# Statistical Analysis Plan for CLE383-P006 / NCT05138783
# Title: Clinical Performance of Two Daily Disposable Soft Contact Lenses

[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 of this study is to demonstrate noninferiority (NI) in visual acuity (VA) at distance when wearing PRECISION1 soft contact lenses (PRECISION1) compared to Biotrue ONEday soft contact lenses (Biotrue).

Decision Criteria for Study Success:

Success of this study will be based on demonstration of noninferiority in distance VA with PRECISION1 when compared to Biotrue, 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 noninferiority in visual acuity at distance when wearing PRECISION1 contact lenses compared to Biotrue contact lenses.

[redacted]

## 1.2 Study Description

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

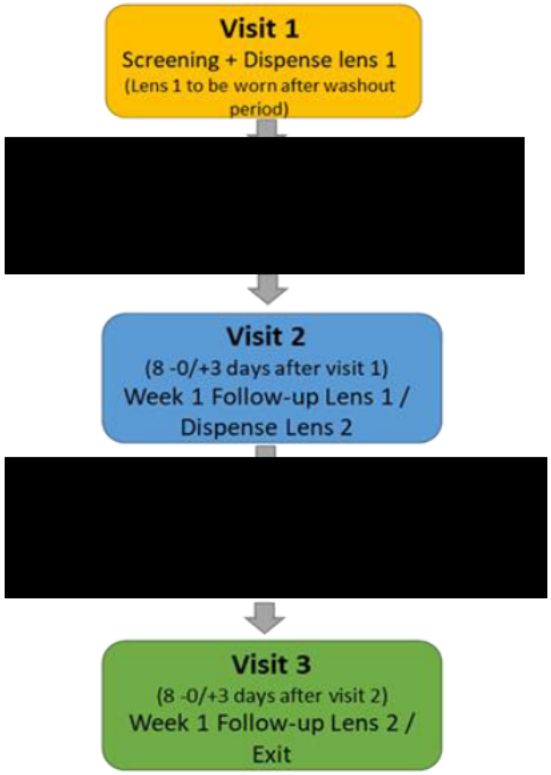
**Table 1-1 Study Description Summary**

| | |
|---|---|
| Study Design | Prospective, randomized, controlled, double-masked, bilateral crossover |
| Study Population | Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous PRECISION1, Biotrue 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.<br>[redacted]<br>Target to complete: 116<br>Planned to enroll: ~128 |
| Number of Sites | ~8<br>US |
| Test Product | PRECISION1 soft contact lenses (PRECISION1) [redacted] |

| | |
|---|---|
| Comparator Product | Biotrue ONEday soft contact lenses (Biotrue) [redacted] |
| Planned Duration of Exposure | ~16 days total duration (test and comparator):<br>Test Product: 8 (-0/+3) days<br>Comparator Product: 8 (-0/+3) days |
| Visits | Pre-Screening (optional)<br>Visit 1: Screening/Baseline/Dispense Lens 1¥<br>Visit 2: Week 1 Follow-up Lens 1/Dispense Lens 2¥ [8 (-0/+3) days after Visit 1]<br>Visit 3: Week 1 Follow-up Lens 2/Exit [8 (-0/+3) days after Visit 2]<br>[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.

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

| **Sequence** | [redacted] | **Lens Name** |
|---|---|---|
| Sequence 1 | [redacted] | PRECISION1/Biotrue |
| Sequence 2 | [redacted] | Biotrue/PRECISION1 |

## 1.4 Masking

This study is double-masked.

[redacted]

[redacted]

# 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]

[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 [redacted] 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 Deviation 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 Characteristics by Lens Sequence
- Baseline Characteristics by Lens Sequence [lens brand, lens solution, power: sphere, Best Corrected Visual Acuity]

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 primary, [redacted] effectiveness endpoint[redacted] effectiveness evaluation[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, as well as confidence intervals/limits as 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, for instance, 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.

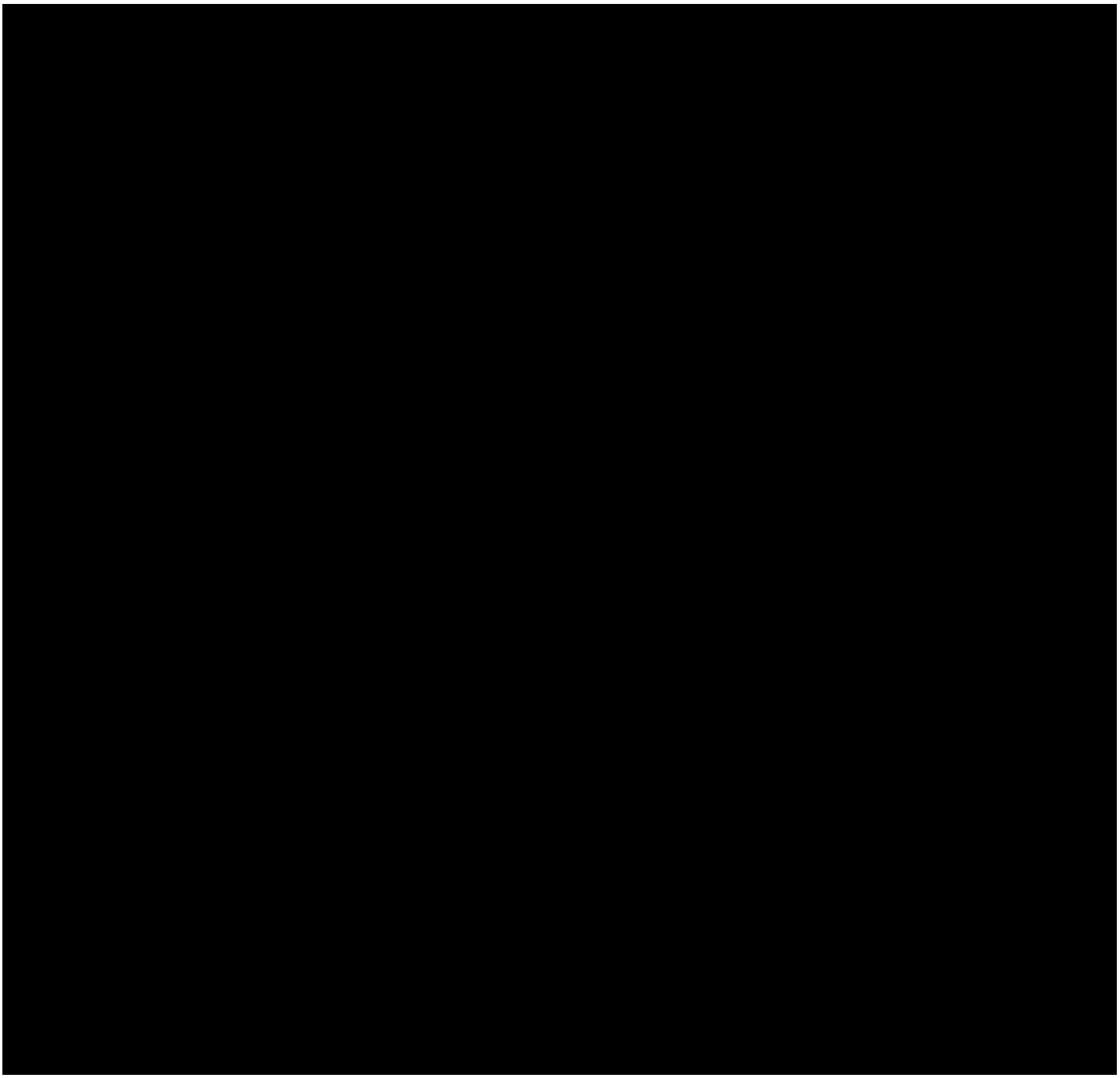
A listing of select effectiveness data will also be provided.

## 4.1 Effectiveness Endpoints

**Primary Effectiveness Endpoint**

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

[redacted]



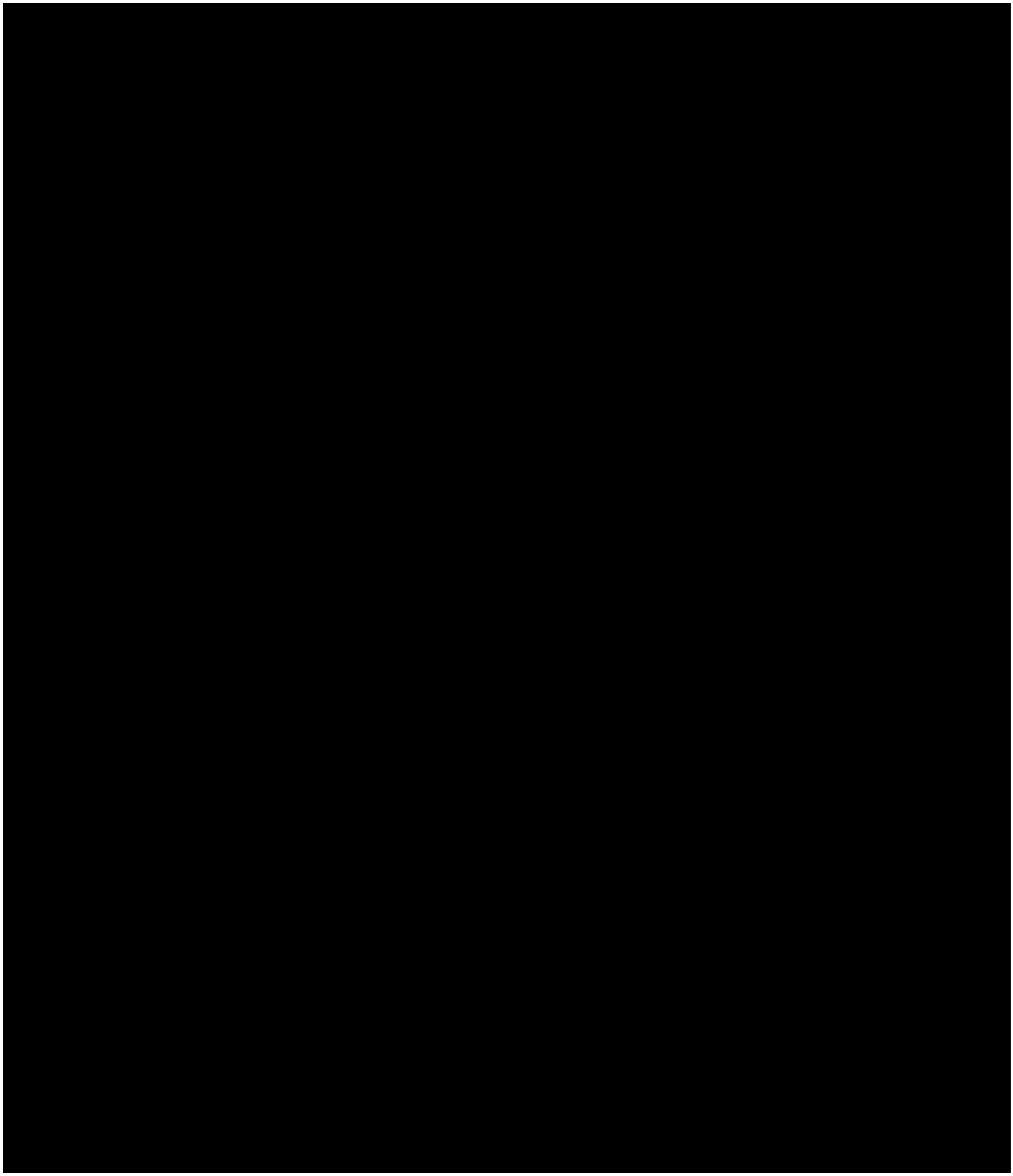
## 4.2 Effectiveness Hypotheses

**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 Biotrue, respectively, on the logMAR scale.



[redacted]

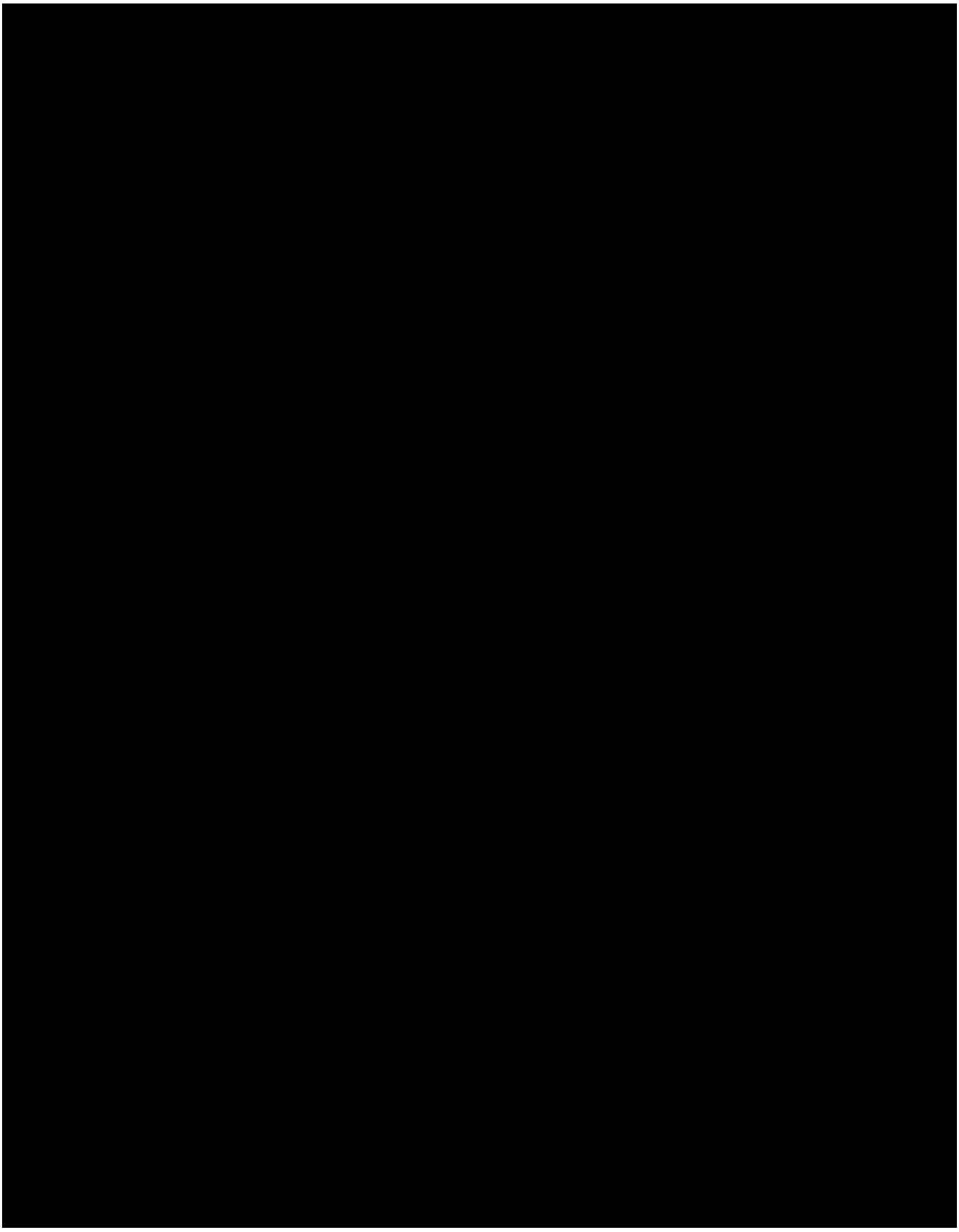
## 4.3 Statistical Methods for Effectiveness Analyses

### 4.3.1 Primary Effectiveness Analysis

A mixed effects repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, period, and sequence. Within-subject correlation due to eye and the crossover design will also be accounted for in the model. Lens difference (PRECISION1 minus Biotrue) 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]



[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 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
    - 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 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.

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 lenses but prior to exposure of Period 2 lenses.

- Treatment-emergent: an event that occurs from exposure to Period 1 study lenses until the 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:

- 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 [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]

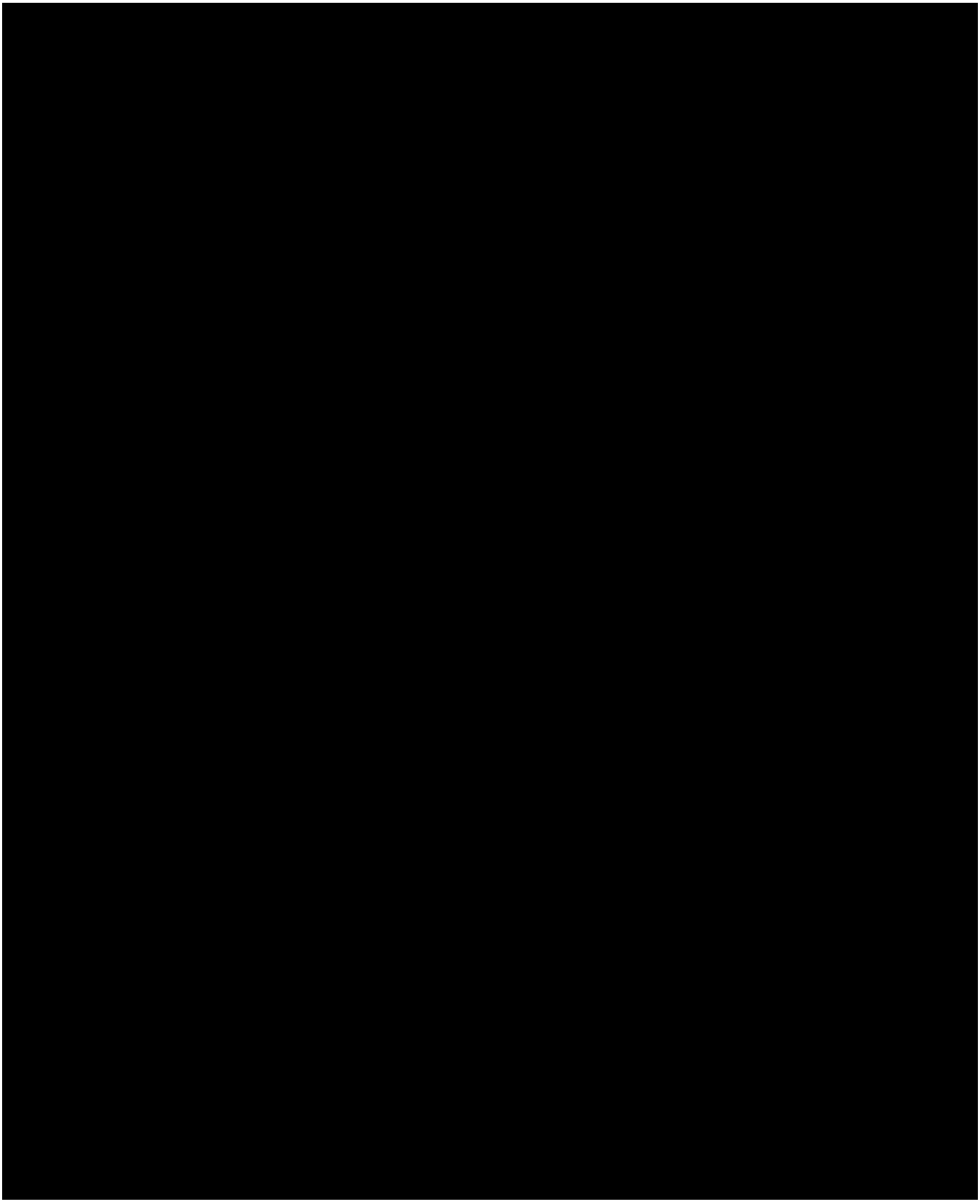
## 7 SAMPLE SIZE AND POWER CALCULATIONS

Sample size calculation is based on a prior clinical study [redacted] which evaluated performance of PRECISION1 and Biotrue. [redacted]

**Primary Effectiveness**

To demonstrate noninferiority (margin = 0.05 in logMAR; ½ line in Snellen) in distance VA as a one-tailed hypothesis with $\alpha$=0.05, and using a standard deviation of 0.0462 for paired differences, 80% power can be attained with a sample size of 8 (4 per sequence).

[redacted]



[redacted]

# 10 APPENDIX

**Table 10-1 Overview of Study Plan**

| 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 | **Early Exit** | **Unscheduled Visit** |
|---|---|---|---|---|---|---|
| | | [redacted] | 8 (-0/+3) days after Visit 1 [redacted] | 8 (-0/+3) days after Visit 2 | **N/A** | **N/A** |
| Informed Consent | | ✓ | | | | |
| Demographics | | ✓ | | | | |
| Medical History‡ | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Concomitant Medications‡ | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Inclusion/Exclusion | | ✓ | | | | |
| Habitual lens information (brand, power, lens solution) | | ✓ | | | | |
| VA with habitual correction (OD, OS, logMAR distance) * | | ✓ | | ✓ (Exit procedure) | ✓ | (✓) |
| Manifest refraction (OD, OS, logMAR distance) * | | ✓ | (✓) | (✓) | (✓) | (✓) |
| BCVA with manifest refraction (OD, OS, logMAR distance) | | ✓ | (✓) | (✓) | (✓) | (✓) |
| Biomicroscopy | | ✓ | ✓ | ✓ | ✓ | ✓ |
| [redacted] | [redacted] | [redacted] | | | | |

| 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 | **Early Exit** | **Unscheduled Visit** |
|---|---|---|---|---|---|---|
| | | [redacted] | 8 (-0/+3) days after Visit 1 [redacted] | 8 (-0/+3) days after Visit 2 | **N/A** | **N/A** |
| Trial lens fitting (Test and Comparator) & assessments: *<br>• VA (logMAR distance)<br>• [redacted] | | ✓ | | | | |
| Randomize✧ | | ✓ | | | | |
| Dispense (provide) study lenses * | | ✓ | ✓ | | | (✓) |
| VA (logMAR distance) with study lenses, (OD, OS) | | | ✓ | ✓ | (✓) | (✓) |
| [redacted] | | | [redacted] | [redacted] | [redacted] | [redacted] |

| 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 | **Early Exit** | **Unscheduled Visit** |
|---|---|---|---|---|---|---|
| | | [redacted] | 8 (-0/+3) days after Visit 1 [redacted] | 8 (-0/+3) days after Visit 2 | **N/A** | **N/A** |
| [redacted] | | | | | | |
| AEs | | ✓ | ✓ | ✓ | ✓ | ✓ |
| Device Deficiencies ~ | | ✓ | ✓ | ✓ | ✓ | ✓ |

| 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 | **Early Exit** | **Unscheduled Visit** |
|---|---|---|---|---|---|---|
| | | [redacted] | 8 (-0/+3) days after Visit 1 [redacted] | 8 (-0/+3) days after Visit 2 | **N/A** | **N/A** |
| Exit Form | | (✓) | (✓) | ✓ | ✓ | (✓) |

(✓) Assessment performed as necessary, e.g., decrease of VA by 2 lines or more with investigational product (IP) compared to BCVA with manifest refraction at Visit 1

[redacted]

✧ Randomization should occur at Visit 1 unless communicated otherwise by the sponsor.

‡ All ocular and targeted systemic meds / medical history

[redacted]