Title:

Statistical Analysis Plan for Protocol CLE383-E002 / NCT04942925

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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 evaluate the overall performance of PRECISION1™ (PRECISION1) contact lenses when compared to INFUSE contact lenses.

Decision Criteria for Study Success**:**

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

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1 STUDY OBJECTIVES AND DESIGN

1.1 Study Objectives

The primary objective of this study is to evaluate the overall performance of PRECISION1 contact lenses when compared to INFUSE contact lenses.

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, parallel group, bilateral, crossover, double-masked, stratified (by symptomatology)
Study Population	Volunteer subjects aged 18 or over who are habitual spherical contact lens wearers (excluding current/previous PRECISION1 and INFUSE 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. [redacted] Target to complete: ~ 52 [redacted] Planned to enroll: ~ 60 [redacted]
Number of Sites	~4 US
Test Product	PRECISION1™ (verofilcon A) soft contact lenses (PRECISION1) [redacted]
Control Product	INFUSE (kalifilcon A) soft contact lenses (INFUSE) [redacted]
Planned Duration of Exposure	~ 16 days in total duration (test and control) Test Product: ~ 8 days Control Product: ~ 8 days
Visits	[redacted]

	Visit 1 – Screening / Baseline / Fitting Set Lens 1 & Lens 2 Dispense Lens 1 [redacted] Visit 2 – Week 1 Follow–up Lens 1/Dispense Lens 2 [redacted] Visit 3 – Week 1 Follow –up Lens 2/ Exit * Optional

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 [redacted] randomized in a 1:1 manner to receive treatment (lens) in a crossover sequence.

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	[redacted]	PRECISION1/INFUSE
Sequence 2	[redacted]	INFUSE/PRECISION1

1.4 Masking

This study is double-masked.

[redacted]

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.

Subjects who are lost to follow-up and their exposure to dispensed study lenses is unknown will be included in the safety analysis data set. The visit date for Dispense (Lens 1 or Lens 2) [redacted] will be used as the first exposure date for the respective Lens.

Adverse events occurring from the time of informed consent but prior to first exposure to study lenses 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

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 [redacted] effectiveness endpoint[redacted] The Safety Analysis Set will be used [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.

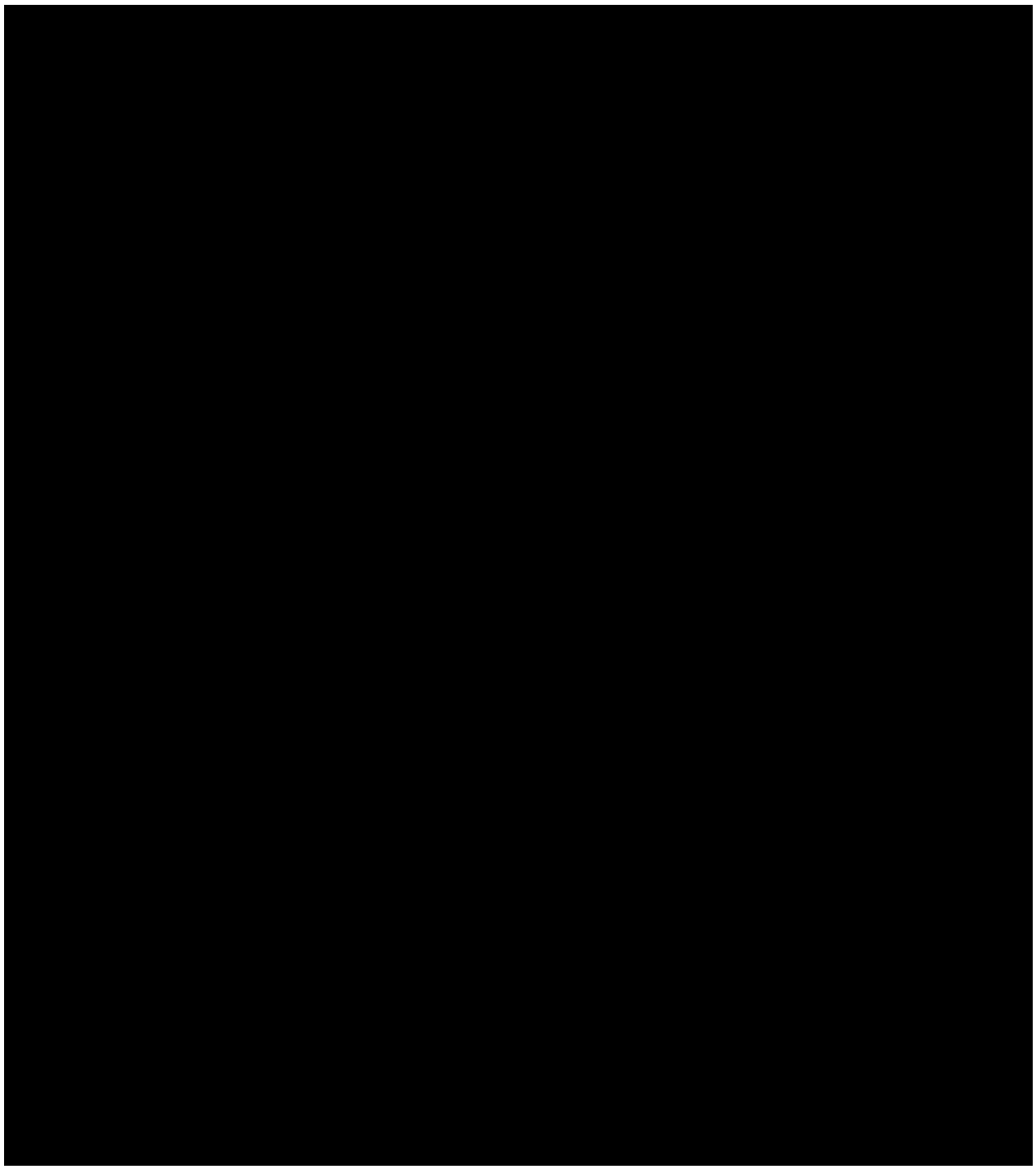
All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out.

A listing of select effectiveness data will also be provided.

4.1 Effectiveness Endpoints

Primary Endpoint

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



[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

Descriptive statistics will be provided.

[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 on 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.

Pre-treatment AEs and between-treatment AEs will be separated from treatment-emergent AEs occurring during the study period. A pre-treatment AE is an event that occurs after signing informed consent but prior to exposure to study lenses. A between-treatment AE is an event that occurs after last exposure to Period 1 lenses but prior to exposure to Period 2 lenses. The period for treatment-emergent AE analysis starts from exposure to study lenses for Period 1 or Period 2 until the subject completes the respective period or is discontinued from the study. Each AE will be summarized under the exposed lens based upon the event onset date/time, up until the start of the next lens in the crossover sequence.

The following tables and supportive listings will be provided:

- Incidence of All Ocular Treatment-Emergent Adverse Events
- Incidence of All Nonocular 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 visit within the crossover period]
- Listings 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

6 ANALYSIS STRATEGY FOR OTHER ENDPOINTS

Not Applicable.

7 SAMPLE SIZE AND POWER CALCULATIONS

No formal sample size calculation is provided given the descriptive and pilot nature of the study.

8 REFERENCES

Not Applicable.

10 APPENDIX

Table 10-1 Schedule of Study Procedures and Assessments

	[redacted]	Visit 1 Screening / Baseline / Fitting [redacted] Lens 1 & Lens 2 Dispense Lens 1 [redacted]	Visit 2 Week 1 Follow–up Lens 1 ‡ / Dispense Lens 2 [redacted]	Visit 3 Week 1 Follow –up Lens 2 ‡ / Exit	Early Exit	Unscheduled Visit
Procedure / Assessment		**Day 0**	**8 (0/+3) days after Visit 1**	**8 (0/+3) days after Visit 2**	**N/A**	**N/A**
[redacted]						
Informed Consent	-	X	-	-	-	-
Demographics	-	X	-	-	-	-
Medical History*	-	X	X	X	X	X
Concomitant Medications*	-	X	X	X	X	X
Inclusion/Exclusion	-	X	-	-	-	-
Habitual lens (brand, power), solution (brand if applicable)*	-	X	-	-	-	-
VA w/habitual correction (OD, OS, logMAR distance)*	-	X	-	X	X	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
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
VA (logMAR distance) with fitting [redacted] lenses (OD, OS)*		X (with both [redacted] lens types)	-	-	-	-
Lens fitting assessments [redacted] *	-	X (with both [redacted] lens types)	-	-	-	-

	[redacted]	Visit 1 Screening / Baseline / Fitting [redacted] Lens 1 & Lens 2 Dispense Lens 1 [redacted]	Visit 2 Week 1 Follow–up Lens 1 ‡ / Dispense Lens 2 [redacted]	Visit 3 Week 1 Follow –up Lens 2 ‡ / Exit	Early Exit	Unscheduled Visit
Procedure / Assessment		**Day 0**	**8 (0/+3) days after Visit 1**	**8 (0/+3) days after Visit 2**	**N/A**	**N/A**
[redacted]						
• Lens movement – primary gaze, peripheral gaze (overall fit) • Lens position (Centration) • Lens surface (front surface wettability, front surface deposits, back surface deposits).						
Keratometry readings	-	X	-	-	-	-
Randomize	-	X	-	-	-	-
Dispense (provide) study lenses*	-	X	X	-	-	(X)
VA w/ study lenses (OD, OS, logMAR distance)	-	-	X	X	(X)	(X)
[redacted]						

	[redacted]	**Visit 1 Screening / Baseline / Fitting [redacted] Lens 1 & Lens 2 Dispense Lens 1 [redacted]**	**Visit 2 Week 1 Follow–up Lens 1 ‡ / Dispense Lens 2 [redacted]**	**Visit 3 Week 1 Follow –up Lens 2 ‡ / Exit**	**Early Exit**	**Unscheduled Visit**
Procedure / Assessment		**Day 0**	**8 (0/+3) days after Visit 1**	**8 (0/+3) days after Visit 2**	**N/A**	**N/A**
[redacted]						
AEs[α]	-	X	X	X	X	X
Device deficiencies	-	X	X	X	X	X
Exit Form	-	(X)	(X)	X	X	(X)

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

* Source only

α Comprehensive details of all AEs will be documented in the source records; however, targeted collection will be utilized in the eCRF.

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