Alcon - Business Use Only Statistical Analysis Plan   **Effective Date:** 30-Apr-2018
Document: TDOC-0055209   **Version:** 1.0; CURRENT; Most-Recent; Effective
Status: Effective

Short Title:

Statistical Analysis Plan
CLE383-C006

Full Title:

Statistical Analysis Plan
CLE383-C006 /
CLE383-C006

Protocol Title:	Clinical Comparison of Two Daily Disposable Soft Contact Lenses
Project Number:	A01660
Protocol TDOC Number:	TDOC-0055048
Author:	██████████ ████████
Template Version:	Version 4.0
Approvals:	See last page for electronic approvals
Job Notes:	

This is the original (Version 1.0) Statistical Analysis Plan for this study. This version of the Statistical Analysis Plan is based on Version 1.0 of the study protocol.

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Executive Summary:

Key Objective:

The primary objective of this study is to evaluate the overall performance of Daily Disposable (DD) T2 Soft Contact Lenses when compared to CooperVision® clariti® 1 day (Clariti 1 Day) 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

PRIMARY OBJECTIVE

The primary objective of this study is to evaluate the overall performance of DD T2 lenses when compared to Clariti 1 Day 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, bilateral crossover, double-masked
Study Population	Volunteer subjects aged 18 or over who are soft daily disposable contact lens wearers (excluding current Clariti 1 Day 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 8 hours per day. Target to complete: 20 Planned to enroll: ~22
Number of Sites	~1 US
Test Product	Daily Disposable T2 Soft Contact Lenses (DD T2)
Control Product	CooperVision® clariti® 1 day (Clariti 1 Day)
Duration of Treatment	~20 days total duration • Test Product: 8 days (-1/+2 days) • Control Product: 8 days (-1/2 days)
Visits	Visit 1, Day 1: Baseline/Dispense Lens 1 Visit 2, Week 1 [Day 8 (-1/+2 Days)]: Follow-up Lens 1/Dispense Lens 2 Visit 3, Week 2 [Day 8 (-1/+ 2 Days)]: Follow-up Lens 2/Exit

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 iMedidata Balance.

Qualifying subjects will be randomized in a 1:1 manner to one of 2 lens sequences consisting of the test lens and control lens as described below. For each sequence, subjects wear 1st lens then crossover to 2nd lens.

Sequence 1: DD T2/Clariti 1 Day
Sequence 2: Clariti 1 Day/DD T2

1.4   Masking

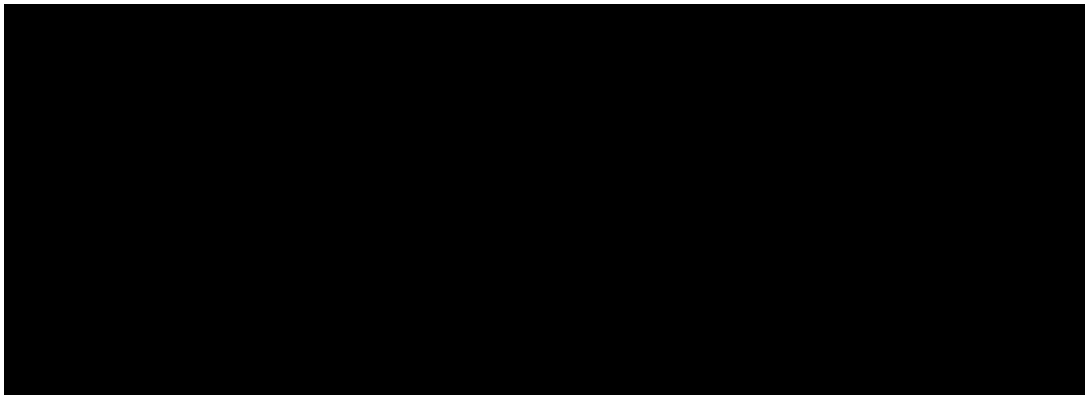This study is double-masked.

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
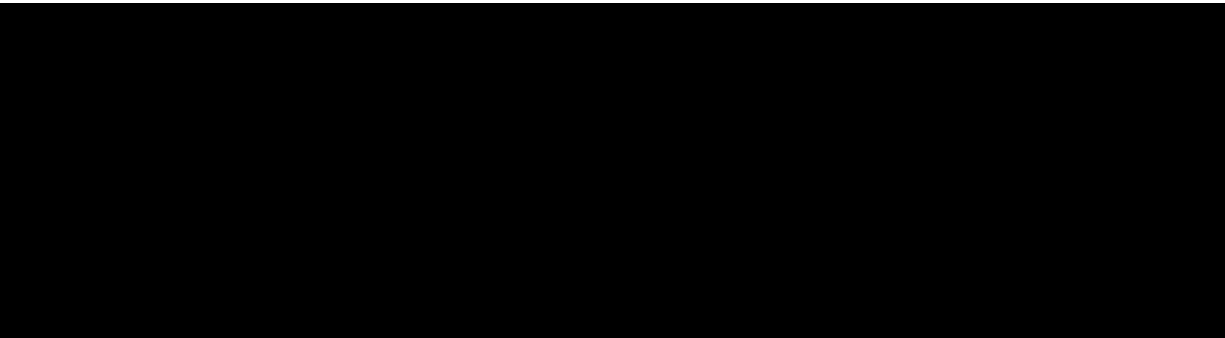
2   Analysis Sets

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. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lens 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.

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4   Effectiveness Analysis Strategy

This study defines one primary endpoint ▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮▮ The Safety Analysis Set will serve as the primary set for all effectiveness analyses.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum, as well as confidence intervals where applicable. Categorical variables will be summarized with counts 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 analysis.

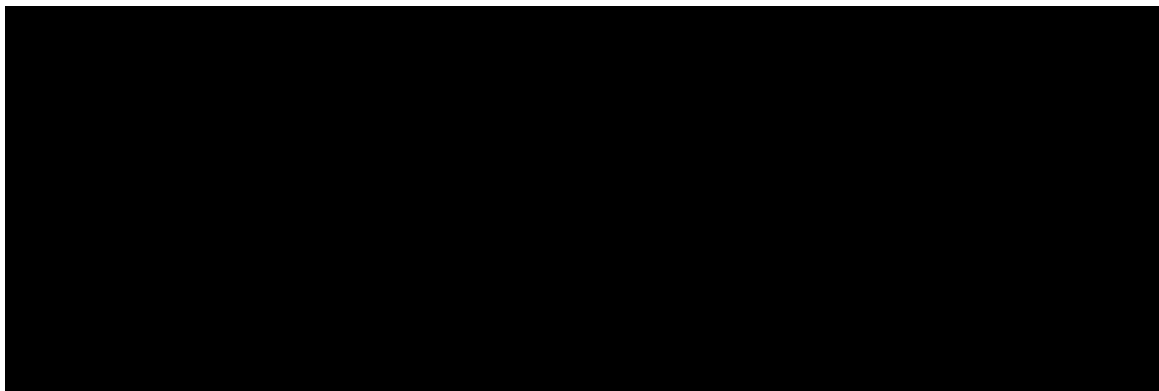A listing of selected effectiveness data will also be provided.
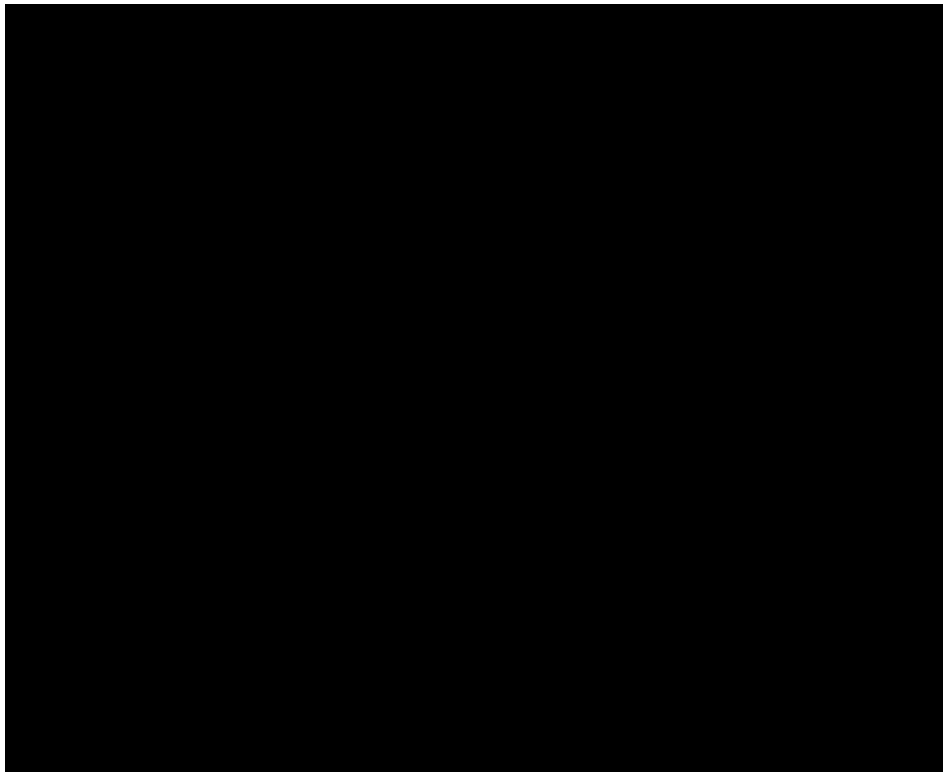
4.1   Effectiveness Endpoints

Primary Endpoint

The primary endpoint is the subjective rating on overall quality of vision, collected binocularly on a scale of 1 (Poor) to 10 (Excellent) at the Day 8 Follow-up visits.

Secondary Endpoint

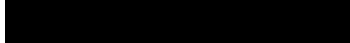No secondary endpoint is defined for this study.

4.2   Effectiveness Hypotheses

Primary Effectiveness

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

4.3   Statistical Methods for Effectiveness Analyses

4.3.1   Primary Effectiveness Analyses

The subjective rating of Overall Quality of Vision will be summarized as both continuous and categorical. As a continuous variable, descriptive statistics as well as a two-sided 95% confidence interval for the mean of each study lens will be provided. As a categorical variable, counts and percentages will be provided for the following categories: 9-10, 7-8, 5-6, 3-4, 1-2.

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4.4 Multiplicity Strategy

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

4.5 Subgroup Analyses and Effect of Baseline Factors

It is not expected that demographic or baseline characteristics will have an impact on the study results in this study. No subgroup analyses are planned.

4.6 Interim Analysis for Effectiveness

No interim analysis is planned for effectiveness endpoints.

5 Safety Analysis Strategy

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

     o 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 the safety analysis set as defined in Section 2.1. Baseline will be defined as the last measurement prior to exposure to study lenses on 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 informed consent to when a subject exits the study will be accounted for in the reporting.

Analysis and presentation of pre-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. The period for treatment-emergent AE analysis starts from exposure to study lenses until the subject completes 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

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 Increased Severity by 1 Grade in Biomicroscopy Findings [This listing will include all relevant visit within the crossover period]
- 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]
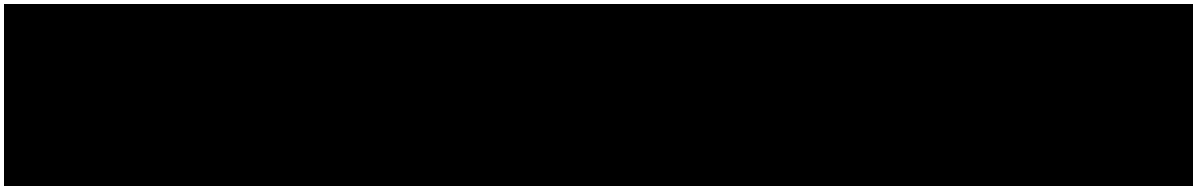- Listings of Subjects with Infiltrates

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.

8   References

Not applicable.

9   Revision History

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10   Appendix

Table 100–1   **Overview of Study Plan**

Procedure/ Assessment	Visit 1, Day 1	Visit 2, Week 1: Day 8 of lens wear (-1/+2 days)		Visit 3, Week 2: Day 8 of lens wear (-1/+2 days)	Unscheduled Visit	Early Exit
	Baseline/ Dispense Lens 1	Follow-up Lens 1	Dispense Lens 2	Follow-up Lens 2/ Exit		
Informed Consent	✓	-	-	-	-	-
Demographics	✓	-	-	-	-	-
Medical History	✓	-	-	-	-	-
Concomitant Medications	✓	(✓)	-	(✓)	(✓)	(✓)
Inclusion/ Exclusion	✓	-	-	-	-	-
Habitual lens (brand, power)*	✓	-	-	-	-	-
VA w/ habitual correction (OD, OS, Snellen distance)*	✓	-	-	✓	(✓)	✓
Biomicroscopy	✓	✓	-	✓	✓	✓
Dispense study lenses	✓	-	✓	-	-	-
VA w/ study lenses (OD, OS, Snellen distance)	✓	✓	✓	✓	(✓)	(✓)

Procedure/ Assessment	Visit 1, Day 1	Visit 2, Week 1: Day 8 of lens wear (-1/+2 days)		Visit 3, Week 2: Day 8 of lens wear (-1/+2 days)	Unscheduled Visit	Early Exit
	Baseline/ Dispense Lens 1	Follow-up Lens 1	Dispense Lens 2	Follow-up Lens 2/ Exit		
████████████████████						
Subjective rating with study lenses: • ████ • ████ • ████ • ████ • overall quality of vision • ████ • ████	-	✓	-	✓	✓	✓
████████████████████						
AEs	✓	✓		✓	✓	✓
Device deficiencies	✓	✓		✓	✓	✓
Exit Form	(✓)	(✓)		(✓)	(✓)	✓

(✓) assessment performed as necessary, eg, decrease of VA by 2 lines or more with investigational product (IP)
* Source only

ⱦ Comments, optional

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
04/27/2018 17:55:39	██████████	█████
04/27/2018 17:57:20	██████████	████
04/27/2018 18:38:29	██████████	█████
04/30/2018 15:53:34	████████	█████████████