Clinical Assessment of a Daily Disposable Soft Silicone Hydrogel Contact Lens

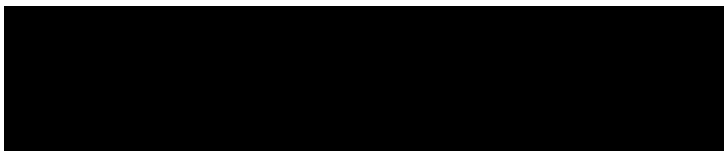
STUDY ID

CLU484-P003

STATISTICAL ANALYSIS PLAN

NCT06044948

Statistical Analysis Plan for CLU484-P003
Title: Clinical Assessment of a Daily Disposable Soft Silicone Hydrogel Contact Lens



This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

Executive Summary:

Key Objective:

To evaluate distance visual acuity (VA) of the DAILIES TOTAL1® (DT1) soft contact lenses over approximately 1 week of wear.

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

PRIMARY OBJECTIVE

To evaluate distance VA of the DT1 soft contact lenses over approximately 1 week of wear.

KEY EXPLORATORY OBJECTIVE

To evaluate subjective performance of the DT1 soft 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, interventional, nonrandomized, single-arm, subject-masked, multicenter
Study Population	Habitual spherical soft contact lens wearers aged 18 or older, with at least 3 months of spherical soft contact lens wearing experience, and who wear their habitual contact lenses for at least 5 days per week and at least 10 hours per day. [redacted] Target to complete: 90 Planned to enroll: ~96

Number of Sites	~6 US
Test Product	DAILIES TOTAL1® spherical soft contact lenses (DT1; delefilcon A; [redacted])
Comparator Product	N/A
Planned Duration of Exposure	6-8 days
Visits	Visit 1: Screen/Baseline/Dispense (Day 1) Visit 2: Week 1 Follow-up/Exit (Day 6 + 2 Days)

1.3 Randomization

Randomization is not applicable for this single product study.

1.4 Masking

This study is subject-masked, with all qualified subjects receiving study product. All members associated with the study (at the site and the study sponsor) are unmasked to the assigned treatment.

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 the study lenses evaluated in this study. Lenses used for power optimization at Visit 1 are not considered study lenses in this context, as they are not used for intended study treatment. Therefore, any adverse event (AE) or device deficiency occurring after Informed Consent and prior to the initial exposure to the study lenses under evaluation in this clinical protocol will be listed as pretreatment.

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 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of the safety analysis set 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
- Analysis Sets
- Subject Accounting
- Demographics
- Baseline Characteristics [lens brand; [redacted]]

In addition, the following subject listings will be provided:

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

4 EFFECTIVENESS ANALYSIS STRATEGY

This study defines 1 primary effectiveness endpoint, [redacted] All effectiveness evaluations will use the safety analysis set as the primary analysis set.

[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 effectiveness analyses.

4.1 Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint is distance VA with study lenses at Week 1, collected for each eye, in Snellen.

[redacted]

4.2 Effectiveness Hypotheses

Primary Effectiveness

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

[redacted]

[redacted]

4.3 Statistical Methods for Effectiveness Analyses

4.3.1 Primary Effectiveness Analyses

Descriptive statistics will be provided as frequency and percentage for each Snellen category. For the converted logMAR values, descriptive statistics will be provided as number of observations, mean, SD, median, minimum, and maximum.

[redacted]

4.4 Multiplicity Strategy

No multiplicity adjustment needs to be considered for the effectiveness endpoints since no formal hypothesis testing will be conducted.

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

- AEs
- Biomicroscopy findings
    - Limbal hyperemia
    - Bulbar hyperemia
    - Corneal staining

  - Conjunctival staining
  - Palpebral conjunctival observations
  - Conjunctival compression/indention
  - Corneal epithelial edema
  - Corneal stromal edema
  - Corneal vascularization
  - Corneal infiltrates
  - Chemosis
  - 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. 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 the 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 and treatment-emergent AEs as defined below:

- Pre-treatment: an event that occurs after signing informed consent but prior to exposure to study lenses

- Treatment-emergent: an event that occurs from first exposure to study lenses until subject exits from the study

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

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

6 Analysis Strategy for Other Endpoints

Not applicable.

7 Sample Size and Power Calculations

Although inferential testing is not planned for the primary [redacted] endpoints, expected precision of the observed results is provided. With a sample size of 90 subjects, degrees of precision achieved with the primary effectiveness endpoint [redacted] are as follows:

<u>Visual acuity</u>

With the assumed standard deviation of 0.08 [redacted], a one-sided 95% CI for the mean of distance VA based on t-statistics will extend 0.015 from the observed mean.

[redacted]

8 References

Not applicable.

[redacted]

10 Appendix

Table 10-1 Schedule of Study Procedures and Assessments

	Visit 1 Screen/Baseline/ Dispense	Visit 2 Week 1 Follow-up/Exit^	Unscheduled Visit(s)	Early Exit
Procedure/ Assessment	**Day 1**	**Day 6 + 2 Days**	**N/A**	**N/A**
Informed Consent	X			
Demographics	X			
Medical History and Concomitant Medications	X	X	X	X
Inclusion/Exclusion	X			
[redacted]				
VA with Habitual Correction (Snellen distance, OD, OS)*	X	X	(X)	(X)
Habitual Lens Brand	X			
Manifest Refraction*	X	(X)	(X)	(X)
BCVA with Manifest Refraction (Snellen distance, OD, OS)*	X	(X)	(X)	(X)
Biomicroscopy	X	X	X	X
Power Optimization and Dispense Study Lens*	X			
VA with Study Lenses (Snellen distance, OD, OS)	X	X	(X)	X
[redacted]				
Collect worn lenses and dispose		X		X
AEs	X	X	X	X

	Visit 1 Screen/Baseline/ Dispense	**Visit 2 Week 1 Follow-up/Exit^**	**Unscheduled Visit(s)**	**Early Exit**
Procedure/ Assessment	**Day 1**	**Day 6 + 2 Days**	**N/A**	**N/A**
Device deficiencies	X	X	X	X
Exit form		X		X

*Source only

^Schedule Exit Visit to occur 6 – 10 hours after lens insertion on that day

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