Alcon

Statistical Analysis Plan for CLY935-C018 / NCT05056987
Title: Clinical Assessment of Two Daily Wear Reusable Soft Silicone Hydrogel Contact Lenses

[redacted]

Executive Summary:

Key Objectives:

The primary objective of this clinical study is to evaluate visual acuity (VA) of the TOTAL30 soft contact lens (TOTAL30) and the ACUVUE OASYS® with HYDRACLEAR® PLUS (AOHP) soft contact lens in a daily wear modality.

Decision Criteria for Study Success:

Not applicable.

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List of Tables

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1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective is to evaluate visual acuity (VA) of the TOTAL30 soft contact lens and the AOHP soft contact lens.

[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, [redacted] bilateral crossover, controlled, subject-masked
Study Population	Volunteer subjects aged ≥ 18 years who are any habitual spherical soft contact lens wearers, have at least 3 months of contact lens wearing experience, and who would be willing to wear the study lenses for at least 5 days per week and at least 8 hours per day. Pregnant and breastfeeding women are excluded for this study. Target to complete: 32 [redacted] Planned to enroll: ~36
Number of Sites	1 UK
Test Product(s)	TOTAL30 soft contact lenses (TOTAL30) [redacted]
Comparator Product	ACUVUE OASYS® with HYDRACLEAR PLUS® soft contact lenses (AOHP) [redacted]
Planned Duration of Exposure	Test Product: 28 days Comparator Product: 14 days

Visits	Pre-screening Visit 1: Screen/Baseline/Dispense Pair 1 [Day 1] Visit 2: Follow-up Pair 1/Dispense Pair 2 [AOHP Day 14 (-3/+7 days); TOTAL30 Day 28 (-3/+7 days)] Visit 3: Follow-up Pair 2/Exit [AOHP Day 14 (-3/+7 days); TOTAL30 Day 28 (-3/+7 days)] [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 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 ratio to receive treatment in crossover sequence of test product then comparator product or comparator product then test product, respectively.

Sequence	[redacted]	**Lens Name**
Sequence 1	[redacted]	TOTAL30/AOHP
Sequence 2	[redacted]	AOHP/TOTAL30

[redacted]

- [redacted]
- [redacted]

1.4 Masking

This is study is subject-masked.

[redacted]

[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 SET

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.

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

3 SUBJECT CHARACTERISTICS AND STUDY CONDUCT SUMMARIES

The following tables will be presented:

- Subject Disposition by Lens Sequence
- Analysis Set by Lens
- Analysis Set by Lens Sequence
- Subject Accounting by Lens Sequence
- Demographics Characteristics by Lens Sequence
- Baseline Characteristics by Lens Sequence [redacted]

In addition, the following subject listings will be provided:

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

4 EFFECTIVENESS ANALYSIS STRATEGY

This study defines one primary endpoint [redacted] will use the Safety Analysis Set.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with frequencies and percentages from each category.

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

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

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

[redacted]

[redacted]

4.2 Effectiveness Hypotheses

Primary Effectiveness

No inferences are to be made on the primary effectiveness endpoint; therefore, no hypotheses are formulated.

[redacted]

4.6 Interim Analysis for Effectiveness

No interim analysis is planned for 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
    - 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 pair 1 and Visit 3 for pair 2.

5.3.1 Adverse Events

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

Analysis and 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 products

- Between-treatment: an event that occurs one day after last exposure to period 1 (Pair 1) study lenses but prior exposure to period 2 (Pair 2) study lenses

- Treatment-emergent: an event that occurs from exposure to period 1 (Pair 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 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:

- Summary Statistics 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
- Listings of Subjects with Infiltrates

5.3.3 Device Deficiencies

The following table and supportive listings will be provided:

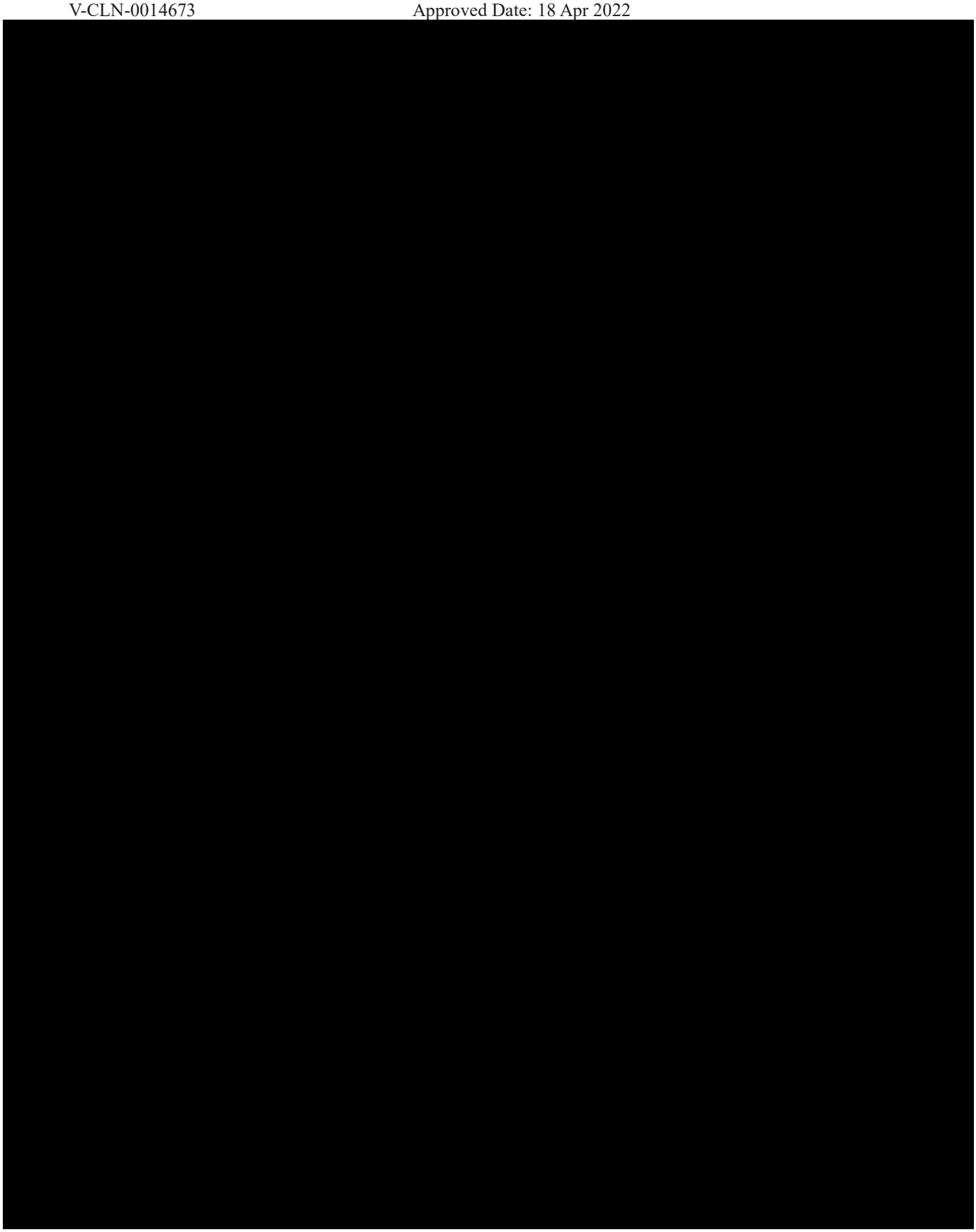
- Frequency of Treatment-Emergent Device Deficiencies
- Listing of Treatment-Emergent Device Deficiencies
- Listing of Device Deficiencies Prior To Treatment Exposure

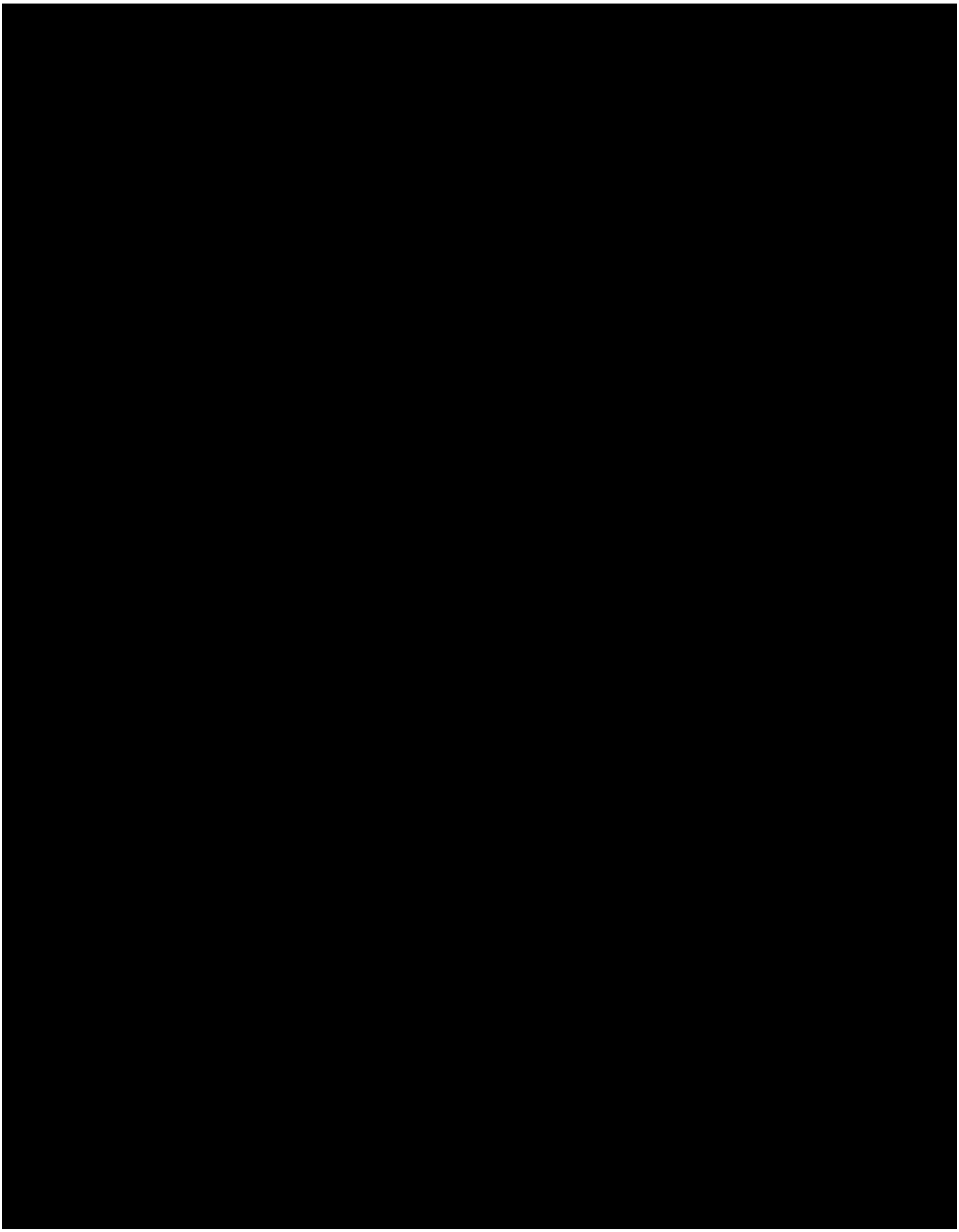
6 ANALYSIS STRATEGY FOR OTHER ENDPOINTS

Not Applicable.

7 SAMPLE SIZE AND POWER CALCULATIONS

Given the feasibility nature of this study, sample size calculation is not relevant.





10 APPENDIX

Table 10-1 Measurement Scales for Ophthalmic Assessments

Procedure/ Assessment	Pre-screening	[redacted]	LENS PAIR 1		[redacted]	LENS PAIR 2	Early Exit	USV
			Visit 1 Screen/Baseline/ Dispense Pair 1	Visit 2 Follow-up Pair 1[$] / Dispense Pair 2		Visit 3 Follow-up Pair 2[$]/Exit		
			Visit Window[Ω]			Visit Window[Ω]		
			Day 1	AOHP = [Day 14 (-3/+7 days)] TOTAL30 = [Day 28 (-3/+7 days)]		AOHP = [Day 14 (-3/+7 days)] TOTAL30 = [Day 28 (-3/+7 days)]		
Pre-Screening Consent	X							
Informed Consent			X					
Demographics			X					
Medical History*			X	X		X	X	X
Pregnancy Form*				(X)		(X)	(X)	X
Concomitant Medications*			X	X		X	X	X
Inclusion/Exclusion			X					
Habitual (lens brand, lens power*, lens care)			X					
Keratometry readings (OD, OS)			X					
Manifest refraction*			X	(X)		(X)	(X)	(X)
BCVA* (OD, OS, logMAR distance with manifest refraction)			X	(X)		(X)	(X)	(X)
Biomicroscopy			X	X		X	X	(X)
[redacted]								
Randomization			X					

Procedure/ Assessment	Pre-screening	[redacted]	LENS PAIR 1		[redacted]	LENS PAIR 2	Early Exit	USV
			Visit 1 Screen/Baseline/ Dispense Pair 1	Visit 2 Follow-up Pair 1$ / Dispense Pair 2		Visit 3 Follow-up Pair 2$/Exit		
			Visit Window Ω			Visit Window Ω		
			Day 1	AOHP = [Day 14 (-3/+7 days)] TOTAL30 = [Day		AOHP = [Day 14 (-3/+7 days)] TOTAL30 = [Day		
[redacted]								
VA w/ study lenses, (OD, OS, logMAR distance)			X (optimization and baseline measurements for both study lens types)	X (lens pair 1)		X (lens pair 2)	X	X
[redacted]								
Slit-lamp photo/video of study lenses*			(X)	(X)		(X)	(X)	(X)
Dispense (provide) study lenses			X	X [redacted]				(X)
[redacted]								

Procedure/ Assessment	Pre-screening	[redacted]	LENS PAIR 1		[redacted]	LENS PAIR 2	Early Exit	USV
			Visit 1 Screen/Baseline/ Dispense Pair 1	Visit 2 Follow-up Pair 1[$] / Dispense Pair 2		Visit 3 Follow-up Pair 2[$]/Exit		
			Visit Window[Ω]			Visit Window[Ω]		
			Day 1	AOHP = [Day 14 (-3/+7 days)] TOTAL30 = [Day		AOHP = [Day 14 (-3/+7 days)] TOTAL30 = [Day		
[redacted]								
AEs[redacted]			X	X		X	X	X
Device deficiencies			X	X		X	X	X
Exit Form			(X)	(X)		X	X	(X)

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

USV = Unscheduled Visit

* Source only

[redacted]

[$] Subjects are required to wear the study lenses at least 6 hrs on the day of follow-up visits prior to the visit. Follow-up visit time to be within ±2 hours of baseline visit time.

[redacted]

[Ω]Visit 2 and 3 visit window and exposure period is dependent on the randomized treatment sequence. AOHP exposure period is to be 14 days (-3/+7 days) and TOTAL30exposure period is to be 28 days (-3/+7 days)