Alcon

Statistical Analysis Plan for CLV201-C002 / NCT05211739
Title: Clinical Assessment of a Daily Wear Monthly Replacement Silicone Hydrogel Toric Contact Lens

[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 is to evaluate visual acuity (VA) of the [redacted] Toric soft contact lenses [redacted] Toric).

Decision Criteria for Study Success:

Decision criteria for study success are not applicable for this study.

Table of Contents

List of Tables

List of Figures

1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

PRIMARY OBJECTIVE

The primary objective of this study is to evaluate visual acuity of the [redacted] Toric soft contact lenses.

[redacted]

1.2 Study Description

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

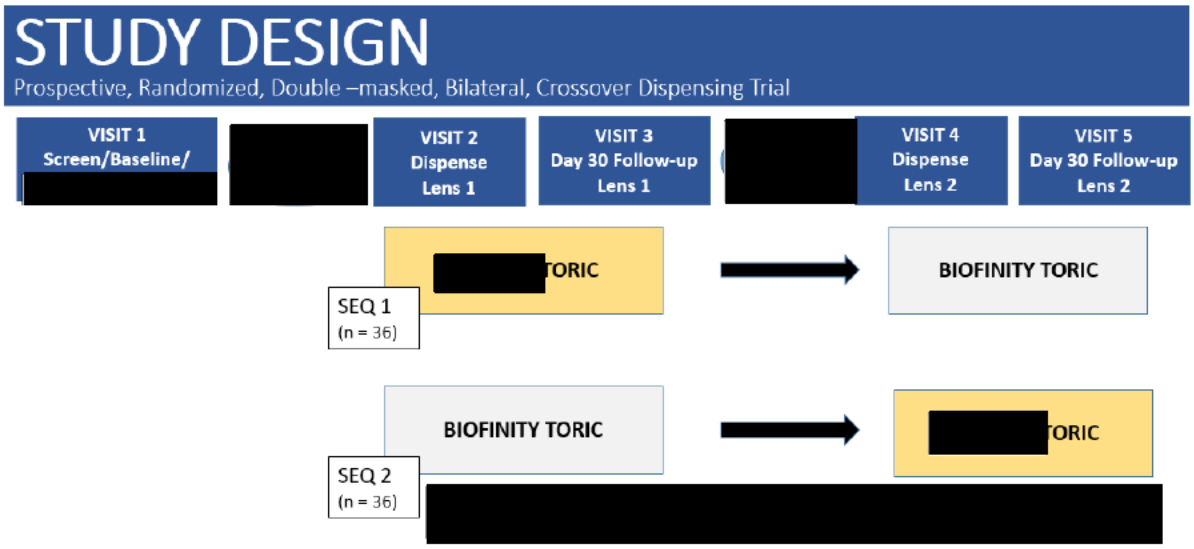
Table 1-1 Study Description Summary

Study Design	Prospective, randomized, double-masked, bilateral crossover
Study Population	Volunteer subjects aged 18 or over who are habitual toric weekly/monthly soft contact 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. Target to complete: 58 Planned to enroll: ~72
Number of Sites	~ 6 US
Test Product	[redacted] Toric soft contact lenses [redacted] Toric; lehfilcon A; LID205255)
Comparator Product	CooperVision® Biofinity® Toric contact lenses (Biofinity Toric; comfilcon A)
Planned Duration of Exposure	~60 days total duration (test and comparator) Test Product: 30 (-1/+3) days Comparator Product: 30 (-1/+3) days
Visits	Visit 1: Screen/Baseline [redacted] Visit 2: Dispense Lens 1 [redacted] [redacted]

	Visit 3: Day 30 Follow-up Lens 1 (Day 30 (-1/+3) Days) Visit 4: Dispense Lens 2 [redacted] Visit 5: Day 30 Follow-up Lens 2 / Exit (Day 30 (-1/+3) Days) [redacted]

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.

Subjects will be randomized in a 1:1 ratio to receive treatment (lens) in crossover sequence of Test product then Comparator product or Comparator product then Test product, respectively.

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	LID205255/Biofinity Toric	[redacted] Toric/Biofinity Toric
Sequence 2	Biofinity Toric/LID205255	Biofinity Toric/[redacted] Toric

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].
Therefore, any AE or device deficiency occurring after Informed Consent and prior to the initial exposure to the study lens (test or comparator) under evaluation in this clinical protocol will be listed as pre-treatment. 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]

[redacted]

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

Subject accounting and demographics characteristics 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

This study defines 1 primar [redacted] effectiveness endpoin[redacted] will use the FAS as the primary analysis set.

[redacted]

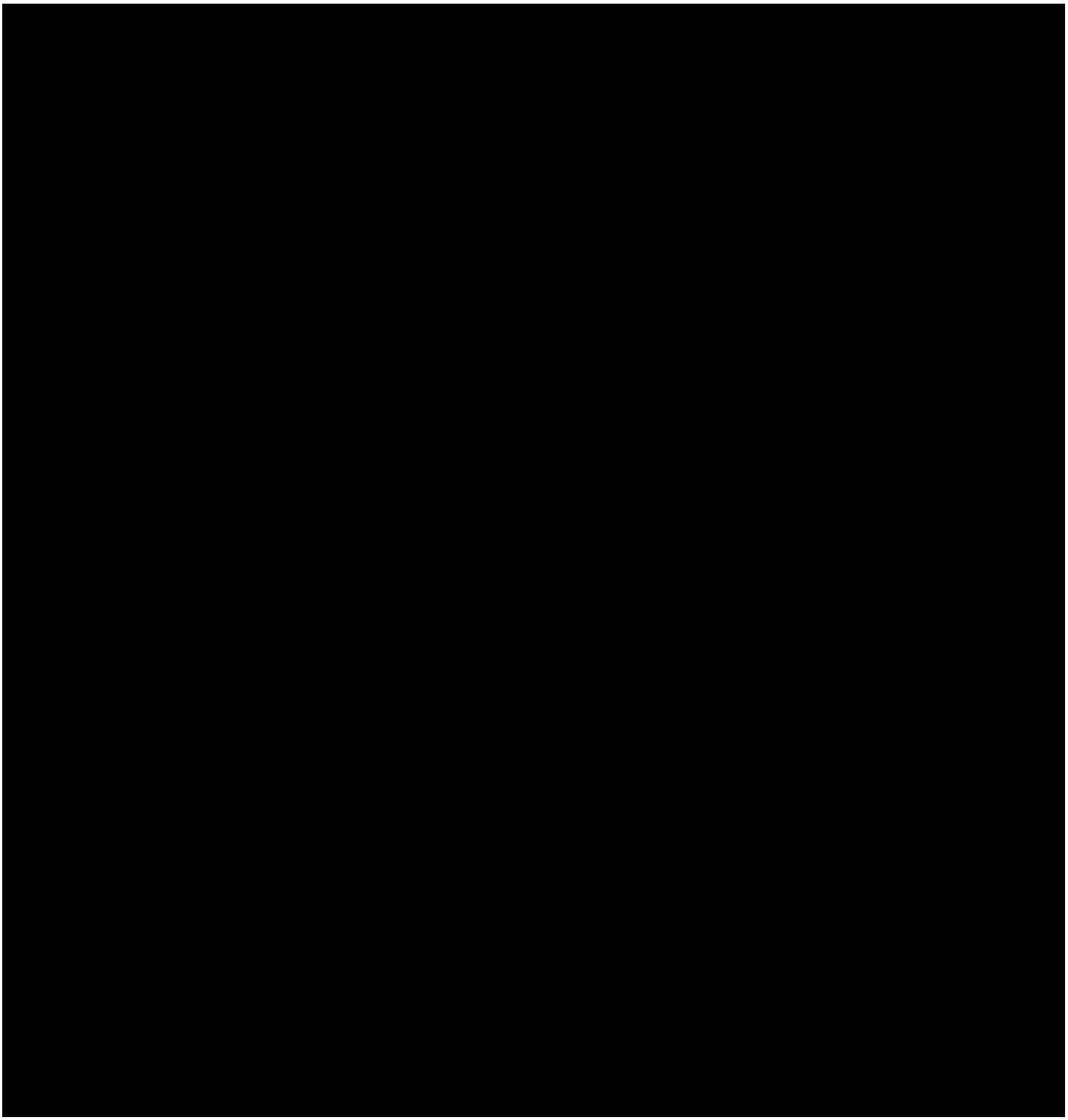
Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with frequencies and percentages from each category. Confidence intervals/limits may be provided as applicable.

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 [redacted] analyses.

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

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

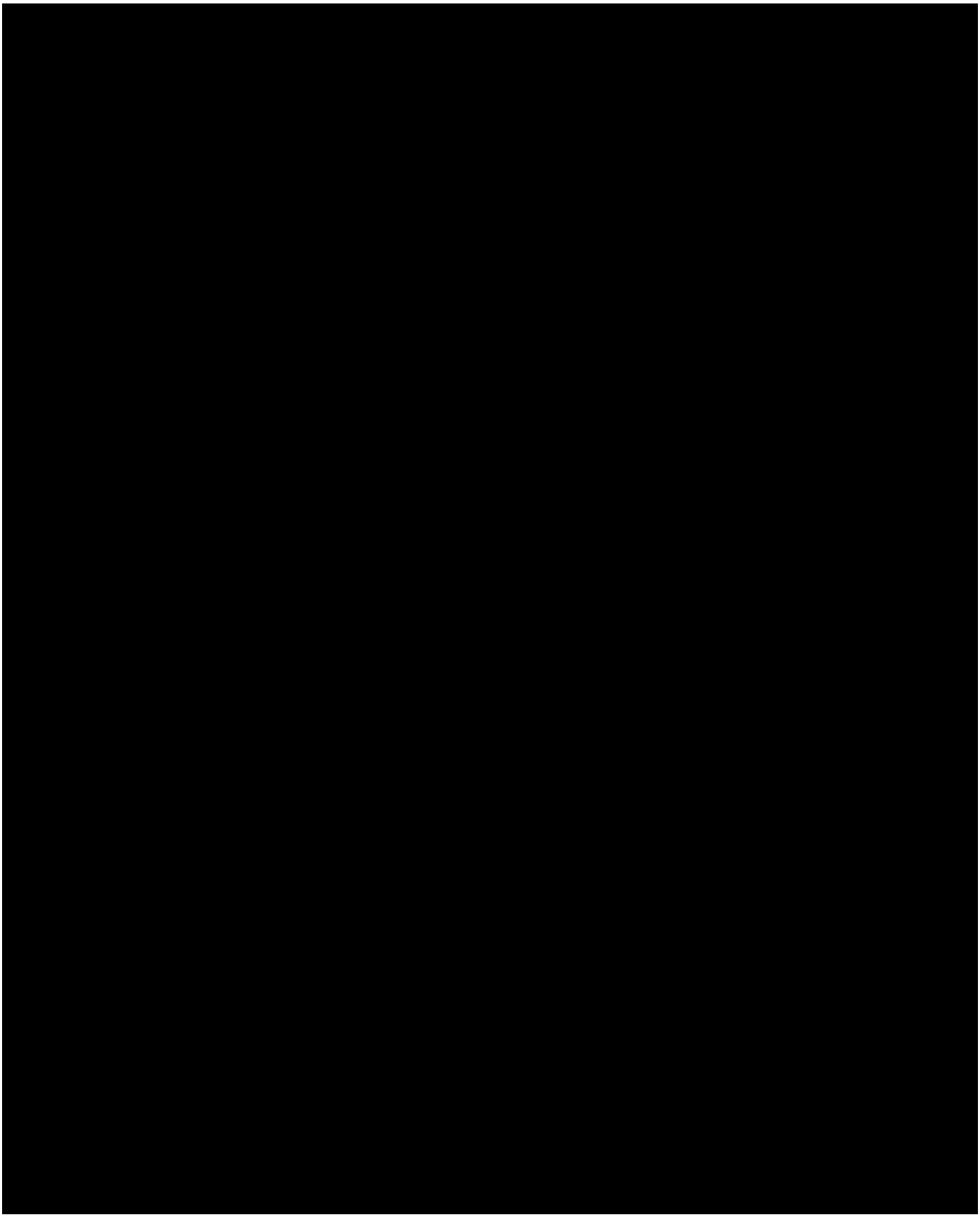
[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analysis

Descriptive statistics used for continuous variables will be presented.

[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 safety hypotheses planned in this study.

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 2 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 when a subject 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 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 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 of Chemosis
- Listing of Subjects With Increased Severity by 2 or More Grades in Biomicroscopy Findings [This listing will include all relevant visits 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

[redacted]

[redacted]

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

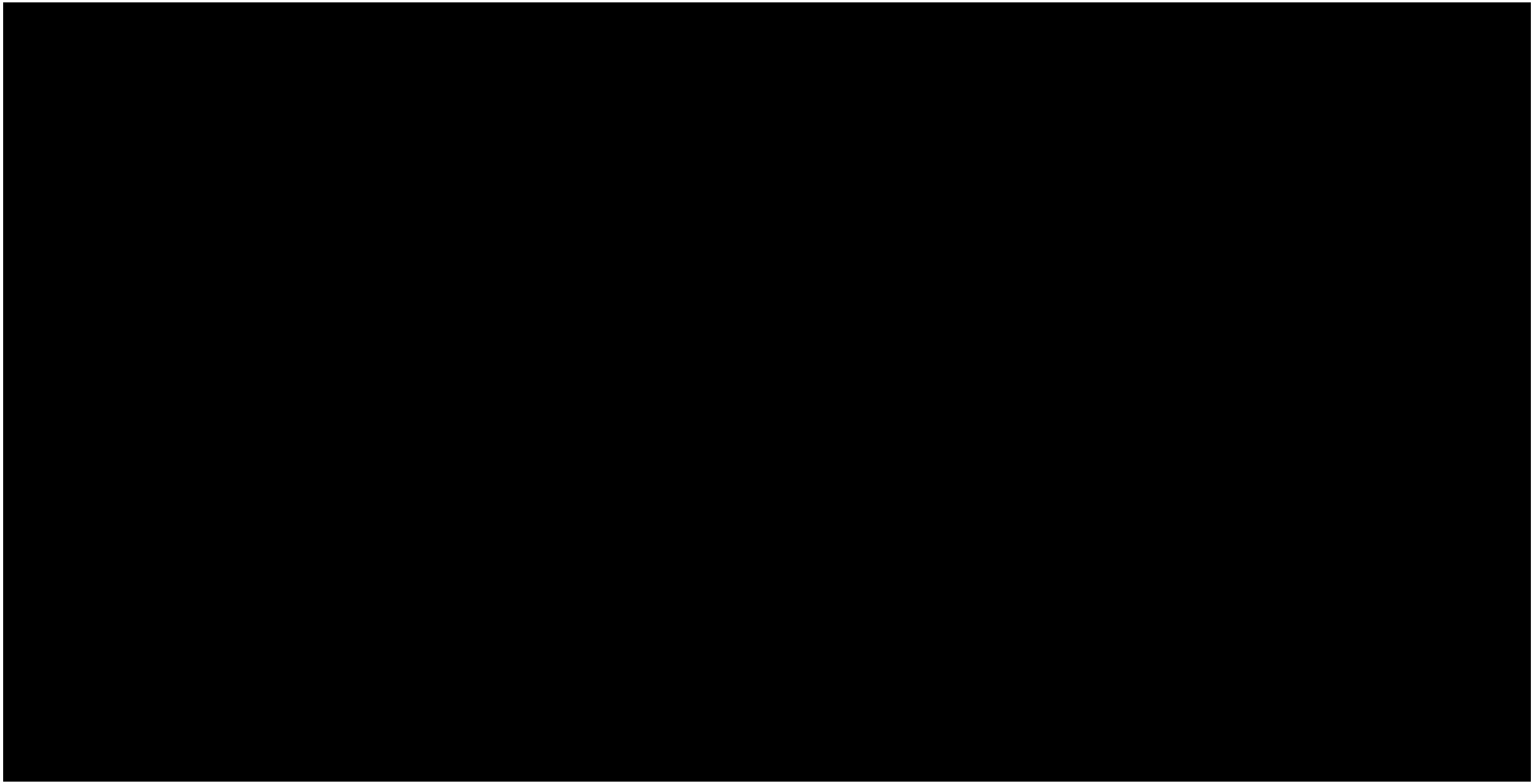
Table 10-1 Schedule of Study Procedures and Assessments

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen / Baseline [redacted]	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled visit**	**Early Exit**
Procedure/ Assessment		**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**Day 1** [redacted] **Visit 3]**	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
Informed Consent	X						
Demographics	X						
Medical History∞	X	X	X	X	X	X	X
Concomitant Medications∞	X	X	X	X	X	X	X
Inclusion/Exclusion	X						
Habitual lens information (brand, power*, lens care)	X						
VA with habitual correction (OD, OS, Snellen distance)*	X				X	(X)	X
Keratometry (OD, OS)	X						
Manifest refraction*	X	(X)	(X)	(X)	(X)	(X)	(X)
BCVA* (OD, OS, Snellen distance with manifest refraction)	X	(X)	(X)	(X)	(X)	(X)	(X)

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen / Baseline [redacted]	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled visit**	**Early Exit**
Procedure/ Assessment		**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
Biomicroscopy	X	X	X	X	X	X *Optional with ULR only*	X
[redacted]							
Randomization	X						
[redacted]							
Determine study lens power parameters*	X						
Dispense study lenses*		X		X		(X)	
[redacted]							

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen / Baseline [redacted] n	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled visit**	**Early Exit**
Procedure/ Assessment		**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
VA w/study lenses (OD, OS, logMAR distance)		X	X	X	X	X	X
[redacted]							

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screen / Baseline [redacted]	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 4 Dispense Lens 2**	**Visit 5 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled visit**	**Early Exit**
Procedure/ Assessment		**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**Day 1** [redacted]	**Day 30 (-1/+3) Days**	**N/A**	**N/A**
[redacted]							
Adverse Events	X	X	X	X	X	X	X
Device deficiencies	X	X	X	X	X	X	X
Exit Form	(X)	(X)	(X)	(X)	X		X



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