Clinical Performance of Two Reusable Silicone Hydrogel Contact Lenses

STUDY ID:

CLL949-E005

PROTOCOL

NCT05431478

Vision Care SEE Protocol for CLL949-E005
Title: Clinical Performance of Two Reusable Silicone Hydrogel Contact Lenses

Sponsor Name and Address:	Alcon Research, LLC and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product(s):	Alcon serafilcon A contact lenses

Investigator Agreement:

- I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described trial in compliance with Good Clinical Practice (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, all applicable regulatory authority regulations, and conditions of approval imposed by the reviewing IRB or regulatory authority.
- I will supervise all testing of the device involving human subjects and ensure that the requirements relating to obtaining informed consent and IRB review and approval are met in accordance with applicable local and governmental regulations.
- I have read and understand the appropriate use of the investigational product(s) as described in the protocol, current Investigator's Brochure, product information, or other sources provided by the sponsor.
- I understand the potential risks and side effects of the investigational product(s).
- I agree to maintain adequate and accurate records in accordance with government regulations and to make those records available for inspection.
- I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements of the sponsor and government agencies.
- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed of their obligations in meeting the above commitments.

Have you ever been disqualified as an investigator by any Regulatory Authority? ☐ No ☐ Yes
Have you ever been involved in a study or other research that was terminated? ☐ No ☐ Yes If yes, please explain here:

Principal Investigator:

Signature Date

Name and professional position:

Address:

1 PROTOCOL SYNOPSIS

Trial Sponsor	Alcon 6201 South Freeway Fort Worth, Texas 76134-2099
Name of Test Product(s)	Alcon serafilcon A contact lenses
Name of Comparator Product(s)	ACUVUE OASYS® 2 Week with HYDRACLEAR® PLUS
Title of Trial	Clinical Performance of Two Reusable Silicone Hydrogel Contact Lenses
Protocol Number	CLL949-E005
Number of Sites Country	~5 US
Clinical Investigation Type	☐ Early Feasibility ☒ Traditional Feasibility ☐ Pivotal (premarket monadic claims) ☐ Postmarket Interventional / Confirmatory ☐ Postmarket Noninterventional / Observational
Planned Duration of Exposure	~28 days total duration (test, comparator) with wash-out Test Product: ~14 days Comparator Product: ~14 days
Number of Subjects	Target to complete: 60 Planned to enroll: ~68
Study Population	Volunteer subjects aged 18 or over who are habitual spherical soft contact lens wearers (excluding current/previous Acuvue Oasys 2 Week with Hydraclear Plus (AOHP) habitual lens wearers and daily disposable 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 8 hours per day. [redacted]
Objective(s)	The objective of this study is to assess the clinical performance of two reusable silicone hydrogel contact lenses when worn on a daily wear modality.

Endpoints	Primary Effectiveness • Visual acuity with study lenses at Week 1 Follow-Up [redacted] Safety • Adverse Events • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness • VA with study lenses (logMAR distance) • Manifest refraction [redacted]

	[redacted] Safety • AEs • Biomicroscopy • Device deficiencies	
Study Design	☒ Prospective	☐ Single-masked (trial subject) ☐ Single-masked (investigator) ☒ Double-masked ☐ Open-label ☐ Other
	☐ Single group ☐ Parallel group ☒ Crossover ☐ Other	
	☐ Contralateral ☒ Bilateral ☐ Monocular lens wear	☒ Randomized
Test Product Details	Primary component/material	serafilcon A
	Product Name	Alcon serafilcon A contact lenses
	LID Number	LID022821
	Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
	Rx Power Range	-1.00 to -6.00 D in 0.25 steps
Comparator Product Details	Primary component/material	senofilcon A
	Product Name	Acuvue Oasys 2 Week with Hydraclear Plus (AOHP)
	LID Number	N/A
	Manufacturer	Johnson & Johnson
	Rx Power Range	-1.00 to -6.00 D in 0.25 steps
	Other	Base Curve: 8.4 mm and 8.8 mm
Inclusion Criteria	1. Subject must be at least 18 years of age.	

	2. Subject must be able to understand and must sign an ICF that has been approved by an IRB. 3. Successful wear of spherical soft contact lenses in both eyes for a minimum of 5 days per week and 8 hours per day during the past 3 months. 4. Manifest cylinder of ≤ 0.75 D in each eye. 5. BCVA 20/25 Snellen (0.10 logMAR) or better in each eye. 6. Subject must be willing to stop wearing their habitual contact lenses for the duration of study participation. 7. Able to wear contact lenses within a range of sphere power from -1.00 to -6.00 D (0.25 D steps) and subject willing and able to wear the study lenses for the full duration of the study. [redacted] 9. Subject must be able to be successfully fit with test and comparator lenses.
Exclusion Criteria	1. Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the investigator. 2. Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the investigator. 3. History of refractive surgery or plan to have refractive surgery during the study or irregular cornea in either eye. 4. Ocular or intraocular surgery (excluding placement of punctal plugs) within the previous 12 months or planned during the study. 5. Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher; presence of corneal infiltrates.

	6. Current or history of pathologically dry eye in either eye that, in the opinion of the investigator, would preclude contact lens wear. 7. Current or history of herpetic keratitis in either eye. 8. Eye injury in either eye within twelve weeks immediately prior to enrollment for this trial. 9. Current or history of intolerance, hypersensitivity or allergy to any component of the study products. 10. Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment. 11. Any use of topical ocular medications and artificial tear or rewetting drops that would require instillation during contact lens wear. 12. The investigator, his/her staff, family members of the investigator, family members of the investigator's staff, or individuals living in the households of the aforementioned persons may not participate in the study. 13. Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial. 14. Habitual AOHP contact lens wearers and/or current habitual wearers of any daily disposable contact lenses. 15. Currently pregnant, as stated by the subject. [redacted]
Associated Materials	• CLEAR CARE® Cleaning & Disinfecting Solution supplied by sponsor to be provided to subjects for use during the study. • Lubrication/re-wetting drops will not be permitted.

Table 1-1 Schedule of Study Procedures and Assessments

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
Informed Consent		X								
Demographics		X								
Medical History*		X	X	X	X	X	X	X	X	X
Concomitant Medications*		X	X	X	X	X	X	X	X	X
Inclusion/ Exclusion		X								
Habitual lens (brand, lens power,		X								

[redacted]

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
VA w/ habitual correction^{+} (OD, OS, logMAR distance)*		X						X	(X)	(X)
[redacted]										
Manifest refraction*		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
[redacted]										
Biomicroscopy		X	X	X	X	X	X	X	X	X

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										
Randomization		X								
Dispense study lenses			X	X		X	X			(X)
VA w/ study lenses (OD, OS, logMAR distance)			X	X	X	X	X	X	(X)	(X)

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										

		Lens 1 (Period 1)				Lens 2 (Period 2)				
Procedure/ Assessment	**Pre-screening**	**Visit 1 Screening / Baseline**	**Visit 2 Dispense Lens 1** [2 (at least 48 hours) - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)]	**Visit 3 Week 1 Follow-up Lens 1** [7 -0/+ 1 days after Visit 2]	**Visit 4 Week 2 Follow- up Lens 1** [7 -0/+ 1 days after Visit 3)]	**Visit 5 Dispense Lens 2** [2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)]	**Visit 6 Week 1 Follow-up Lens 2** [7 -0/+ 1 days after Visit 5]	**Visit 7 Week 2 Follow-up Lens 2 /Exit** [7 -0/+ 1 days after Visit 6)]	**Early Exit**	**Unscheduled Visit**
[redacted]										
Unplanned lens replacement with reason			(X)	(X)	(X)	(X)	(X)			(X)
AEs [α]		X	X	X	X	X	X	X	X	X
Device deficiencies		X	X	X	X	X	X	X	X	X
Exit Form								X	X	

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

1.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
AOHP	Acuvue Oasys 2 Week with Hydraclear Plus
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CIP	Clinical investigation plan
eCRF	Electronic case report form
D	Diopter(s)
D/C	Discontinue
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICF	Informed consent form
IEC	Independent Ethics Committee
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
LID	Lens identification
LogMAR	Logarithm of the minimum angle of resolution
[redacted]	[redacted]
MOP	Manual of Procedures
N/A	Not applicable
OD	Right eye
OS	Left eye
OU	Both eyes
SAE	Serious adverse event
SADE	Serious adverse device effect
SiHy	Silicon hydrogel
US or USA	United States of America
USADE	Unanticipated serious adverse device effect
VA	Visual acuity
[redacted]	[redacted]

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3 INTRODUCTION

3.1 Study Rationale and Purpose

The investigational contact lens is intended for the optical correction of refractive ametropia in persons with nondiseased eyes.

The purpose of this study is to assess the clinical performance of the investigational Alcon serafilcon A contact lenses with marketed AOHP contact lenses. [redacted] The design of this study is justified based upon preclinical and clinical testing, as described within the Investigator's Brochure. AOHP contact lenses were chosen as the comparator product because these lenses also are reusable contact lenses (see Package Insert for AOHP contact lenses).

[redacted].

3.2 Trial Objective

The objective of this study is to assess the clinical performance of two reusable silicone hydrogel contact lenses when worn on a daily wear modality.

3.3 Risks and Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Material properties and design characteristics of the Alcon serafilcon A contact lens are features consistent with successful contact lens wear.

A summary of the known potential risks and benefits associated with the investigational Alcon serafilcon A contact lens can be found in the Investigator's Brochure (see Package Insert for AOHP contact lenses). Risks are minimized by compliance with the eligibility criteria and study procedures, and through close supervision by a licensed clinician during exposure to the study lenses. The potential harms associated with on-eye exposure to the new lens materials include toxicity response, blurred vision and ocular discomfort. In general, the risks with the investigational contact lens are anticipated to be similar to other marketed soft contact lenses.

The site personnel will educate subjects on proper hygiene and lens handling, and compliance with the use of contact lenses according to the protocol. Subjects should be instructed not to wear contact lenses while sleeping or swimming. The site personnel will also advise the subjects to remove contact lenses and return for prompt follow-up of symptoms, such as ocular discomfort, foreign body sensation, excessive tearing, vision changes, or hyperemia.

3.4 Subject Population

The study population includes approximately 68 volunteer subjects to be enrolled at approximately 5 sites, with approximately 14 subjects enrolled per site. The study population will consist of subjects with normal eyes (other than the need for optical correction for myopia), who are adapted, existing wearers of soft contact lenses in both eyes for at least the past 3 months and who wear contact lenses at least 5 days per week and at least 8 hours per day.

Subjects must be screened according to the full list of inclusion/exclusion criteria in Section 1 of this protocol.

Rescreening of subjects is not allowed in this study.

3.5 Outline of Study

This will be a multi-site, prospective, randomized, double-masked, bilateral, crossover study comparing 2 reusable soft contact lenses. The expected duration of subject participation in the study approximately 28 days (~14 days per each lens type), with 7 scheduled visits. Subjects will be asked to wear their habitual spectacles only (no contact lens wear) during the washout periods of 2 (at least 48 hours) to 4 days after Visit 1 and after Visit 4.

4 TREATMENTS ADMINISTERED

Subjects will be randomized in a 1:1 manner to receive treatment (lens) in crossover sequence Test product then Comparator product or Comparator product then Test product, respectively.

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	LID022821/AOHP	Alcon serafilcon A/AOHP

Sequence 2	AOHP/LID022821	AOHP/Alcon serafilcon A

4.1 Identity of Study Treatments

DESCRIPTION OF TEST AND COMPARATOR PRODUCTS		
	Test	Comparator
LID Number	LID022821	N/A
Lens	Alcon serafilcon A contact lenses	Acuvue Oasys 2 Week with Hydraclear Plus (AOHP) contact lenses
Material	serafilcon A	senofilcon A
Water Content	55 ± 2%	38%
Base Curve (mm)	8.4 mm (Targeted)	8.4 mm and 8.8 mm
Diameter (mm)	14.2 mm (Targeted)	14.0 mm
Packaging, Labeling, and Supply	• Blister foil pack • Foil label includes at a minimum: - material name and/or identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - investigational device statement - sponsor information - country of origin. • Provided in packages of ~ 25 lenses per power per package, identified with the following at a minimum:	• Commercial packaging • Commercial foil • Lenses should be stored at room temperature.

	- a color coded label stating the protocol number - LID number - power - an investigational use only statement - handling unit. • Lenses should be stored at room temperature.	
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: o Test: ~7-day replacement o Comparator: ~14-day replacement o The unmasked staff must maintain the subject and Investigator masking to the study product being used. • Replacement lenses will not be provided to the subject. In the event a lens needs to be replaced, the subject must return to the site for a replacement lens. Until the replacement lens is obtained, the subject must store both study lenses in the provided lens care solution and wear their habitual spectacles. • Exposure: Study lenses are to be worn during typical contact lens wearing hours, on all days during the study lens wearing period, at least 10 hours per day, over each treatment period (7 day (-0/+1) for test and 14 day (-0/+1) for comparator, according to randomization assignment). [redacted] • Lens Care: Cleaned and disinfected with CLEAR CARE Cleaning & Disinfecting Solution after each use.	

Comparator lens procurement	• Sites will procure the comparator product.

4.2 Accountability Procedures

Upon receipt of the study lenses, the investigator or delegate will conduct an inventory. Designated study staff will provide the study lenses to the subjects in accordance with their randomization schedule. Throughout the study, the investigator or delegate must maintain records of study treatment dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation.

The investigator should make every effort to collect unused lenses, foils, and supplies from subjects.

It is the investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner.
- All unused products are available for return to the Study sponsor, as directed.
- Any study lenses associated with a device deficiency or with any product-related adverse event [i.e., ADE or SADE] are returned to the study sponsor for investigation. Refer to Section 7.3 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

4.3 Worn Lens Collection, Storage and Return

Worn lenses from designated sites are to be returned to the study sponsor as indicated in the MOP.

5 STUDY PROCEDURES AND ASSESSMENTS

5.1 Unscheduled Visits

Any visit that occurs between regularly scheduled visits is an Unscheduled Visit. If a subject requires an Unscheduled Visit, he/she must be advised to return to the office wearing the study lenses, if at all possible (unless he/she is experiencing a sign or symptom [as indicated

in Section 3.3 Risks and Benefits]). During all unscheduled visits, the investigator must conduct all procedures specified in Table 1-1 Schedule of Study Procedures and Assessments.

The investigator may perform additional procedures for proper diagnosis and treatment of the subject. The investigator must document this information in the subject's source documents.

If during an Unscheduled Visit the subject is discontinuing from the study, the investigator must refer to 5.2 Discontinued Subjects.

Unplanned Lens Replacement is to be used in the event of a device deficiency or if a lens is lost or damaged, so as to maintain lens wear until the follow-up visit.

5.2 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after signing the informed consent, including screen failures. Subjects may discontinue from the study at any time for any reason. Subjects may also be discontinued from the study at any time if, in the opinion of the investigator, their continued participation poses a risk to their health. Discontinued subjects will not be replaced (i.e., their subject numbers will not be reassigned/reused).

Should a subject exhibit any clinically relevant signs, symptoms, or other clinical observations that possibly could be associated with suspected sensitivity or intolerance to one of the study treatments, the investigator must document those observations on an AE Form.

Any subject who exits early from the study (excluding screen failures) must undergo all procedures outlined in Table 1-1, as possible.

The investigator must document the reason for study or treatment discontinuation in the subject's case history source documents.

To ensure the safety of all subjects who discontinue early, investigators must assess each subject and, if necessary, advise them of any therapies and/or medical procedures that may be needed to maintain their health.

5.3 Clinical Study Termination

The study sponsor reserves the right to close the investigational site or terminate the study in its entirety at any time, for reasonable cause.

If the clinical study is prematurely terminated or suspended by the study sponsor:

- The study sponsor must:
    - Immediately notify the investigator(s) and subsequently provide instructions for study termination.
    - Inform the investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension, as applicable.
- The investigator must:
    - Promptly notify the IRB of the termination or suspension and of the reasons.
    - Provide subjects with recommendations for poststudy treatment options as needed.

The investigator may terminate a site's participation in the study for reasonable cause.

6 ANALYSIS PLAN

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.

Any deviations to this analysis plan will be updated during the course of the study as part of a protocol amendment or will be detailed in the clinical study report.

6.1 Subject Evaluability

The final subject evaluability will be determined prior to breaking of the code for masked treatment (lens) sequence assignment and locking the database, based on the Deviations and Evaluability Plan.

6.2 Analysis Data Sets

6.2.1 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.

6.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the Safety Analysis Set. Baseline data pertaining to habitual lenses, BCVA, and keratometry readings will be summarized on the Safety Analysis Set as well.

6.4 Effectiveness Analyses

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

Select effectiveness endpoints will also be summarized by period.

6.4.1 Primary Effectiveness

The objective of this study is to assess the clinical performance of two reusable SiHy contact lenses when worn on a daily wear modality. The primary endpoint is VA with study lenses at Week 1 Follow-Up, collected at distance for each eye in logMAR.

6.4.1.1 Statistical Hypotheses

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

6.4.1.2 Analysis Methods

Descriptive statistics will be provided, at each visit.

6.5 Subgroup Analyses

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

6.6 Handling of Missing Data

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

6.7 Multiplicity

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

6.8 Safety Analysis

The safety endpoints for this study are AEs, biomicroscopy findings, and device deficiencies.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Descriptive summaries (frequencies and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. AEs leading to study discontinuation, significant nonserious AEs, and SAEs will be identified. Individual subject listings will be provided, as necessary.

Individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to study lenses.

Each biomicroscopy parameter will be tabulated by its grade. For each applicable biomicroscopy parameter, frequencies and percentages of eyes that experience an increase of ≥ 2 grades from baseline (last assessment prior to study lens exposure) to any subsequent visit within the same period will be presented. A supportive listing will be generated which will include all biomicroscopy data from all visits within the same period for these eyes experiencing the increase.

Two listings (prior to exposure of study lenses and treatment-emergent) of device deficiencies, as recorded on the Device Deficiency Form, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

6.9 Interim Analyses

There are no plans to conduct an interim analysis, and no criteria by which the study would be terminated early based upon statistical determination.

6.10 Sample Size Justification

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

7 ADVERSE EVENTS AND DEVICE DEFICIENCIES

Terms and Definitions

Adverse Event (AE)	Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device or comparator and whether anticipated or unanticipated. *Note: For subjects, this definition includes events related to the investigational medical device, comparator, or the procedures involved. For users or other persons, this definition is restricted to the use of investigational medical devices or comparator.*

Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device or comparator *Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse.*
Anticipated Serious Adverse Device Effect (ASADE)	An effect which by its nature, incidence, severity, or outcome has been identified in the risk assessment.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling related to the investigational medical device or the comparator.*
Malfunction	Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan (CIP), or investigator's brochure (IB).
Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in the health of the subject, users or other persons as defined by one or more of the following: a) a life-threatening illness or injury *Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, i.e., it*

	does not include an event which hypothetically might have caused death had it occurred in a more severe form. b) any potentially sight-threatening event or permanent impairment to a body structure or a body function including chronic diseases. c) in-patient hospitalization or prolonged hospitalization. d) a medical or surgical intervention to prevent a) or b). e) any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, congenital abnormality, or birth defect including physical or mental impairment. *Note: Planned hospitalization for a preexisting condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.* *Refer to Section7.1 for additional SAEs.*
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons *Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.*
Significant Nonserious Adverse Event	A symptomatic, device-related, non-sight-threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 7.1 for additional Significant Nonserious AEs.*
Unanticipated Serious Adverse	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the risk assessment.

Device Effect (USADE)	
Use Error	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. *Note:* *a) Use error includes the inability of the user to complete a task.* *b) Use errors can result from a mismatch between the characteristics of the user, user interface, task, or use environment.* *c) Users might be aware or unaware that a use error has occurred.* *d) An unexpected physiological response of the patient is not by itself considered a use error.* *e) A malfunction of a medical device that causes an unexpected result is not considered a use error.*

7.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test *product*). Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 7–1 Categorization of All AEs

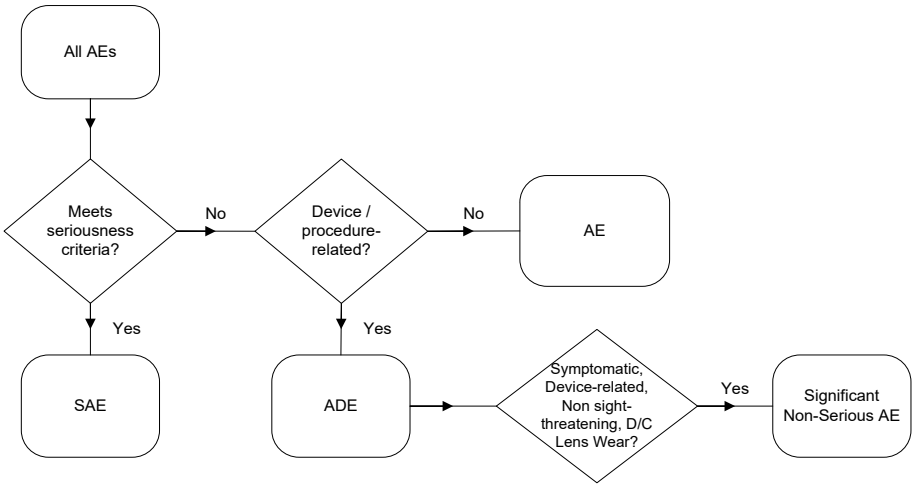
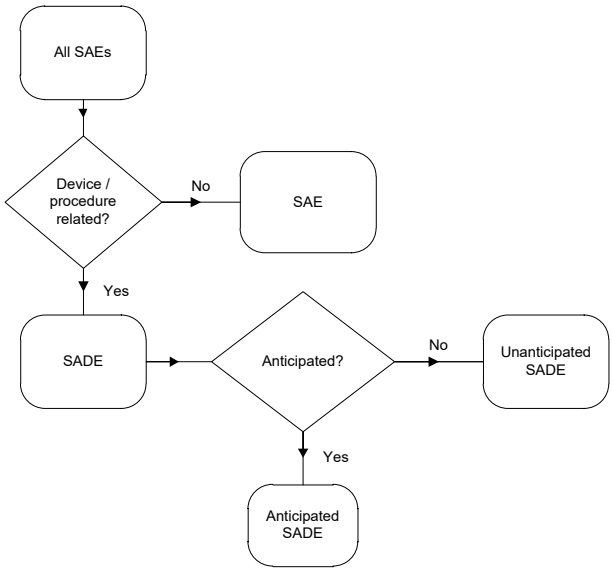


Figure 7-2 Categorization of All Serious Adverse Events



Specific Events Relevant to this Protocol

Serious Adverse Events

In addition to reporting all AEs (serious and nonserious) meeting the definitions, the investigator must report any occurrence of the following as an SAE:

- An ocular infection including a presumed infectious ulcer with any of the following characteristics:
    - Central or paracentral location
    - Penetration of Bowman's membrane
    - Infiltrates > 2 mm diameter
    - Iritis
    - Increase in intraocular pressure
    - Culture positive for microorganisms
    - Increasing size or severity at subsequent visits
- Any central or paracentral corneal event (such as neovascularization) that results in permanent opacification
- Hypopyon
- Hyphema
- Neovascularization within the central 6 mm of the cornea
- Permanent vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting ≥ 50% of corneal surface area

Significant Nonserious Adverse Events

A significant nonserious AE is a symptomatic, device-related, non-sight-threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. In addition, the investigator must report any occurrence of the following as a Significant Nonserious AE:

- Peripheral nonprogressive noninfectious ulcers
- All symptomatic corneal infiltrative events
- Corneal staining score greater than or equal to Grade 3 (Refer to MOP for grading scales)
- Temporary vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that persists for 2 or more weeks

- Neovascularization score greater than or equal to Grade 2

The above events are based upon the categories provided in the ISO 11980 and the US FDA Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (i.e., ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The investigator should determine the applicable category listed in the Device Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. Examples of device deficiencies include the following:

- Failure to meet product specifications (e.g., incorrect lens power/diameter/base curve/color)
- Lens/solution cloudy
- Lens surface/edge defect
- Torn lens during handling/in pack
- Packaging deficit (e.g., mislabeled product, tampered seal, leaking bottle/container)
- Suspect product contamination

7.2 Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the investigator should inquire about AEs by asking the standard questions shown below and report as applicable:

- “Have you had any health problems since your last study visit?”
- “Have there been any changes in the medicines you take because of a new health issue since your last study visit?”

Additionally, changes in *any protocol-specific parameters and/or questionnaires* evaluated during the study are to be reviewed by the investigator. Any untoward (unfavorable and unintended) change in *a protocol-specific parameter or questionnaire response* that is clinically relevant, in the opinion of the investigator, is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

7.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent. Any preexisting medical conditions or signs/symptoms present in a subject prior to the start of the study (i.e., before informed consent is signed) are not considered AEs in the study and should be recorded in the Medical History section of the eCRF.

In addition, temporary lens awareness or visual changes during the fitting process are not considered AEs if the investigator assesses that the symptom(s) can reasonably resolve within the anticipated adaptation period.

For each recorded event, the ADEs and SAEs documentation must include: date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the investigator must document all device deficiencies reported or observed with test and comparator products on the Device Deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the study sponsor immediately as follows:

- ADEs or SAEs are documented on the *Serious Adverse Event and Adverse Device Effect* eCRF within 24 hours of the investigator's or site's awareness.
- Device deficiencies are documented on the *Device Deficiency* eCRF within 24 hours of the investigator's or site's awareness.
- A printed copy of the completed *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* eCRF must be included with product returns.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death, etc., if applicable, in narrative section of the *Serious Adverse Event and Adverse Device Effect* eCRF.

Note: Should the EDC system become nonoperational, the site must complete the appropriate paper *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* Form. The completed form is emailed to the study sponsor at msus.safety@alcon.com according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for nonstudy marketed devices/products (i.e., CLEAR CARE Cleaning & Disinfecting Solution) will be considered and processed as spontaneous

(following the postmarket vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study sponsor representatives may be contacted for any protocol-related question.

Further, depending upon the nature of the AE or device deficiency being reported, the study sponsor may request copies of applicable portions of the subject's medical records. The investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

Intensity and Causality Assessments

Where appropriate, the investigator must assess the intensity (severity) of the AE based upon medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

Mild	An AE is mild if the subject is aware of but can easily tolerate the sign or symptom.
Moderate	An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.
Severe	An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

For every AE in the study, the investigator must assess the causality (Related or Not Related to the medical device or study procedure). An assessment of causality will also be performed by study sponsor utilizing the same definitions, as shown below:

Causality

Related	An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.
Not Related	An AE classified as not related may either be definitely unrelated or simply unlikely to be related (i.e., there are other more likely causes for the AE).

The study sponsor will assess the AEs and may upgrade the investigator's assessment of seriousness and/or causality. The study sponsor will notify the investigator of any AEs that are upgraded from nonserious to serious or from unrelated to related.

7.4 Return product analysis

Alcon products associated with device deficiencies and/or product related AEs should be returned and must include the Complaint # which will be provided by study sponsor after the case is entered in the study sponsor's Global Product Complaint Management System. These products should be returned to the sponsor at the end of the study, unless instructed otherwise by the sponsor.

7.5 Follow-Up of Subjects with Adverse Events

The investigator is responsible for adequate and safe medical care of subjects during the study and for ensuring that appropriate medical care and relevant follow-up procedures are maintained after the study.

The investigator should provide the study sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ongoing at time of subject discontinuation or exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (i.e., database lock).

Any additional data received up to 1 month after subject discontinuation or exit must be documented and available upon the study sponsor's request. All complaints received after this time period will be considered and processed as spontaneous and should be communicated to the medical device's manufacturer as per local requirements.

The investigator should also report complaints on non-Alcon products directly to the manufacturer as per the manufacturer's instructions or local regulatory requirements.

7.6 Pregnancy in the Clinical Study

Women who are pregnant at the time of study entry are excluded from participation. However, pregnancy should be included in the pregnancy eCRF when a woman becomes pregnant during the study. Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case–by-case basis.

8 CONFIDENTIALITY, BIAS, AND MASKING

8.1 Subject Confidentiality and Methods Used to Minimize Bias

The investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the investigator must keep an enrollment log with confidential identifying information that corresponds to the subject numbers and initials of each study participant. All documents submitted to the sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information should be transmitted to the sponsor.

This study is double-masked with subjects randomized to use Alcon serafilcon A or AOHP contact lens for the duration of 2-week treatment period.

The investigator and sponsor personnel (other than site monitors, clinical operations lead, person responsible for generating the randomization schedule, and unmasked clinical data managers) involved in reporting, obtaining, and/or reviewing the clinical evaluations will be masked to the identity of the contact lens being administered. This level of masking will be maintained throughout the conduct of the study. Unmasking will occur only after all planned study data have been validated, and the database locked.

8.2 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study. In the event of a medical emergency where the knowledge of subject treatment is required, individual investigator(s) will have the ability to unmask the treatment assignment for a specific subject. If time allows, the appropriate study sponsor representative should be contacted prior to unmasking. The study sponsor must be informed of all cases in which the code was broken and of the circumstances involved. Additionally, the study sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting requirements.

9 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

9.1 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the eCRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Study monitors are appointed by the study sponsor and are independent of study site staff. If electronic records are maintained, the method of verification must be determined in advance of starting the study.

At a minimum, source documents should include the following information for each subject:

- Subject identification (name, sex, race/ethnicity)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of study parameters, as required by the protocol
- IP accountability records
- Documentation of AEs and other safety parameters (if applicable)
- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation, if applicable

It is required that the author of an entry in the source documents be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the eCRF are consistent with the original source data.

Only designated individuals may complete the eCRFs. The eCRFs will be submitted at regular intervals following the clinical study visit schedule. It is expected that all data reported will have corresponding entries in the source documents. The principal investigator is responsible for reviewing and certifying that the eCRFs are accurate and complete. The only subject identifiers recorded on the eCRFs will be subject number and subject demographic information.

9.2 Data Review and Clarifications

Upon completion of the eCRFs, a targeted review of the eCRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. Additional data clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's eCRFs.

9.3 Regulatory Documentation and Records Retention

The investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the sponsor and the investigator's files will be reviewed as part of the ongoing study monitoring. Financial disclosure is not subject to regulatory inspection and should be kept separately.

Additionally, the investigator must keep study records and source documents until the sponsor provides written approval for their destruction. If the investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records, the sponsor must be notified, and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations (generally 2 years after discontinuing clinical development or after the last marketing approval).

10 ETHICS AND COMPLIANCE

This trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the referenced directives, regulations, guidelines, and/or standards.

10.1 Compliance

The investigator must ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience. The investigator and all clinical study staff must conduct the clinical study in compliance with the protocol. Deviations from this protocol, regulatory requirements, and/or GCP must be recorded and reported to the sponsor prior to database lock. If needed, corrective and preventive action should be identified, implemented, and documented within the study records.

10.2 Institutional Review Board (IRB)

This trial requires IRB approval prior to initiation. This protocol, subject informed consent, and subsequent amendments will be reviewed and approved by an IRB.

Before clinical study initiation, this protocol, the ICF (and assent form, if applicable), any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IRB. The investigator must provide documentation of the IRB approval to the study sponsor. The approval must be dated and must identify the applicable protocol, amendments (if any), ICF, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. The IRB must be provided with a copy of the Investigator's Brochure, any periodic safety updates, and all other information as required by local regulation and/or the IRB. At the end of the study, the investigator must notify the IRB about the study's completion. The IRB also must be notified if the study is terminated prematurely. Finally, the investigator must report to the IRB on the progress of the study at intervals stipulated by the IRB.

Voluntary informed consent must be obtained from every subject (and/or legal representative, as applicable) prior to the initiation of any screening or other study-related procedures. The investigator must have a defined process for obtaining consent. Specifically, the investigator, or delegate, must explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the investigator, and if required by local regulation, other qualified personnel. The investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and sponsor-designated personnel. The investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject according to local regulations. Following this study, the subject will return to their eye care professional for their routine eye care and contact lenses.

12 REFERENCES

The following are references that may be applicable in whole or in part for this clinical trial.

- ISO 11980:2012 Ophthalmic optics - Contact lenses and contact lens care products - Guidance for clinical investigations
- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 812 - Investigational Device Exemptions
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators

13 APPENDIX

Not applicable.