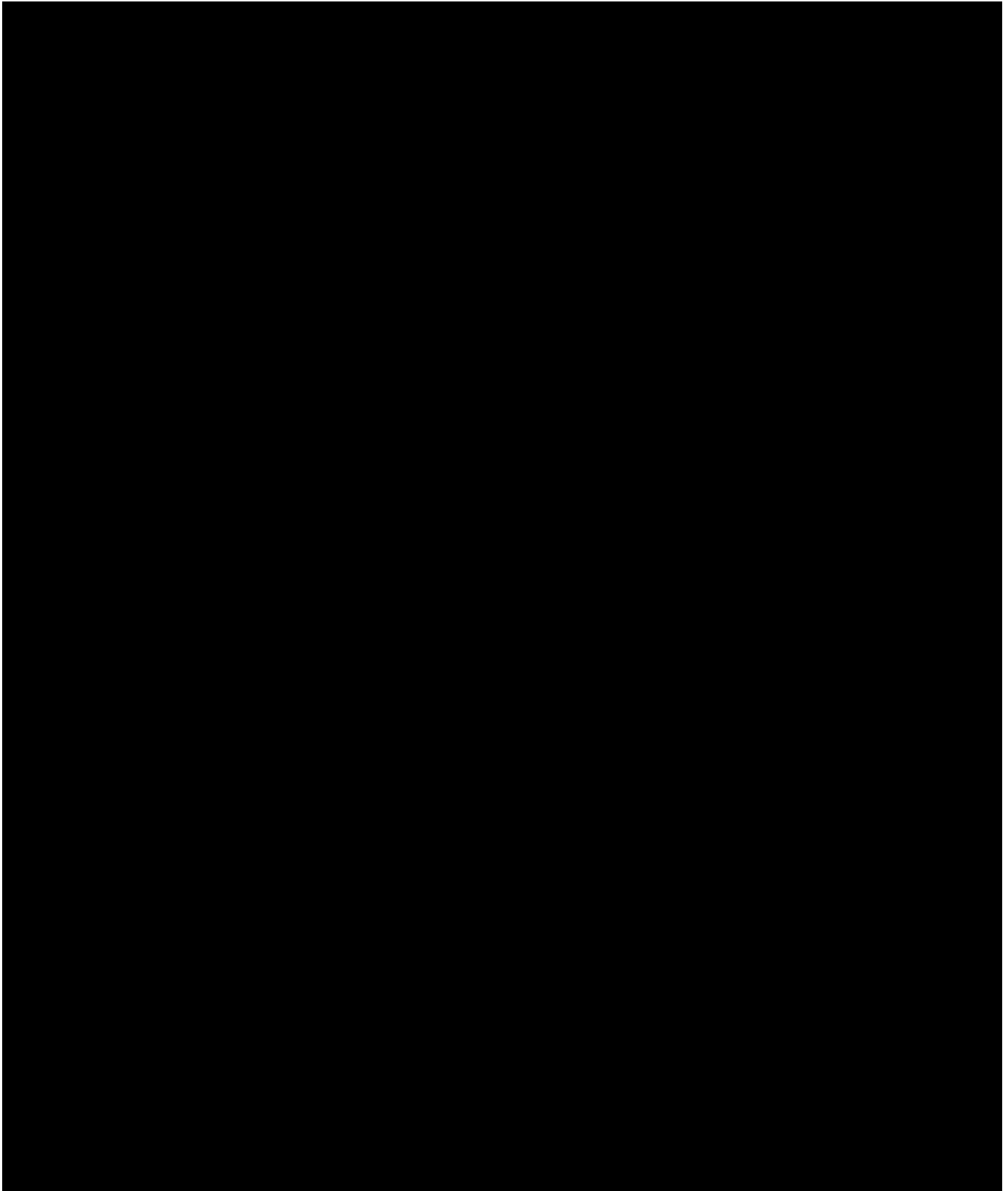
4.4 Multiplicity Strategy

The primary effectiveness endpoint of distance VA will be tested at one-sided $\alpha = 0.05$ for NI and will serve as the gatekeeper for subsequent testing of the key effectiveness endpoints.

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4.5 Subgroup Analyses and Effect of Baseline Factors

It is not expected that demographics or baseline characteristics will have an impact on study results in this study. No subgroup analyses are planned.

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:

- AEs

- Biomicroscopy findings
    - 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 2 for Period 1 and Visit 5 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 the informed consent to the time of their study exit will be accounted for in the reporting.

Presentation of AEs will be separated into pre-treatment AEs, between-treatment AEs, and treatment-emergent AEs as defined below:

- Pre-treatment: an event that occurs after signing informed consent but prior to exposure to study lenses

- Between-treatment: an event that occurs one day after last exposure to Period 1 study lenses but prior to exposure of Period 2 study lenses.

- Treatment-emergent: an event that occurs from first exposure to Period 1 study lenses until subject exits from the study, excluding those classified as between-treatment

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 Ocular Significant Nonserious 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

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
- Listing of Subjects with Infiltrates

5.3.3   Device Deficiencies

The following tables and supportive listings will be provided:
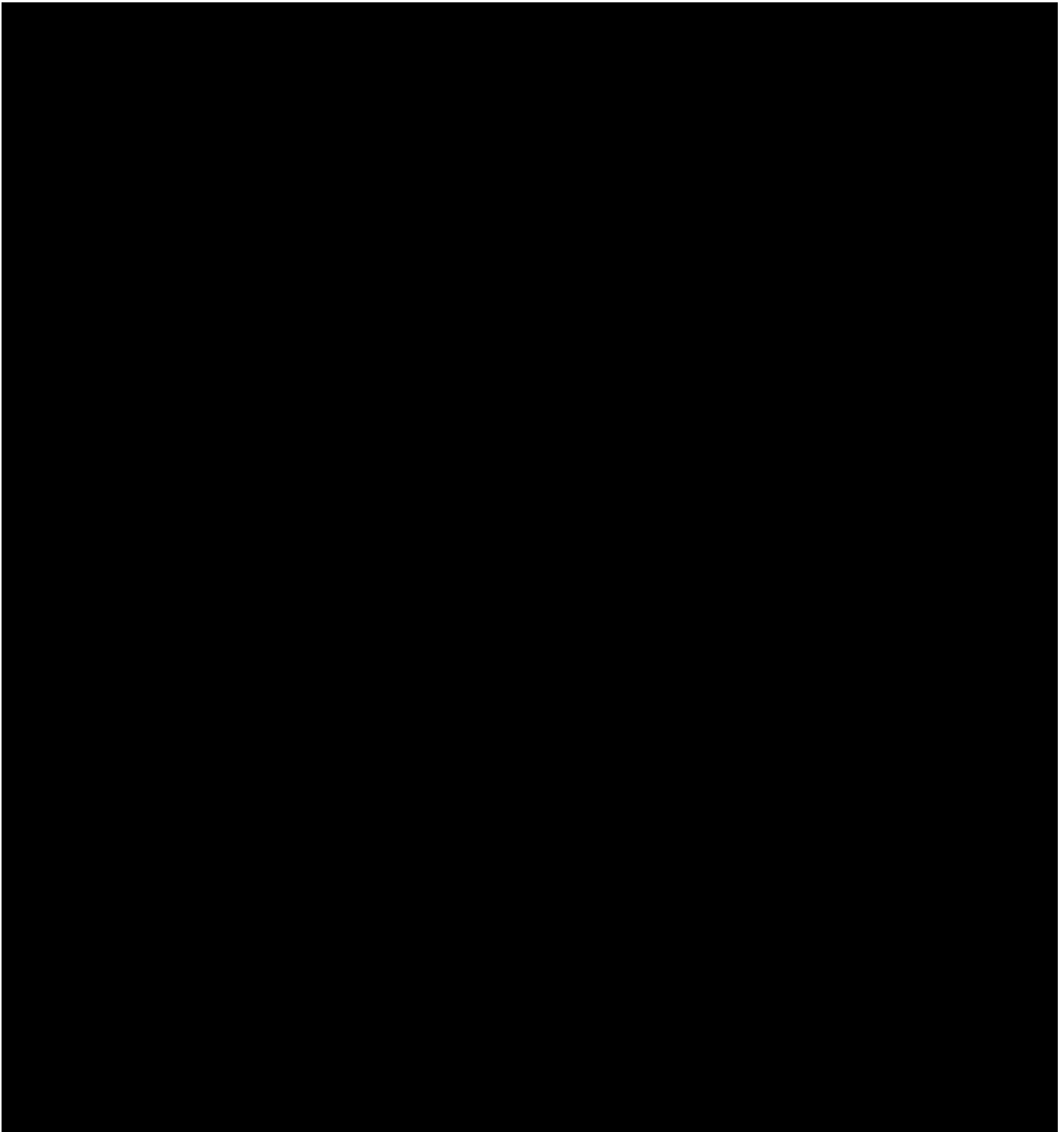
- Frequency of Treatment-Emergent Device Deficiencies
- Listing of Treatment-Emergent Device Deficiencies
- Listing of Device Deficiencies Prior To Treatment Exposure

7   SAMPLE SIZE AND POWER CALCULATIONS

Sample size calculation is based on a prior clinical study (▮▮▮▮▮▮▮ which evaluated performance of Alcon serafilcon A and AOHP.
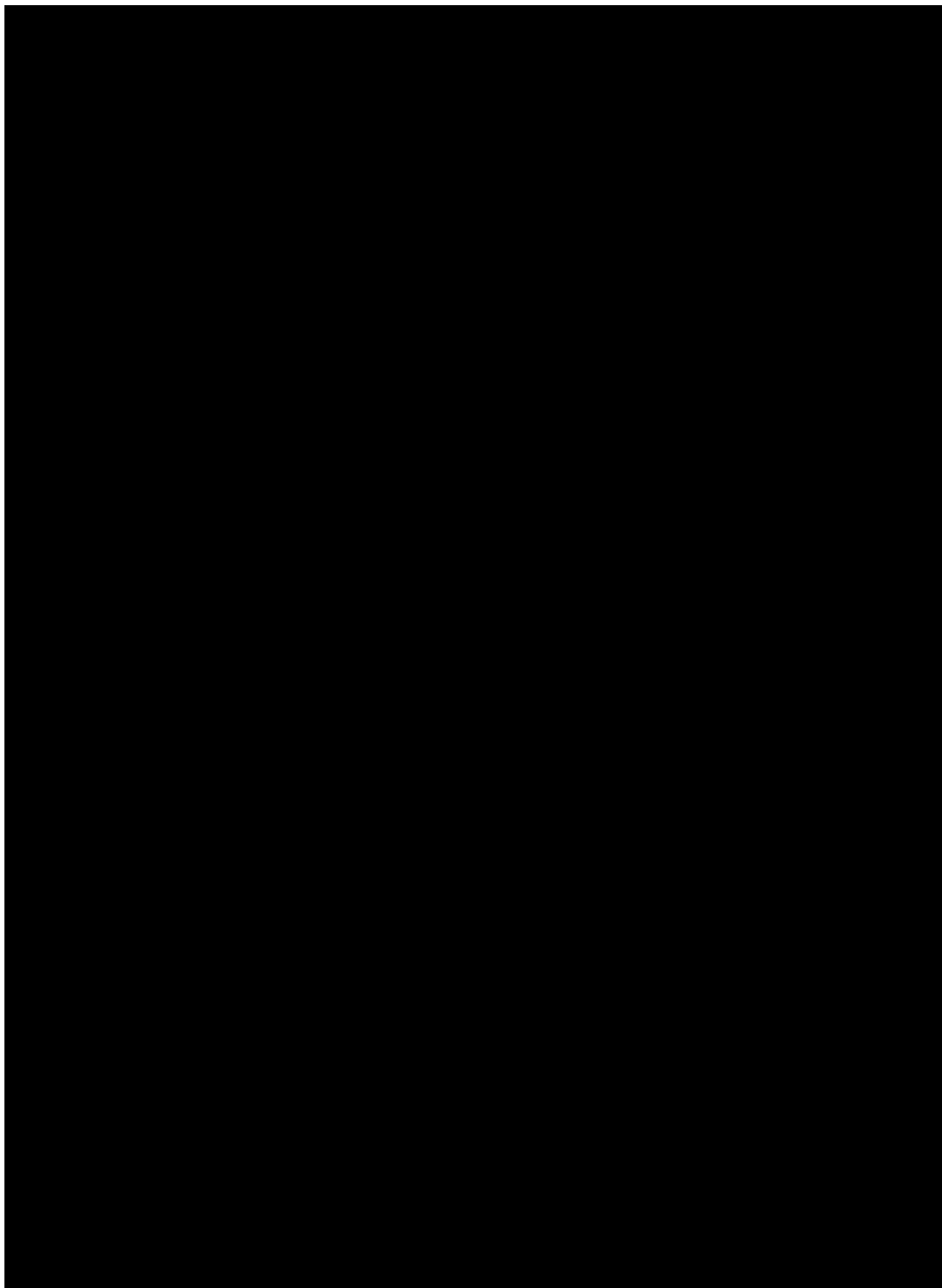
8 REFERENCES

Not applicable.

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 2.0 of the study protocol.
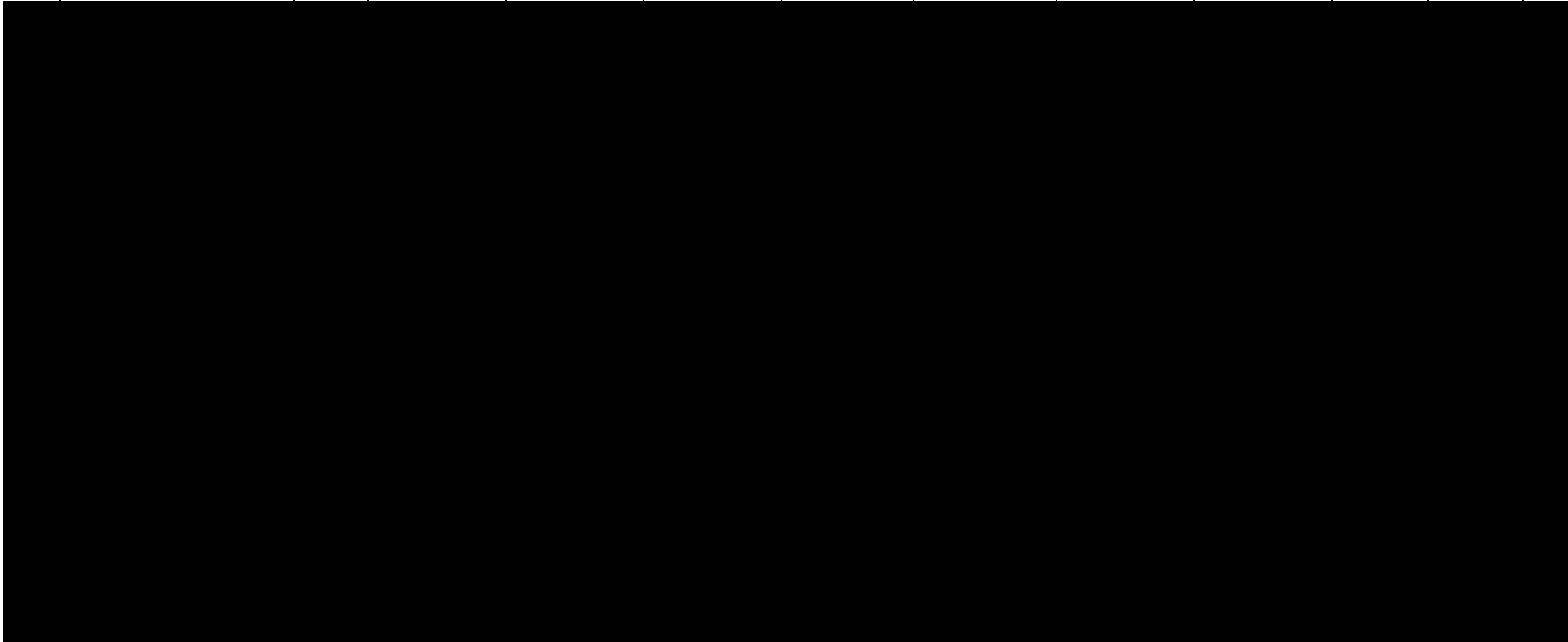
10 APPENDIX

Table 10-1   **Schedule of Study Procedures and Assessments**

Procedure/ Assessment	Pres cree ning	Visit 1 Screening / Baseline	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unsche duled Visit
			Visit 2 Dispense Lens 1 [2 (at least 48 hours) – 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	Visit 3 Week 1 Follow-up Lens 1 [7 -0/+ 1 days after Visit 2]	Visit 4 Week 2 Follow- up Lens 1 [7 -0/+ 1 days after Visit 3)]	Visit 5 Dispense Lens 2 [2 (at least 48 hours) – 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	Visit 6 Week 1 Follow-up Lens 2 [7 -0/+ 1 days after Visit 5]	Visit 7 Week 2 Follow-up Lens 2 /Exit [7 -0/+ 1 days after Visit 6)]		
Informed Consent		X								
Demographics		X								
Medical History		X	X	X	X	X	X	X	X	X
Concomitant Medications		X	X	X	X	X	X	X	X	X
Inclusion/ Exclusion		X								
Habitual lens (brand, lens power, lens care)		X								
In office subjective questionnaire • Habitual lens wear and rewetting drop usage		X								

Procedure/ Assessment	Pres cree ning	Visit 1 Screening / Baseline	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unshe duled Visit
			Visit 2 Dispense Lens 1 [2 (at least 48 hours) – 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	Visit 3 Week 1 Follow-up Lens 1 [7 -0/+ 1 days after Visit 2]	Visit 4 Week 2 Follow- up Lens 1 [7 -0/+ 1 days after Visit 3)]	Visit 5 Dispense Lens 2 [2 (at least 48 hours) – 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	Visit 6 Week 1 Follow-up Lens 2 [7 -0/+ 1 days after Visit 5]	Visit 7 Week 2 Follow-up Lens 2 /Exit [7 -0/+ 1 days after Visit 6)]		
Keratometry		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
VA w/ habitual correction+ (OD, OS, logMAR distance)*		X						X	X	(X)
Manifest refraction*		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
BCVA (OD, OS, logMAR distance with manifest refraction)		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
Biomicroscopy		X	X	X	X	X	X	X	X	X

Procedure/ Assessment	Pres cree ning	Visit 1 Screening / Baseline	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unsche duled Visit
			Visit 2 Dispense Lens 1 [2 (at least 48 hours) – 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	Visit 3 Week 1 Follow-up Lens 1 [7 -0/+ 1 days after Visit 2]	Visit 4 Week 2 Follow- up Lens 1 [7 -0/+ 1 days after Visit 3)]	Visit 5 Dispense Lens 2 [2 (at least 48 hours) – 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	Visit 6 Week 1 Follow-up Lens 2 [7 -0/+ 1 days after Visit 5]	Visit 7 Week 2 Follow-up Lens 2 /Exit [7 -0/+ 1 days after Visit 6)]		
Fitting of investigational products (trial assessments): (Test and Comparator)* - VA (logMAR distance) - Lens movement (Overall fit- primary and peripheral gazes) - Lens position (Centration)		X								
Randomization		X								
Dispense study lenses			X	X		X	X			(X)
VA w/study lenses, (OD, OS, logMAR distance)			X	X	X	X	X	X	(X)	(X)

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	Pres cree ning	Visit 1 Screening / Baseline	Visit 2 Dispense Lens 1 [2 (at least 48 hours) – 4 days after Visit 1 (Washout period with habitual spectacles only after	Visit 3 Week 1 Follow-up Lens 1 [7 -0/+ 1 days after Visit 2]	Visit 4 Week 2 Follow- up Lens 1 [7 -0/+ 1 days after Visit 3)]	Visit 5 Dispense Lens 2 [2 (at least 48 hours) – 4 days after Visit 4 (Washout period with habitual spectacles only after	Visit 6 Week 1 Follow-up Lens 2 [7 -0/+ 1 days after Visit 5]	Visit 7 Week 2 Follow-up Lens 2 /Exit [7 -0/+ 1 days after Visit 6)]	Early Exit	Unsche duled Visit

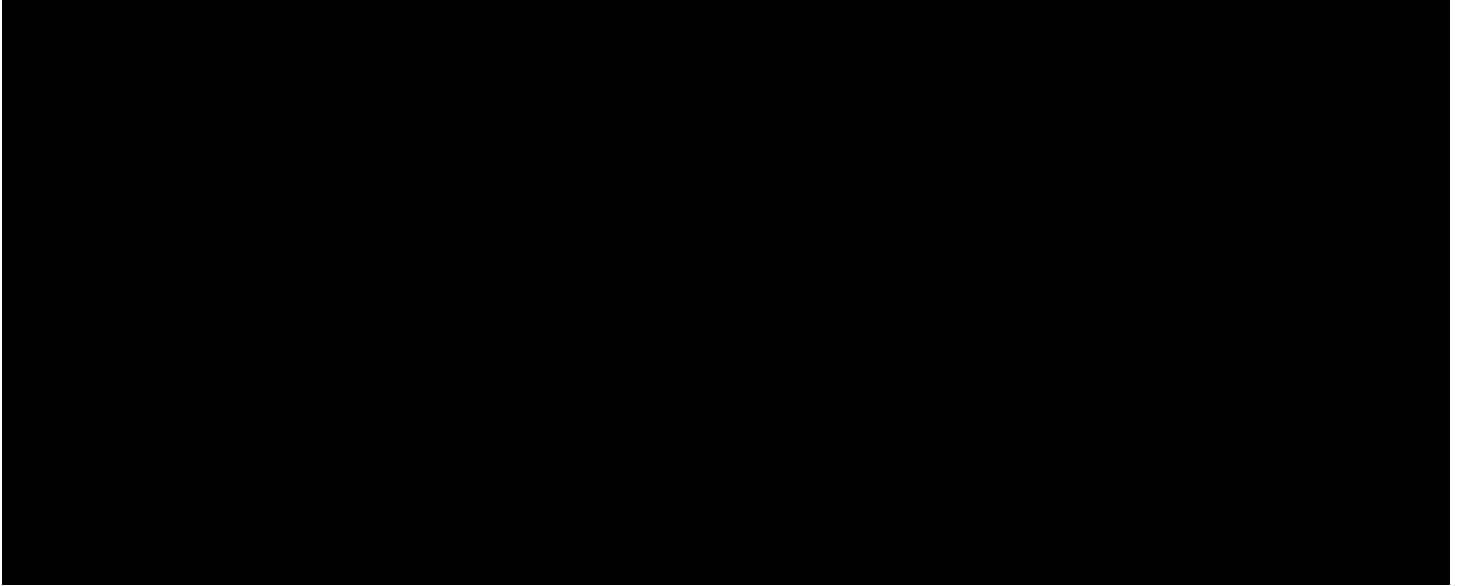| Procedure/ Assessment	Pres cree ning	Lens 1 (Period 1)				Lens 2 (Period 2)			Early Exit	Unsche duled Visit
		Visit 1 Screening / Baseline	Visit 2 Dispense Lens 1 [2 (at least 48 hours) – 4 days after Visit 1 (Washout period with habitual spectacles only after	Visit 3 Week 1 Follow-up Lens 1 [7 -0/+ 1 days after Visit 2]	Visit 4 Week 2 Follow- up Lens 1 [7 -0/+ 1 days after Visit 3)]	Visit 5 Dispense Lens 2 [2 (at least 48 hours) – 4 days after Visit 4 (Washout period with habitual spectacles only after	Visit 6 Week 1 Follow-up Lens 2 [7 -0/+ 1 days after Visit 5]	Visit 7 Week 2 Follow-up Lens 2 /Exit [7 -0/+ 1 days after Visit 6)]		
AEs [a]		X	X	X	X	X	X	X	X	X
Device deficiencies		X	X	X	X	X	X	X	X	X
Exit Form		(X)	(X)	(X)	(X)	(X)	(X)	X	X	(X)

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(X) Assessment performed as necessary, e.g., decrease of VA by 2 lines or more with investigational product (IP)

* Source only (source transferred to the sponsor upon request)

α Comprehensive details of all AEs will be documented in the source records, however limited collection will be utilized in the eCRF (see MOP for details).

Signature Page for V-CLN-0038497 v1.0

Signature Page for V-CLN-0038497 v1.0