Title:

Statistical Analysis Plan for Protocol CLY935-C020 / NCT04532099

This version of the Statistical Analysis Plan is based on Version 6.0 of the study protocol.

Executive Summary:

Key Objective:

The primary objective of this study is to evaluate the overall performance of an investigational silicone hydrogel lens when compared to ACUVUE OASYS® with HYDRACLEAR® PLUS (AOHP).

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 an investigational silicone hydrogel lens when compared to AOHP.

[redacted]

1.2 Study Description

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

Table 1-1 Study Description Summary

Study Design – Part A	Prospective, randomized, parallel group, crossover, double-masked, bilateral, [redacted]
Study Design – Part B	Prospective, single group [redacted] single-masked, bilateral
Study Population	Volunteer subjects aged 18 or over who are habitual spherical weekly/monthly soft 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]

	Number of Subjects – Part A Target to complete: 60 (~30 per each parallel group) Planned to enroll: ~66 Number of Subjects – Part B Target to complete: 60 (~30 per each parallel group) Planned to enroll: ~66
Number of Sites	~4 US
Test Product	LID018869
Control Product	Control Product 1 (Part A): ACUVUE OASYS® with HYDRACLEAR® PLUS (AOHP) Control Product 2 (Part B): CooperVision® Biofinity® (Biofinity)
Planned Duration of Exposure – Part A	~60 days total duration (test and control): Test Product: ~30 days Control Product 1: ~30 days (2x ~15 days)
Planned Duration of Exposure – Part B	~30 days total duration (control only): Control Product 2: ~30 days
Visits – Part A	Pre-Screening* Visit 1: Screen/Baseline/Dispense Lens 1 Visit 2: Day 15 Follow-up Lens 1 [redacted] Visit 3: Day 30 Follow-up Lens 1/Dispense Lens 2 [redacted] Visit 4: Day 15 Follow-up Lens 2 [redacted] Visit 5: Day 30 Follow-up Lens 2/Exit [redacted] *Optional
Visits – Part B	Pre-Screening* Visit 1: Screen/Baseline/Dispense Lens 1 Visit 2: Day 15 Follow-up Lens 1 [redacted] Visit 3: Day 30 Follow-up Lens 1/Exit [redacted] *Optional

1.3 Randomization

[redacted]

Subjects for Part A of the study will be [redacted] randomized in a 1:1 manner to receive treatment (lens) in a crossover sequence. No randomization will be implemented in Part B.

1.4 Masking

Part A of this study is double masked and Part B of the study is single masked (trial subject).

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

3 Subject Characteristics and Study Conduct Summaries

The following tables will be presented for Part A [by lens Sequence or by Lens] and Part B separately:

- 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] (habitual lens brand, habitual lens care brand, [redacted]

In addition, the following subject listings will be provided for Part A and Part B separately:

- 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 endpoint [redacted] The Safety Analysis Set will be used for all effectiveness analyses.

Part A and Part B will be summarized and presented separately.

Continuous variables will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum. 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 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]

[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 presented.

[redacted]

4.4 Multiplicity Strategy

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

[redacted]

5 Safety Analysis Strategy

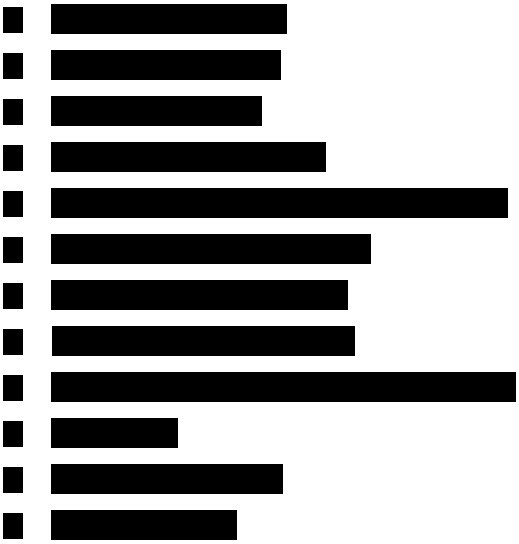
The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of adverse events as well as the other listed parameters. Therefore, no inferential testing will be done for the safety analysis.

Part A and Part B will be summarized and presented separately.

5.1 Safety Endpoints

The safety endpoints are

- Adverse events (AE)
- Biomicroscopy Findings/Slit Lamp Examinations



- 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. 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 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
- 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

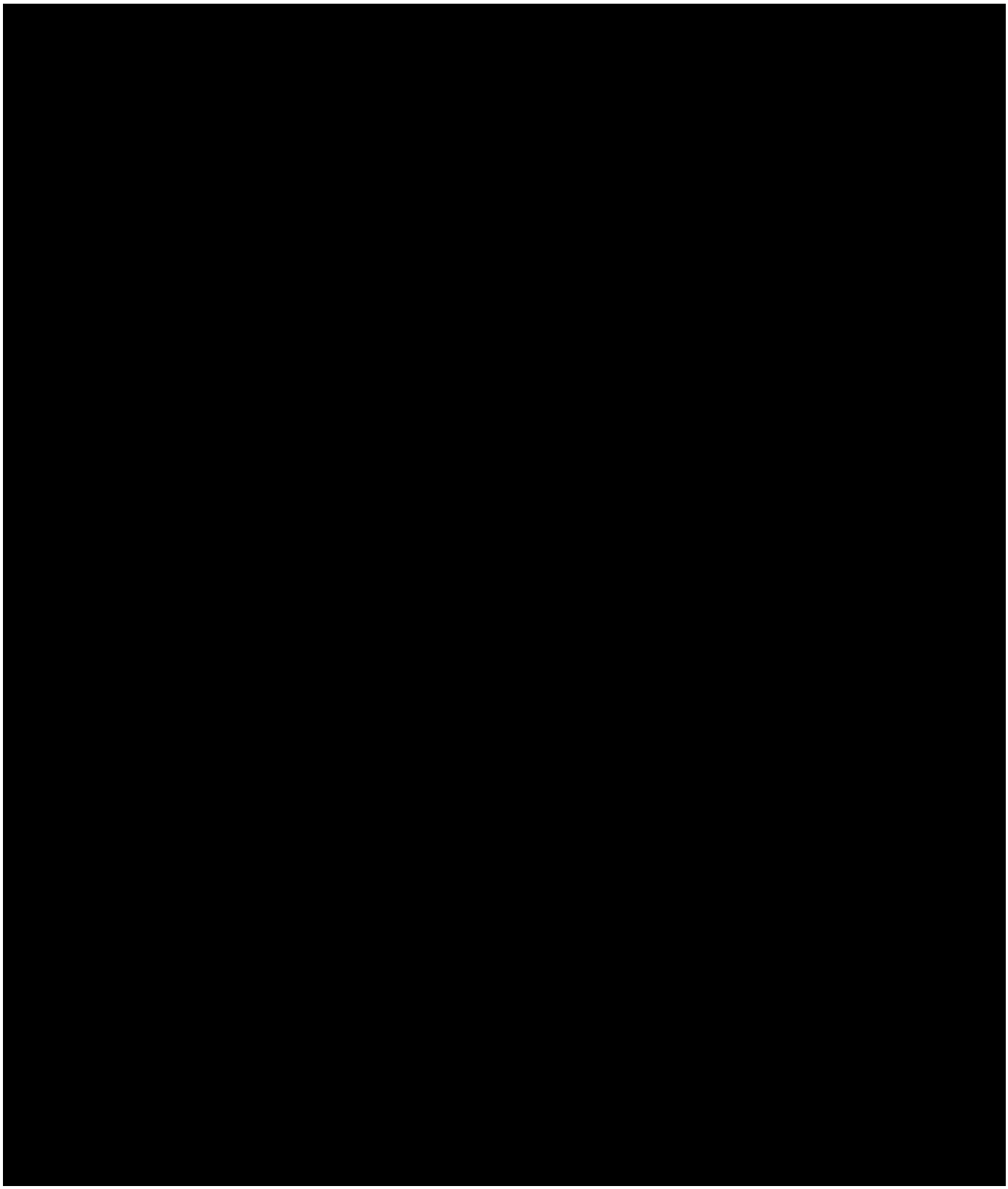
Not applicable.

7 Sample Size and Power Calculations

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 – Part A

Procedure/ Assessment	PRESCREENING	LENS 1			LENS 2			
		Visit 1 Screen/ Baseline/ Dispense Lens 1	Visit 2 Day 15 Follow-up Lens 1 [redacted]	Visit 3 Day 30 Follow-up Lens 1 [redacted] Dispense Lens 2		Visit 4 Day 15 Follow-up Lens 2 [redacted]	Visit 5 Day 30 Follow-up Lens 2 /Exit^ [redacted]	USV
				Follow-up Lens 1	Dispense Lens 2			
Informed Consent		X						
Demographics		X						
Medical History*		X	X	X		X	X	X
Concomitant Medications*		X	X	X		X	X	X
Inclusion/ Exclusion		X						
Habitual (lens brand, lens power*, lens care)		X						
VA w/ habitual correction* (OD, OS, Snellen distance)		X					X	(X)
Manifest Refraction and BCVA with manifest refraction* (OD, OS, Snellen distance)		X	(X)	(X)		(X)	(X)	(X)
Biomicroscopy		X	X	X		X	X	X
[redacted]	[redacted]	[redacted]						
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Randomization and record lens power*		X						
Dispense study lenses		X	(X)$^{\Omega}$		X	(X)$^{\Omega}$		(X)
VA w/ study lenses (OD, OS, logMAR distance)		X	X	X	X	X	X	(X)

Procedure/ Assessment	PRESCREENING	LENS 1			LENS 2			
		Visit 1 Screen/ Baseline/ Dispense Lens 1	**Visit 2** Day 15 Follow-up Lens 1	**Visit 3** Day 30 Follow-up Lens 1 / Dispense Lens 2		**Visit 4** Day 15 Follow-up Lens 2	**Visit 5** Day 30 Follow-up Lens 2 /Exit^	**USV**
				Follow-up Lens 1	Dispense Lens 2			
AEs§		X	X	X	X	X	X	X
Device deficiencies		X	X	X	X	X	X	X
Exit Form		(X)	(X)	(X)	(X)	(X)	X	(X)

USV = Unscheduled visit

[redacted]

Table 10-2 Schedule of Study Procedures and Assessments – Part B

Procedure/ Assessment	PRESCREENING	Visit 1 Screen/ Baseline/ Dispense Lens 1	Visit 2 Day 15 Follow-up Lens 1 [redacted]	Visit 3 Day 30 Follow-up Lens 1/Exit^ [redacted]	USV
Informed Consent		X			
Demographics		X			
Medical History*		X	X	X	X
Concomitant Medications*		X	X	X	X
Inclusion/ Exclusion		X			
[redacted]		[redacted]			
Habitual (lens brand, lens power*, lens care)		X			
VA w/ habitual correction* (OD, OS, Snellen distance)		X		X	(X)
Manifest Refraction and BCVA with manifest refraction* (OD, OS, Snellen distance)		X	(X)	(X)	(X)
Biomicroscopy		X	X	X	X
[redacted]	[redacted]	[redacted]			
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Record lens power*		X			
Dispense study lenses		X	(X)		(X)
VA w/ study lenses (OD, OS, logMAR distance)		X	X	X	(X)
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
AEs§		X	X	X	X
Device deficiencies		X	X	X	X

Procedure/ Assessment	PRESCREENING	Visit 1 Screen/ Baseline/ Dispense Lens 1	Visit 2 Day 15 Follow-up Lens 1 [redacted]	Visit 3 Day 30 Follow-up Lens 1/Exit^ [redacted]	USV
Exit Form		(X)	(X)	(X)	(X)

USV = Unscheduled visit

[redacted]

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