Clinical Performance Evaluation of Two Frequent Replacement

Silicone Hydrogel Toric Contact Lenses

STUDY ID

CLN109-C001

STATISTICAL ANALYSIS PLAN

NCT05959200

Alcon

Statistical Analysis Plan for CLN109-C001
Title: Clinical Performance Evaluation of Two Frequent Replacement Silicone Hydrogel Toric Contact Lenses

This version of the Statistical Analysis Plan is based on Version 3.0 of the study protocol.

Executive Summary:

Key Objectives:

To evaluate the percentage of Alcon serafilcon A Toric (LID226397) contact lenses with axis orientation within ±30 degrees from the 90º axis (ideal location), 10 minutes (min) after lens insertion at dispense visit.

Decision Criteria for Study Success:

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

Table of Contents

[redacted]

List of Tables

List of Figures

[redacted]

1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

PRIMARY OBJECTIVE

To evaluate the percentage of LID226397 contact lenses with axis orientation within ±30 degrees from the 90º axis (ideal location), 10 min after lens insertion at dispense visit.

[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, double-masked, multicenter.
Study Population	Volunteer subjects aged 18 or over who are habitual soft toric contact lens wearers (excluding AOfAHP habitual lens wearers and habitual daily disposable lens wearers) with normal eyes (other than correction for refractive error). Subjects should have at least 3 months wearing experience, wear these lenses at least 5 days per week and at least 10 hours per day.

	Target to complete: 80 Planned to enroll: ~92
Number of Sites	~6 United States
Test Product(s)	Alcon serafilcon A toric contact lenses (serafilcon A; LID226397)
Comparator Product(s)	ACUVUE® OASYS for ASTIGMATISM with HYDRACLEAR® PLUS contact lenses (AOfAHP; 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/Trial fit Visit 2: Dispense Lens 1 [3 – 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

[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.

[redacted]

Qualifying subjects will be randomized in a 1:1 ratio to receive treatment (lens) in one of the following crossover sequences:

- Sequence 1: LID226397/AOfAHP
- Sequence 2: AOfAHP/LID226397

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.

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, except for lenses used for lens fitting at Visit 1.

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; [redacted] keratometry readings; C[redacted]]

Subject accounting and demographics table 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 primary effectiveness [redacted]Effectiveness evaluations will use the FAS as the primary analysis set, except for endpoints relating to lens fitting, which will be summarized for all randomized subjects.

[redacted]

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 [redacted] effectiveness analyses.

[redacted]

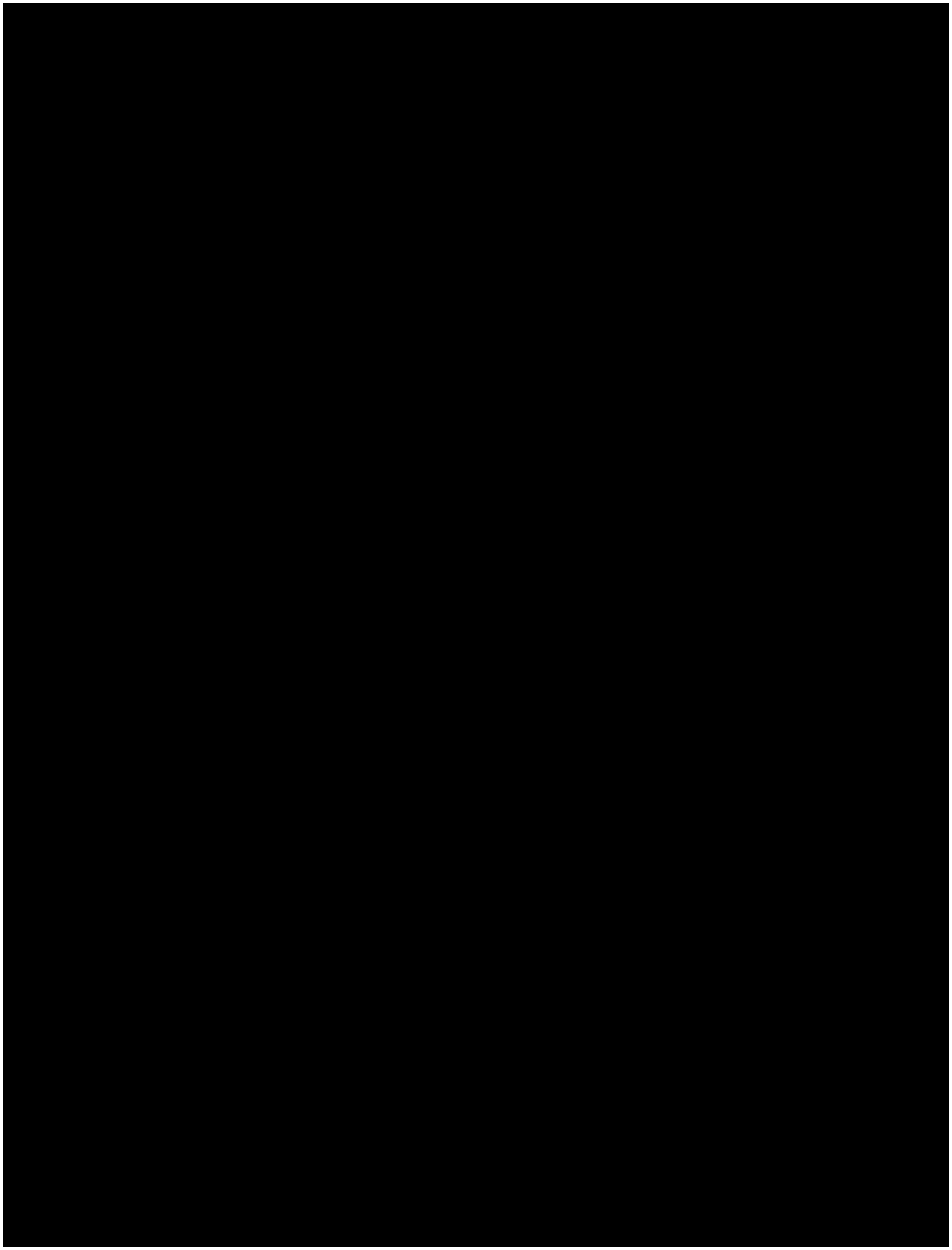
A listing of select effectiveness data will also be provided.

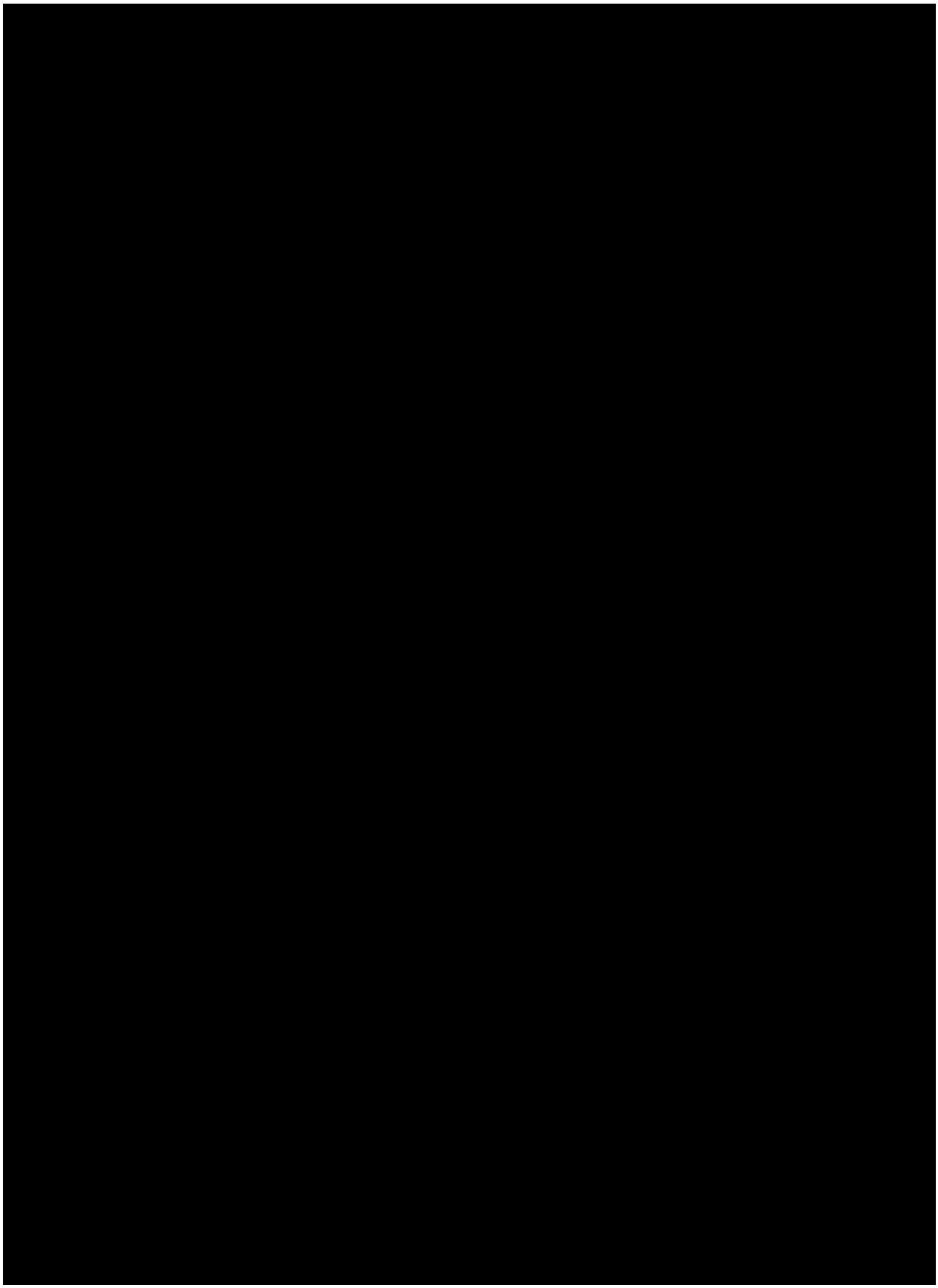
4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint is the percentage of LID226397 contact lenses with axis orientation, recorded as deviations from 90° axis, between -30 degrees and +30 degrees, inclusive, assessed at the dispense visit, 10 min after lens insertion.

[redacted]

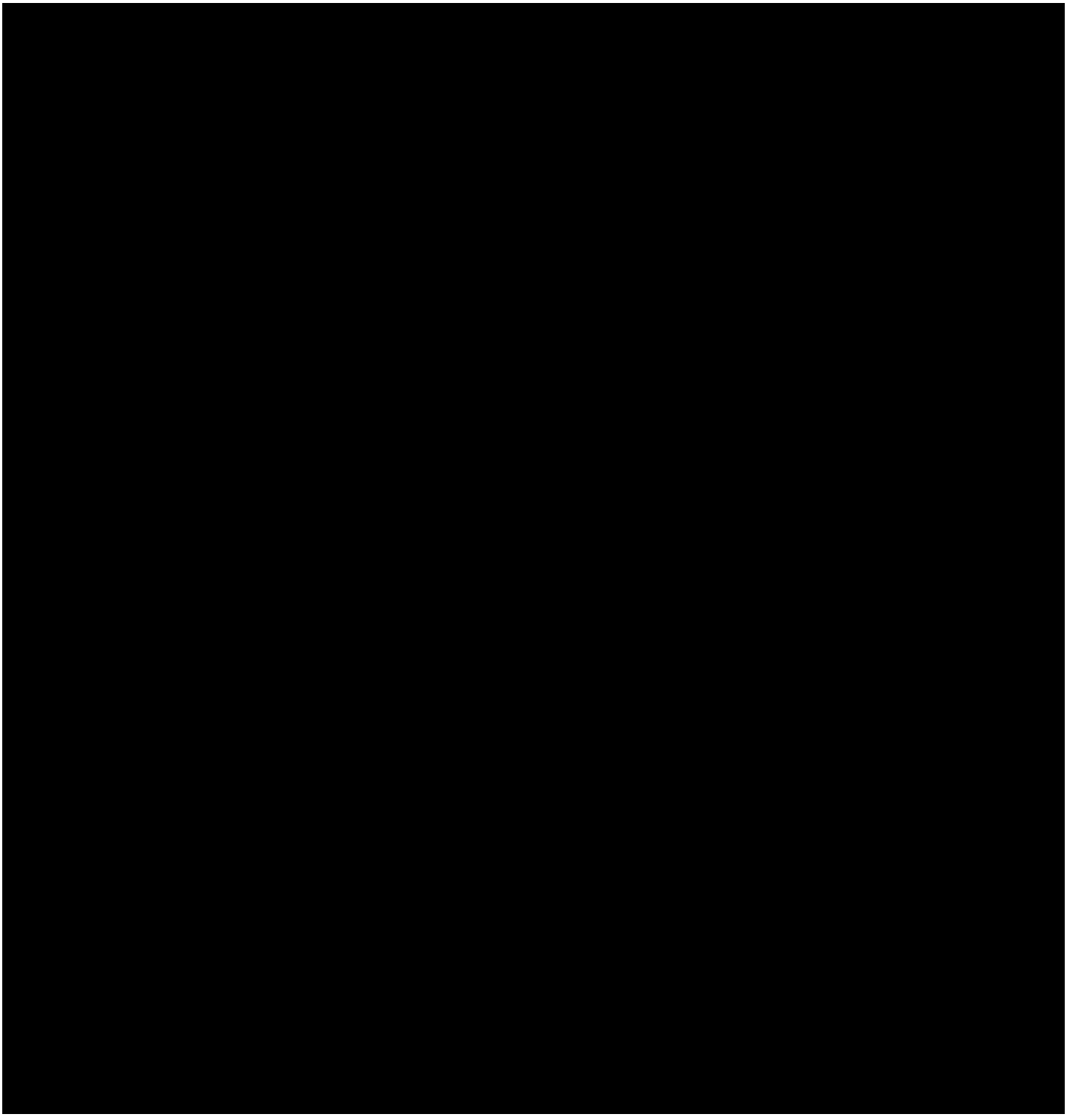




4.2 Effectiveness Hypotheses

Primary Effectiveness

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



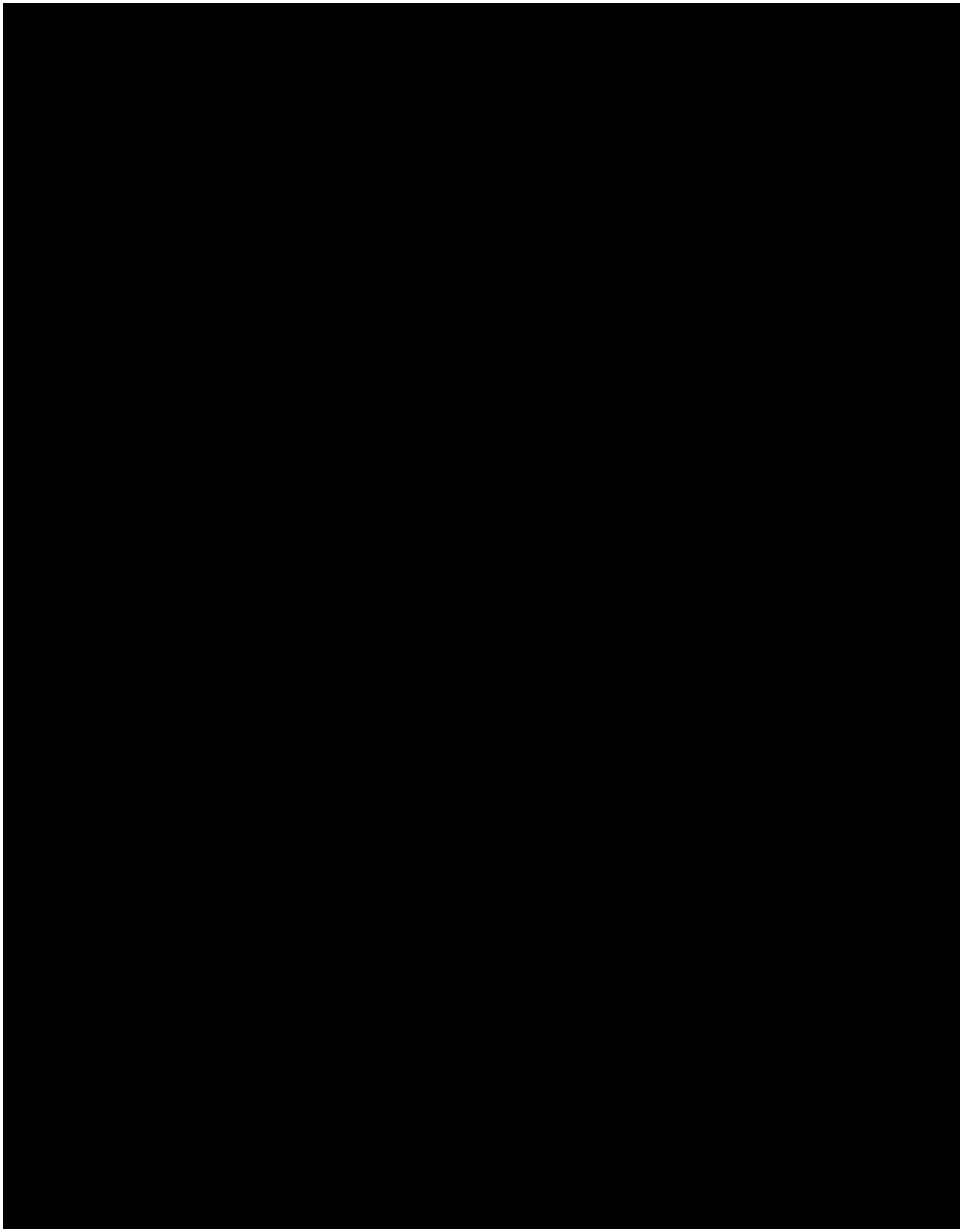
[redacted]

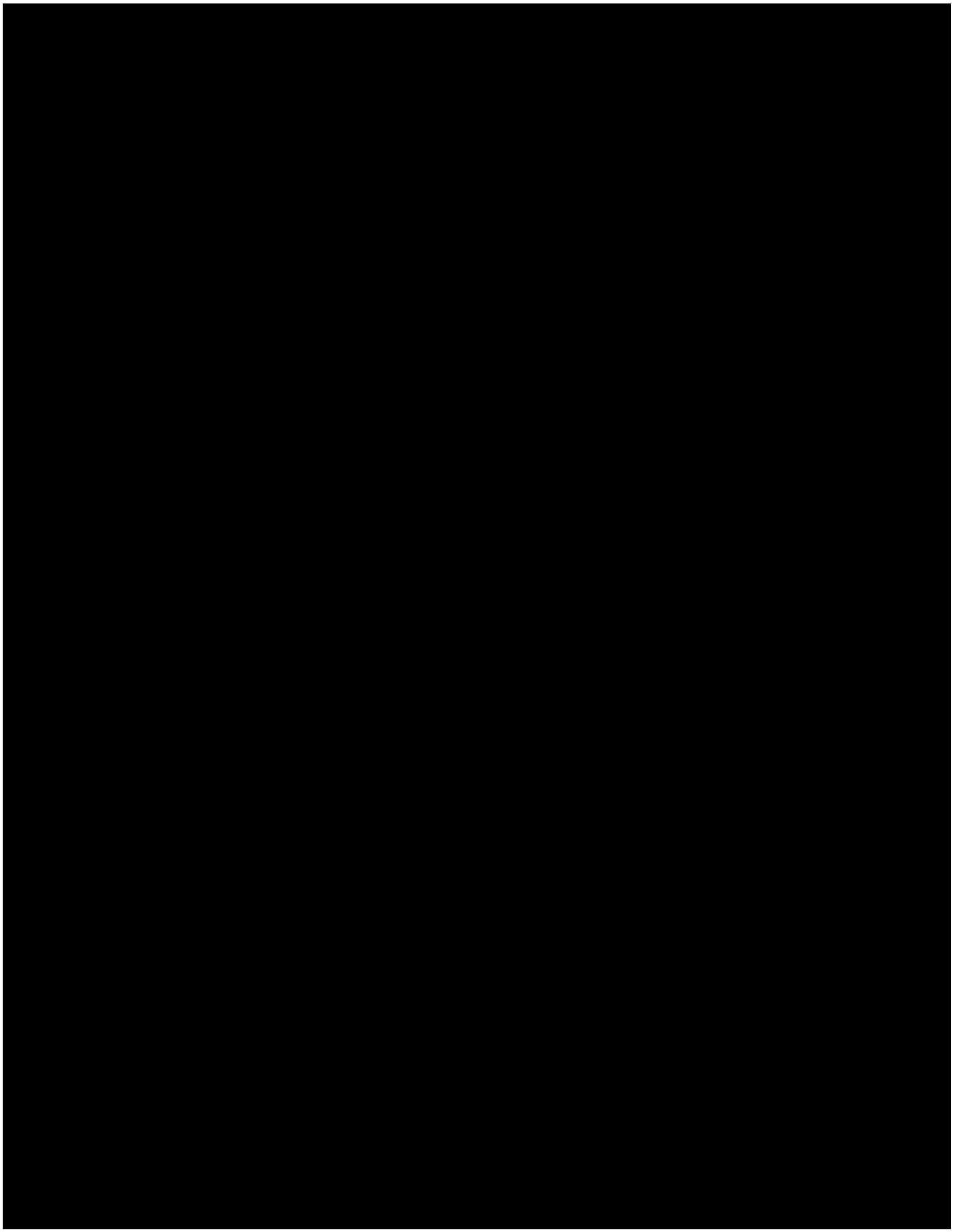
4.3 Statistical Methods for Effectiveness Analyses

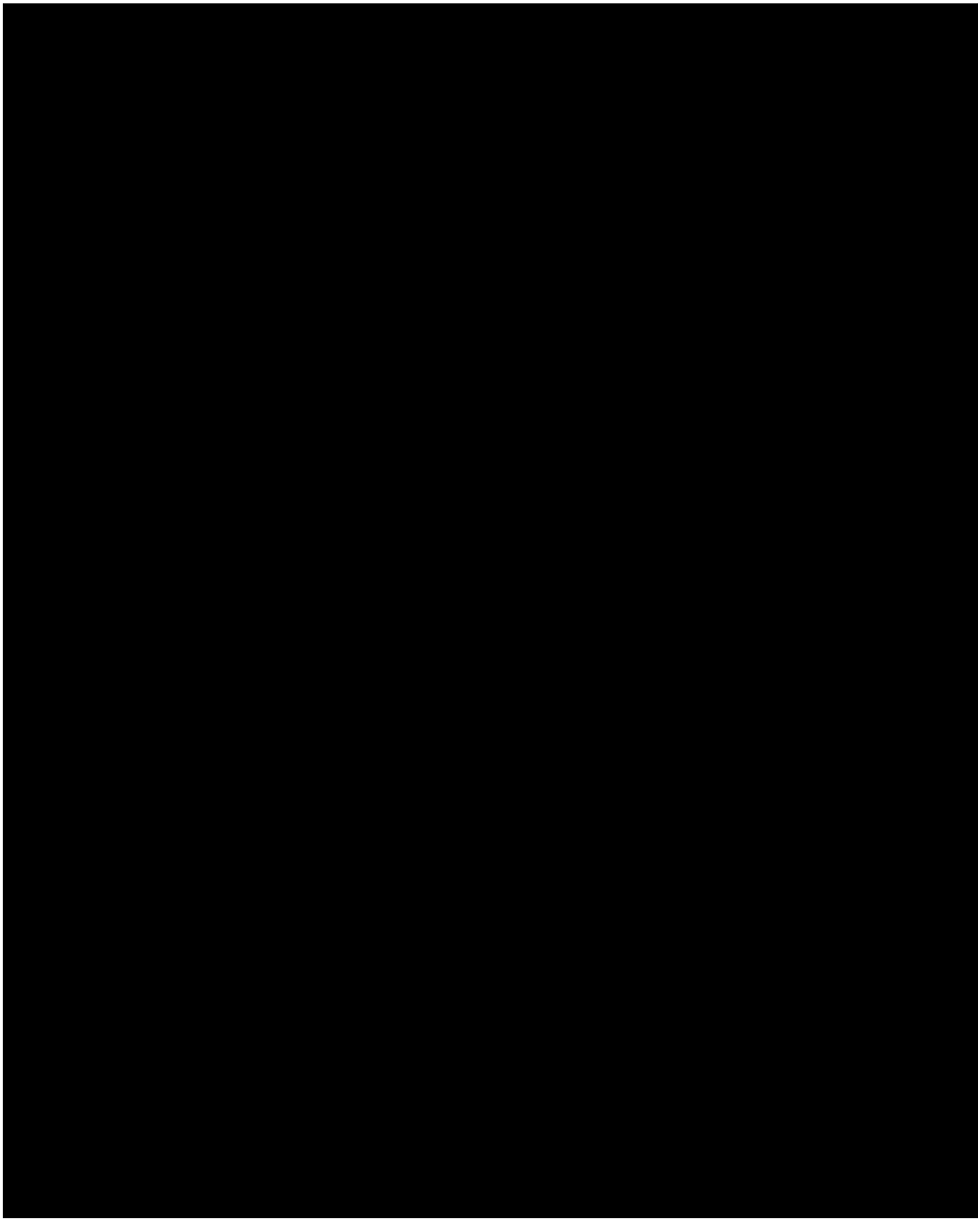
4.3.1 Primary Effectiveness Analyses

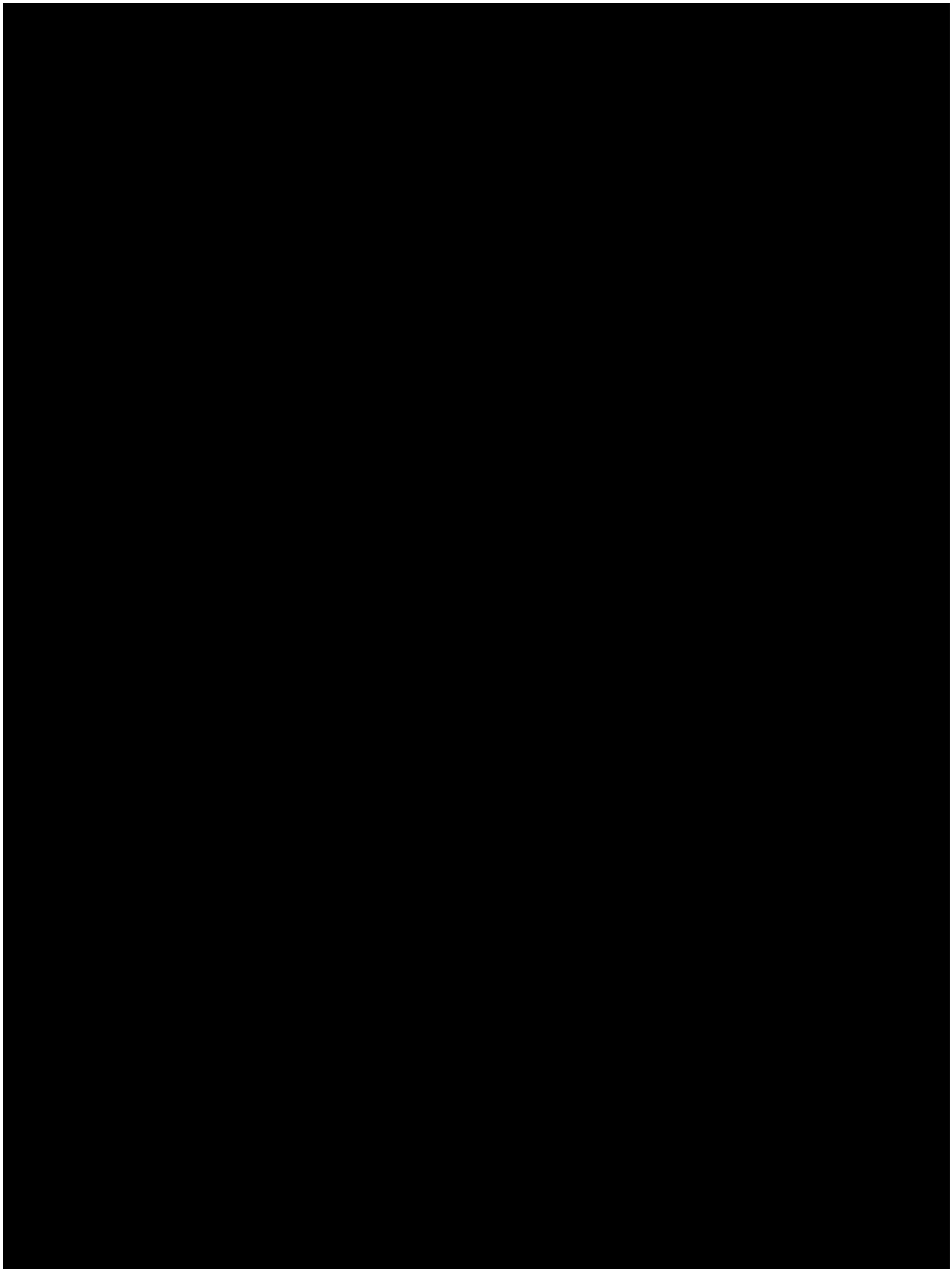
Frequencies and percentages will be provided, [redacted]

[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 carried out on the safety data.

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 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 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

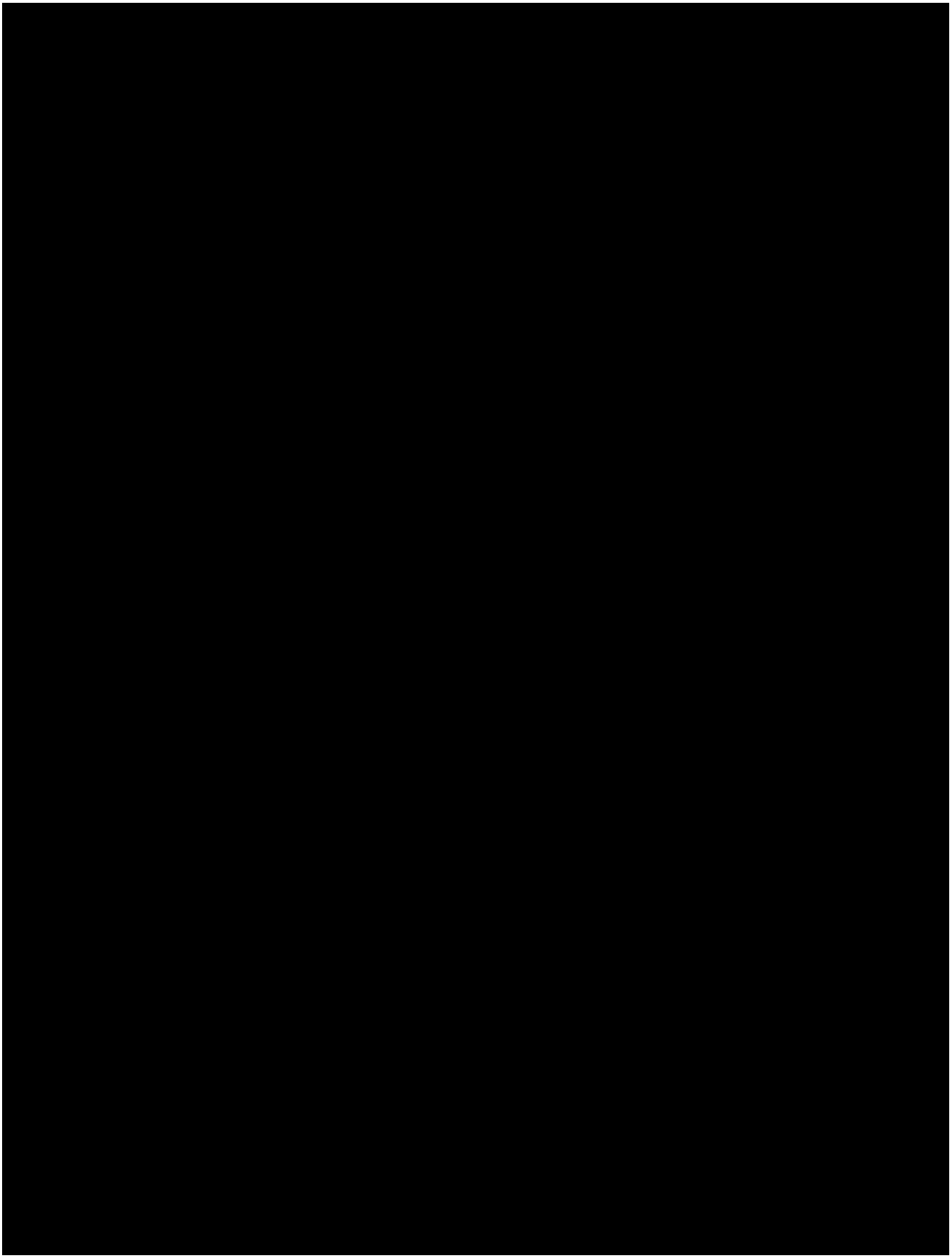
5.3.3 Device Deficiencies

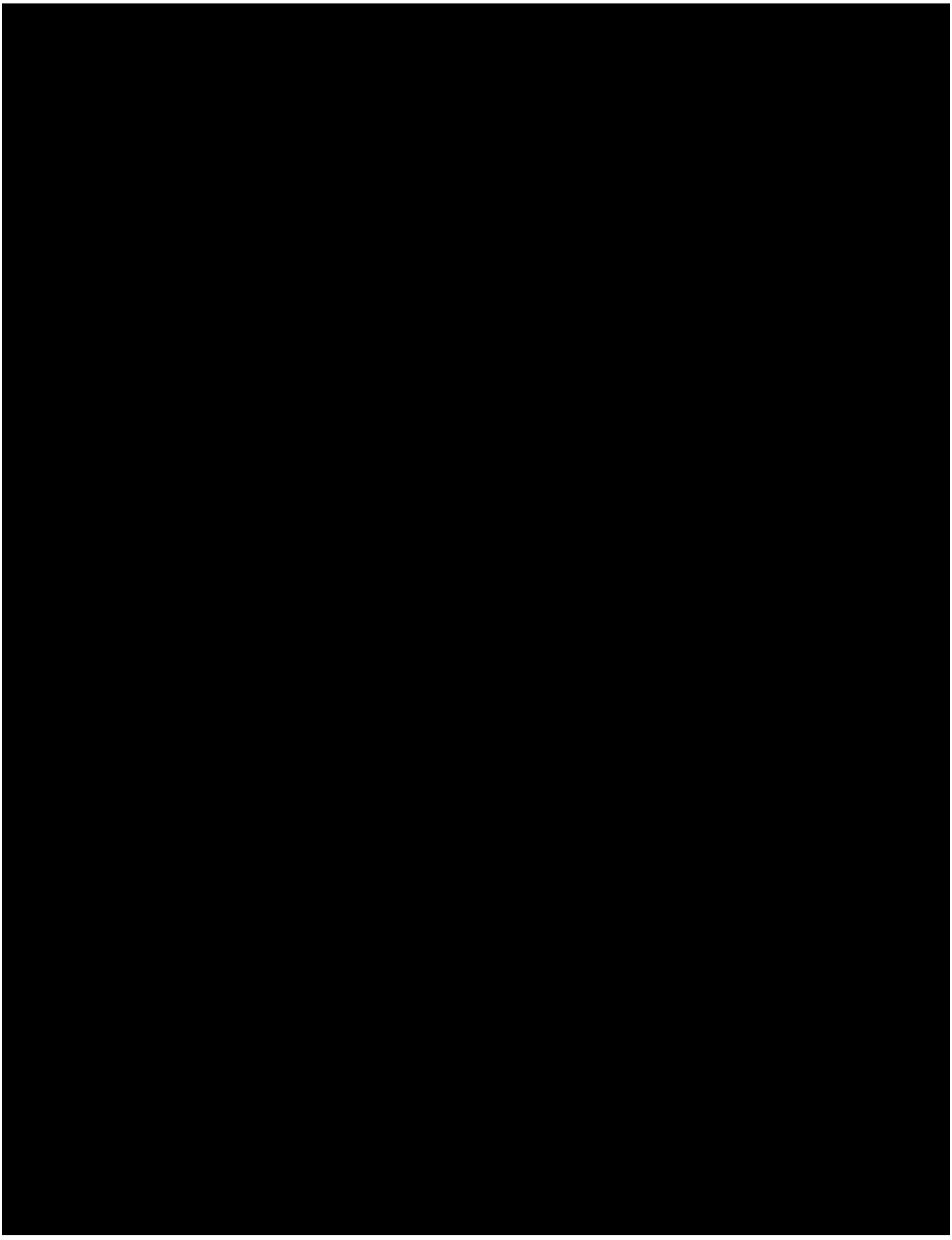
The following tables and supportive listings will be provided:

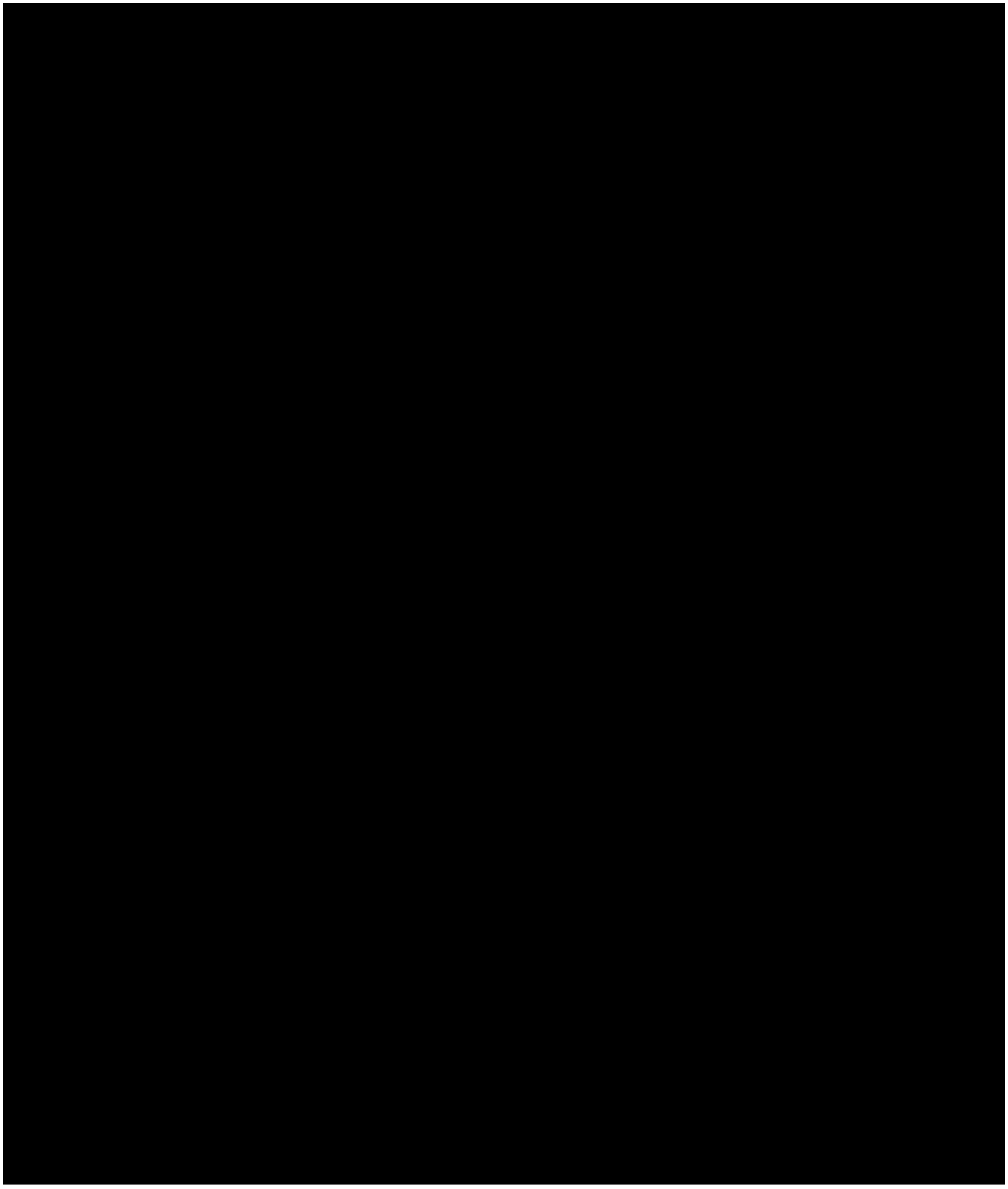
- Frequency of Treatment-Emergent Device Deficiencies
- Listing of Treatment-Emergent Device Deficiencies
- Listing of Device Deficiencies Prior To Treatment Exposure

8 REFERENCES

Not applicable.







10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening/ Baseline/ Trial fit**	**Visit 2 Dispense Lens 1** (3 - 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)	**Early Exit**	**Unscheduled Visit**
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								
[redacted]										
Habitual Lens wear & Drop Usage*		X								
Keratometry (OD, OS)		X								
VA w/ habitual correction+ (OD,		X						X	X	(X)

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening/ Baseline/ Trial fit**	**Visit 2 Dispense Lens 1** (3 - 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)	**Early Exit**	**Unscheduled Visit**
OS, logMAR distance)*										
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
Randomization		X								
Fitting of investigational products (trial assessments): (Test and Comparator)* • VA (OD, OS, logMAR, distance) • Lens movement (overall fit- primary and peripheral gazes) • Lens position (centration; decentration – direction and amount)		X								

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening/ Baseline/ Trial fit**	**Visit 2 Dispense Lens 1** (3 - 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)	**Early Exit**	**Unscheduled Visit**
Study lens power to be dispensed		X								
[redacted]										
Dispense study lenses**			X	X		X	X			(X)
Axis orientation at [redacted] 10 min after lens insertion			X			X				
[redacted]										

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening/ Baseline/ Trial fit**	**Visit 2 Dispense Lens 1** (3 - 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)	**Early Exit**	**Unscheduled Visit**
[redacted]										

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening/ Baseline/ Trial fit**	**Visit 2 Dispense Lens 1** (3 - 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)	**Early Exit**	**Unscheduled Visit**
[redacted]										
Lens wear calendar*			X	X	X	X	X	X	X	X

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening/ Baseline/ Trial fit**	**Visit 2 Dispense Lens 1** (3 - 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)	**Early Exit**	**Unscheduled Visit**
			(Dispense Calendar)	(Review Calendar)	(Collect & Review Calendar)	(Dispense Calendar)	(Review Calendar)	(Collect & Review Calendar)	(Collect & Review Calendar)	(Review Calendar)
Collect worn study lenses*				X	X		X	X	X	(X)
[redacted]										
AEs		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)

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

* Source only

+ Subject must have visual acuity with habitual correction of 0.30 logMAR (20/40) or better OU in order to leave the office

[redacted]