Clinical Performance Evaluation of Two Frequent Replacement Silicone Hydrogel Multifocal Contact Lenses

STUDY ID

CLN705-C001

PROTOCOL

NCT05338333

Alcon

Device Protocol for CLN705-C001
Title: Clinical Performance Evaluation of Two Frequent Replacement Silicone Hydrogel Multifocal Contact Lenses

Protocol Number:	CLN705-C001
Clinical Investigation Type:	Pivotal
Test Product:	[redacted] Multifocal contact lenses
Sponsor Name and Address:	Alcon Research, LLC, and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099

[redacted]

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 Practices; applicable international and national regulations, laws, guidelines, and standards; the conditions of approval imposed by the reviewing IRB or regulatory authority; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki.
- 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:

Phone Number:

Off-hours Emergency Phone Number:

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[redacted]

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1 GLOSSARY OF TERMS

Names of test product(s)	Throughout this document, test product(s) will be referred to as [redacted] Multifocal ([redacted] MF) contact lenses.
Name of Comparator Product(s)	AIR OPTIX® plus HydraGlyde® Multifocal (AOHG MF) contact lenses.
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device (investigational product) or comparator product. *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.*
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: 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 events related to the use of investigational medical device or comparator.* Requirements for reporting Adverse Events in the study can be found in Section 11.
Anticipated Serious Adverse Device Effect (ASADE)	An effect which by its nature, incidence, severity, or outcome has been identified in the risk assessment.

Clinical Investigation Plan (CIP)	The document(s) stating the rationale, objectives, design, and prespecified analysis, methodology, organization, monitoring, conduct, and record-keeping of the clinical investigation. *Note: The protocol and other documents referenced in the protocol (for example, the Statistical Analysis Plan, the Manual of Procedures, the Deviations and Evaluability Plan, and the Protocol Monitoring Plan) comprise the CIP.*
Clinical Investigation Report (CIR) / Clinical Study Report	The document describing the design, execution, statistical analysis, and results of a clinical investigation. The Clinical Investigation Report is synonymous with the Clinical Study Report.
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.* Requirements for reporting Device Deficiencies in the study can be found in Section 11.
Enrolled Subject	Any subject who signs an informed consent form for participation in the study.
Point of Enrollment	The time at which, following recruitment and before any clinical investigation-related procedures are undertaken, a subject signs and dates the informed consent form.

Interventional Clinical Trial	A pre- or postmarket clinical investigation where the assignment of a subject to a particular medical device is decided in advance by a clinical investigation plan, or diagnostic or monitoring procedures requested in the CIP are in addition to those available as normal clinical practice and burden the subject.
Investigational Product	A preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or comparator product in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
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).
Noninterventional Study	Clinical investigation that draws inferences about the possible effect of an intervention on subjects, but the investigator has not assigned subjects into intervention groups based on a protocol and has not made any attempts to collect data on variables beyond those available throughout the course of normal clinical practice and burden to the subject. NOTE: The term "noninterventional" is synonymous with "observational."
Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.

Product Complaint	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling, or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
Randomized Subject	Any subject who is assigned a randomized treatment.
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) inpatient 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 Section 11 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 11 for additional Significant Nonserious AEs.*
Study Start	The start of the study is considered to coincide with the enrollment of the first patient.
Study Completion	The completion of the study is considered to coincide with the study-level last subject last visit or the decision to terminate the trial, whichever is later.
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the risk assessment.

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."*
Vulnerable Subject	An individual who is unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response.

2 LIST OF ACRONYMS AND ABBREVIATIONS

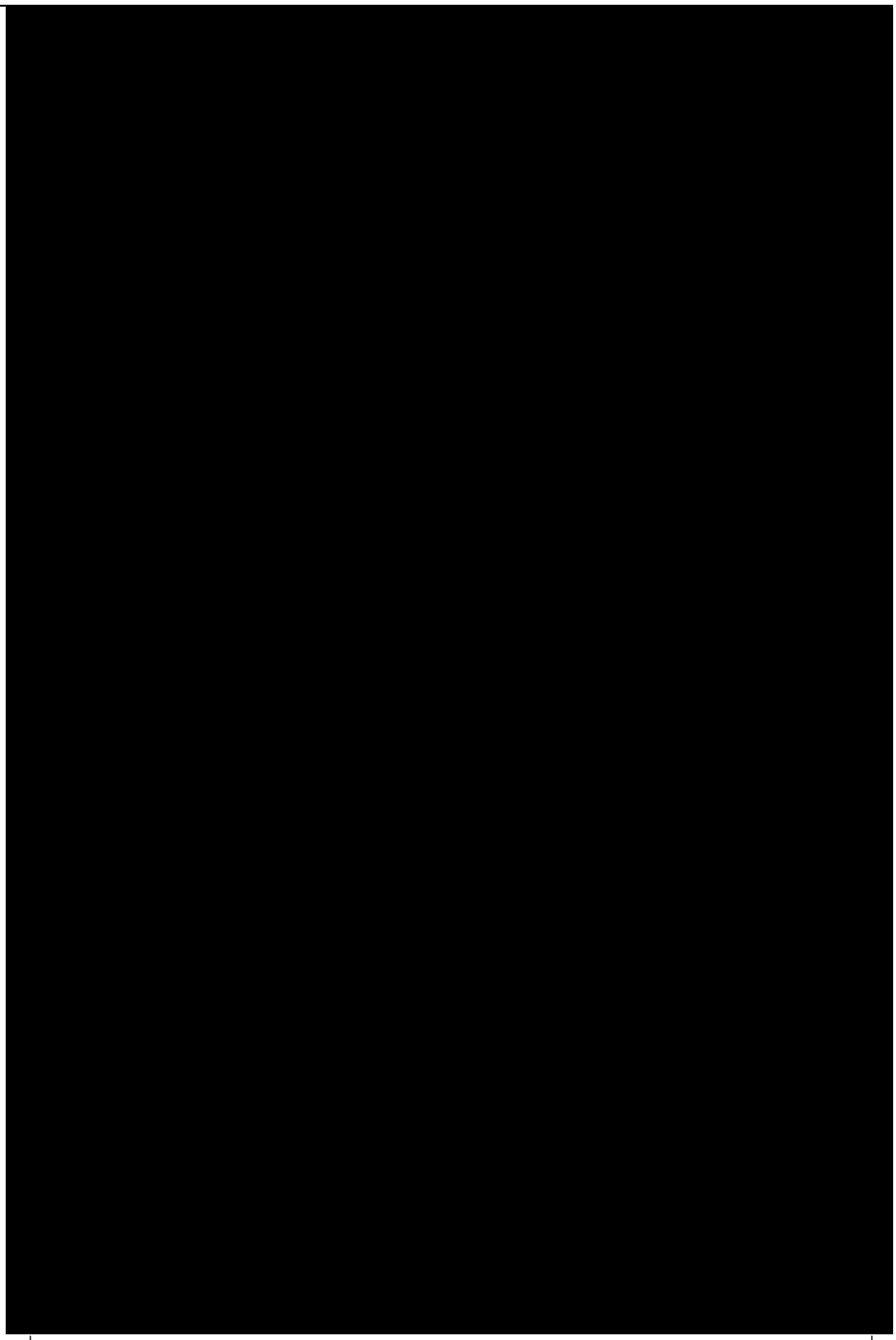
Table 2–1 List of Acronyms and Abbreviations Used in This Protocol

Abbreviation	Definition
ADD	Addition
ADE	Adverse device effect
AE	Adverse event
AOHG MF	AIR OPTIX® plus HydraGlyde® Multifocal contact lenses (lotrafilcon B)
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CIP	Clinical investigation plan
CIR	Clinical investigation report
[redacted]	[redacted]
COL	Clinical operation lead
CRF	Case report form
CSM	Clinical site manager
CTT	Clinical trial team
D	Diopters
EC	European Commission
ECP	Eye care professional
eCRF	Electronic case report form
EDC	Electronic data capture
FAS	Full analysis set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
HC/HI	High Contrast/High Illumination
HI	High
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
LO	Low
LogMAR	Logarithm of the minimum angle of resolution
m	Meters
MED	medium
MedDRA®	Medical Dictionary for Regulatory Activities
MF	Multifocal
[redacted]	[redacted]

Abbreviation	Definition
MOP	Manual of procedures
N	Number of subjects
N/A	Not applicable
NI	Noninferiority
OD	Oculus dexter (right eye)
OS	Oculus sinister (left eye)
OU	Oculus uterque (both eyes)
[redacted] MF	[redacted] Multifocal contact lenses (lehfilcon A)
PI	Principal investigator
PP	Per protocol
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SLE	Slit lamp examination
SOP	Standard operating procedure
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: [redacted] Multifocal contact lenses Comparator Product: AIR OPTIX plus HydraGlyde Multifocal contact lenses
Purpose and Scientific Rationale for the Study	To compare the clinical performance of [redacted] MF contact lenses with AOHG MF contact lenses, both utilizing Alcon's Precision Profile® Multifocal Design, [redacted]
Objective(s)	The primary objective of this study is to demonstrate noninferiority in visual acuity at distance when wearing [redacted] MF contact lenses compared to AOHG MF contact lenses, after 30 days of wear. [redacted] r. The safety objective of this study is to describe the safety profile of the investigational products.
Endpoint(s)	Primary Effectiveness • Binocular high contrast/high illumination (HC/HI) visual acuity (VA; logMAR) at distance (4 m or 3 m) at Day 30 [redacted] [redacted]

	
	Safety • Adverse events • Biomicroscopy findings • Device deficiencies

Assessment(s)	Effectiveness • Binocular [redacted] logMAR HC/HI Distance (4 m or 3 m) VA [redacted] Safety • Biomicroscopy • Adverse Events • Device deficiencies

Study Design	This is a prospective, randomized, [redacted], bilateral, crossover, double-masked, dispensing trial comparing [redacted] MF and AOHG MF contact lenses. Subjects will be expected to attend 4 office visits and will be dispensed study lenses (test and comparator lenses) for a 30 day duration of bilateral wear each (total of approximately 60 days of lens wear). [redacted] Subjects will be [redacted] randomized 1:1 to receive one of two sequences: Sequence 1 = LID210464/AOHG MF Sequence 2 = AOHG MF/ LID210464
Subject population	Planned number of subjects enrolled/consented: ~96 Planned number of completed subjects: 84 The subject population consists of volunteer subjects aged ≥ 40 years, who are habitual daily disposable and biweekly/monthly replacement soft multifocal contact lens wearers for at least past 3 months and wear their habitual lenses at least 5 days per week and at least 8 hours per day.
Sites and Locations	Planned number of clinical sites: ~ 8 Planned locations (initial list of locations, which may change during start up or conduct according to study needs): United States
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Habitual daily disposable & biweekly/monthly replacement soft multifocal contact lens (including AOHG MF) wearers aged ≥ 40 years with normal eyes (other than correction for refractive error). Subjects should have at least 3 months wearing experience, wear these lenses at least 5 days per week and at least 8 hours per day. • Subjects must have a manifest cylinder ≤ 0.75 D in each eye. • Subjects must have a BCVA of 20/25 or better in each eye at distance with a spherical refractive error between -1.00 and -4.00 D, and requiring a near ADD of LO, MED or HI (ADD of +0.75 D to +2.50 D) in each eye.

<table>
<tr><td>Key exclusion criteria
(See Section 8.2 for a complete list of exclusion criteria)</td><td>

Currently pregnant or lactating
Any history of amblyopia, strabismus or binocular vision abnormalities
Monovision contact lens wearers and wearers of contact lens in one eye only.

</td></tr>
<tr><td>Data analysis and sample size justification</td><td>
Planned Data Analysis
[redacted] planned analyses are summarized below:
<table>
<tr><th>Endpoint</th><th>Comparison</th><th>Statistical Model</th></tr>
<tr><td>Primary</td><td></td><td></td></tr>
<tr><td>Binocular HC/HI VA at</td><td>[redacted] MF vs AOHG MF</td><td>Mixed effects repeated measures</td></tr>
</table>
[redacted]
Sample Size Justification
Sample size calculation is based on 2 prior clinical studies which evaluated performance of several marketed multifocal contact lenses. Of the endpoints with planned inferential testing, VA at near yields the largest required sample size of 42/sequence at 90% power, one-sided α=0.05, with NI margin of 0.05.
</td></tr>
<tr><td>Associated materials</td><td>

CLEAR CARE® Cleaning & Disinfecting Solution
Lubrication/rewetting drops will not be permitted during lens wear. However, habitual lubrication/rewetting drop usage is allowed up to 10 minutes prior to lens insertion and any time after lens removal.
No lubrication/rewetting drop use will be allowed during clinic visits.
LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.

</td></tr>
</table>

Table 3–1 Schedule of Study Procedures and Assessments

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screening / Baseline / Lens Fit	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 3 Dispense Lens 2**	**Visit 4 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled Visit**	**Early Exit**
Procedure/ Assessment		**Day 1 [3-5 days after Visit 1** [redacted]	**Day 30 (-2/+1) Days**	**Day 1 [same day as Lens 1 Day 30 Follow-up visit]**	**Day 30 (-2/+1) Days**	**N/A**	**N/A**
Informed Consent	X						
Demographics	X						
Medical History∞	X	X	X		X	X	X
Concomitant Medications∞	X	X	X		X	X	X
Habitual lens information (brand, power, lens solution*)	X						
VA with habitual correction (OD, OS, Snellen distance)*	X				X	(X)	X
Keratometry (OD, OS)*	X						
Manifest refraction*	X	(X)	(X)	(X)	(X)	(X)	(X)
BCVA (OD, OS, Snellen distance and near with manifest refraction)*	X	(X)	(X)	(X)	(X)	(X)	(X)
Biomicroscopy	X	X	X		X	X	X

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screening / Baseline / Lens Fit	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 3 Dispense Lens 2**	**Visit 4 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled Visit**	**Early Exit**
Procedure/ Assessment		**Day 1 [3-5 days after Visit 1** [redacted]	**Day 30 (-2/+1) Days**	**Day 1 [same day as Lens 1 Day 30 Follow-up visit]**	**Day 30 (-2/+1) Days**	**N/A**	**N/A**
						Optional with Unplanned Lens Replacement only	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Inclusion/Exclusion criteria	X						
Randomize	X						
Study lens parameters optimization and fitting per randomization scheme (Test and Comparator)* • [redacted]	X						
[redacted]	[redacted]						

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screening / Baseline / Lens Fit	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 3 Dispense Lens 2**	**Visit 4 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled Visit**	**Early Exit**
Procedure/ Assessment		**Day 1 [3-5 days after Visit 1** [redacted]	**Day 30 (-2/+1) Days**	**Day 1 [same day as Lens 1 Day 30 Follow-up visit]**	**Day 30 (-2/+1) Days**	**N/A**	**N/A**
Study lens power to be dispensed	X						
[redacted]	[redacted]						
Dispense study lenses per randomization scheme		X		X		(X)	
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
LogMAR HC/HI VA at: • Distance (4 m or 3 m; [redacted] OU) [redacted]		X	X	X	X	(X)	X

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screening / Baseline / Lens Fit	Visit 2 Dispense Lens 1	Visit 3 Day 30 Follow-up Lens 1	Visit 3 Dispense Lens 2	Visit 4 Day 30 Follow-up Lens 2 / Exit	Unscheduled Visit	Early Exit
Procedure/ Assessment		Day 1 [3-5 days after Visit 1 [redacted]	Day 30 (-2/+1) Days	Day 1 [same day as Lens 1 Day 30 Follow-up visit]	Day 30 (-2/+1) Days	N/A	N/A
[redacted]		■	■	■	■		■
[redacted]		■	■	■	■		■
[redacted]		■		■			
[redacted]			■		■		■
[redacted]			■		■		■
[redacted]			■		■		■
[redacted]			■		■		■
[redacted]		■	■	■		■	

		LENS 1 (Period 1)		LENS 2 (Period 2)			
	Visit 1 Screening / Baseline / Lens Fit	**Visit 2 Dispense Lens 1**	**Visit 3 Day 30 Follow-up Lens 1**	**Visit 3 Dispense Lens 2**	**Visit 4 Day 30 Follow-up Lens 2 / Exit**	**Unscheduled Visit**	**Early Exit**
Procedure/ Assessment		**Day 1 [3-5 days after Visit 1** [redacted]	**Day 30 (-2/+1) Days**	**Day 1 [same day as Lens 1 Day 30 Follow-up visit]**	**Day 30 (-2/+1) Days**	**N/A**	**N/A**
Adverse Events	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) assessment performed as necessary, e.g., decrease of VA by 2 lines or more with investigational product (IP), for example when comparing between V3 and V2 for Distance VA with Lens 1 and between V4 and V3 for Distance VA with Lens 2.

* Source only (source provided to sponsor upon request).

∞ Concomitant medications (past 30 days) and Medical History (past year) must be fully documented and collected in the subject source documents with targeted collection in EDC.

4 PROTOCOL AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments must be created by the study sponsor and must be approved by the IRB/IEC and global and regional Health Authorities, as applicable, prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all subjects currently enrolled in the study must sign the approved, revised informed consent (re-consent), as required by the IRB/IEC.

[redacted]

5 INTRODUCTION

5.1 Rationale and Background

Presbyopia is a refractive error condition that develops as part of normal aging in which the natural crystalline lens of the eye progressively loses the focusing ability, resulting in difficulty at focusing for close objects and for activities like reading. The signs of presbyopia become noticeable around the age of 40 years. Presbyopia could be corrected with single-vision, bifocal or progressive spectacles, progressive addition lenses, monovision contact lenses or multifocal contact lenses.

To address the growing needs of prebyopic population, [redacted] MF soft contact lenses, a new monthly replacement water gradient contact lens has been developed. These multifocal lenses use the center-near aspheric Unique Precision Profile® Multifocal design, which has been successfully adopted for DAILIES® Total1® MF, DAILIES® AquaComfort® Plus MF and AIR OPTIX® plus HydraGlyde® MF contact lenses.

[redacted] MF soft contact lenses are indicated for the optical correction of presbyopia, with or without refractive ametropia (myopia and hyperopia) in phakic (having the natural eye lens) or aphakic (not having the natural eye lens) persons with non-diseased eyes who may require a reading addition of +3.00 D or less and who may have up to 1.50 D of astigmatism that does not interfere with visual acuity.

The lenses are intended for daily wear (less than 24 hours while awake) with removal for disposal, or cleaning and disinfection (chemical, not heat) prior to reinsertion, as recommended by an eye care professional. Lenses should be discarded and replaced with a new pair after one month or more often, if recommended by an eye care professional.

The [redacted] MF contact lens possesses unique material properties and inherently wettable core material with a water gradient surface to provide sustained long-lasting performance. These new silicone hydrogel lenses have been designed to provide favorable performance for daily wear with 1-month replacement.

In this clinical study, the clinical performance of the investigational [redacted] MF contact lens will be assessed and compared to the Alcon's commercially available AOHG MF contact lens, which also utilizes the Precision Profile multifocal design, in a crossover dispense trial, both to be worn in a daily wear modality and replaced on a monthly basis.

5.2 Purpose of the Study

The study will compare the clinical performance of [redacted] MF contact lenses with AOHG MF contact lenses, both utilizing Alcon's Precision Profile® Multifocal Design, [redacted]

At the end of the study, a clinical study report will be prepared in accordance with applicable regulatory requirements and standards.

[redacted]

Alcon reserves the right of prior review of any publication or presentation of information related to the study. The author(s) of the publication will be the individual with substantial contribution to the conception or design of the work, or the acquisition, analysis, or interpretation of data. Additionally, the author will draft the work or revise it critically for important intellectual content; provide final approval of the version to be published; and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

5.3 Risks and Benefits

Risk management principles have been applied to both the planning and the intended conduct of the clinical investigation, in order to ensure the reliability of the clinical data generated and the safety of the subjects.

The clinical investigation process risks are managed through appropriate training and monitoring according to the protocol-specific monitoring plan. Investigational device risks, including risks associated with use of device and methods and procedures for application of device, are defined in the investigator's brochure and/or product labeling and are managed through review of safety assessments outlined in this protocol.

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Material properties and design characteristics of [redacted] contact lenses are features consistent with successful contact lens wear. Based upon nonclinical testing and documented rationale for applicability of test results, [redacted] MF contact lenses, which are made of the same material as [redacted] sphere contact lenses, are assessed to be non-toxic and biocompatible for on-eye use.

In the US, AIR OPTIX plus HydraGlyde contact lenses have approved indications for use for both daily wear and extended wear for up to 6 continuous nights. Further details on any known potential risks and benefits can be found in the product package insert.

A summary of the known potential risks and benefits associated with [redacted] MF contact lenses can be found in the IB. The potential harms associated with on-eye exposure to the new lens materials include toxicity response, blurred vision, and ocular discomfort. In general, when worn for daily wear, the risks with [redacted] MF contact lenses are anticipated to be similar to other marketed soft contact lenses worn for daily wear.

There may also be unknown risks to use of [redacted] MF contact lenses. Any risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria and study procedures, clinical oversight, and monitoring. Site personnel will educate subjects on proper hygiene and lens handling, and compliance with the use of contact lenses for daily wear according to the protocol. Subjects should be instructed not to wear contact lenses while swimming due to increased risk of infection or while sleeping. Site personnel should 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.

Refer to the IB for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
To demonstrate noninferiority in visual acuity at distance when wearing [redacted] MF contact lenses compared to AOHG MF contact lenses, after 30 days of wear.	Binocular high contrast/high illumination (HC/HI) visual acuity (VA; logMAR) at distance (4 m or 3 m) at Day 30

6.2 Secondary Objective(s)

Not applicable.

[redacted]

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

Objective(s)	Endpoint(s)
To describe the safety profile of the investigational products.	• Adverse events • Biomicroscopy findings • Device deficiencies

7 INVESTIGATIONAL PLAN

7.1 Study Design

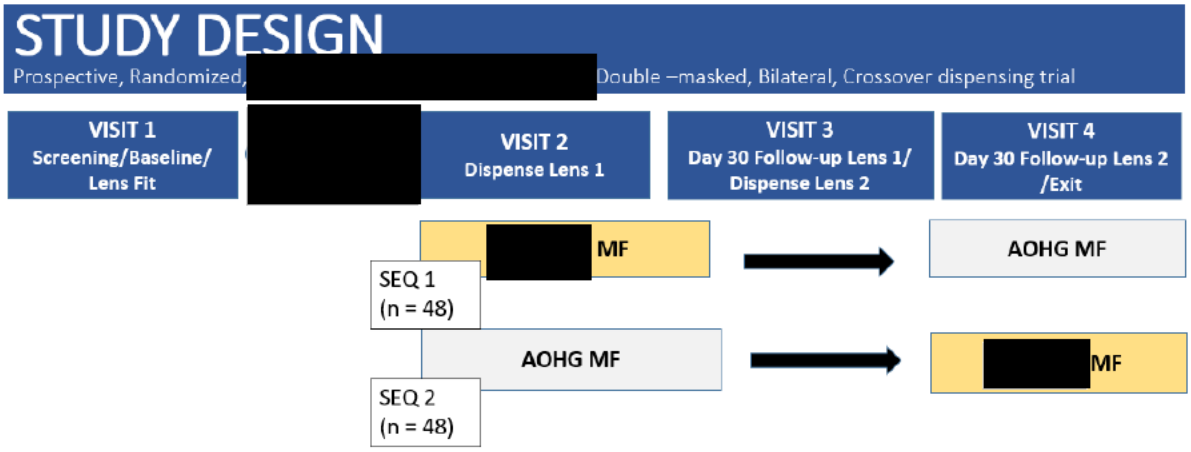
This is a prospective, randomized, [redacted] bilateral, crossover, double-masked, trial comparing the [redacted] MF and AOHG MF contact lenses.

Subjects will be randomized in 1 of 2 crossover sequences and exposed to both test and comparator lenses for bilateral wear. Subjects will be expected to attend 4 office visits and will be dispensed study lenses (test and comparator lenses) for a 30 day duration of bilateral wear with each study lens (~60 days total of study lens wear). Subjects will be expected to wear their study contact lenses for at least 8 hours per day, at least 5 days per week, over a 30 day period per study lens.

In this trial, both the investigator and subject will be masked and an unmasked site coordinator will prepare the lenses for both lens fitting and dispensing.

All study contact lenses will be prescribed according to the subject's prescription. CLEAR CARE Cleaning & Disinfecting Solution will be provided for use during the duration of the study.

Figure 7-1 Study Design



7.2 Rationale for Study Design

This study design is justified based upon an evaluation of the results of relevant preclinical and clinical testing, as described within the IB.

The bilateral, crossover study design will ensure that the same subject is exposed to both the test and comparator lens materials during the study visits and wearing period; therefore, objective and subjective assessments can be obtained for both lenses from the same subject.

The study will include only those subjects who are successful wearers of soft multifocal contact lenses in both eyes during the past 3 months for a minimum of 5 days per week and 8 hours per day. This will avoid confounding safety responses in non-adapted subjects. Habitual AOHG MF contact lens wearers are allowed to participate in this trial and can constitute up to approximately 50% of the total subject population. Habitual daily disposable multifocal soft contact lens wearers will be allowed to participate as well, and can constitute up to approximately 20% of the total subject population. The study will exclude subjects who are monovision contact lens and wearers of contact lens in one eye only.

Lubrication/rewetting drops will not be permitted during study lens wear or at study visits, as this may confound the primary effectiveness [redacted]. However, habitual lubrication/rewetting drop usage is allowed up to 10 minutes prior to lens insertion and any time after lens removal during the study.

Currently pregnant or lactating women and participants with any history of amblyopia, strabismus or binocular vision abnormalities will be excluded from the trial, to prevent confounding the safety/effectiveness endpoints. Subjects who become pregnant during the study will not be discontinued; however, data will be excluded from the effectiveness analyses because pregnancy can alter refraction and visual acuity results.

7.3 Rationale for Duration of Treatment/Follow-Up

The primary [redacted] will be assessed on Day 30. Hence, subjects will wear each study product bilaterally for approximately 30 days.

7.4 Rationale for Choice of Comparator Product

The AOHG MF contact lenses have been chosen as the comparator product because these lenses utilize the same Precision Profile MF design, and have the same wear modality and monthly replacement schedule as [redacted] MF contact lenses.

8 STUDY POPULATION

The study population consists of volunteer subjects, of at least 40 years of age who are habitual biweekly or monthly soft multifocal 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 8 hours per day. It is aimed to enroll (consent) approximately 96 subjects at

approximately 8 sites in the United States, with a target of 84 total subjects completed. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 4 weeks; however, unanticipated circumstances may shorten or lengthen this time and would not require amendment of this protocol.

Habitual AOHG MF contact lens wearers are allowed to participate in this trial and can constitute up to approximately 50% of the total subject population. If enrollment exceeds approximately 50% of the target for AOHG MF habitual contact lens wearers, a subject may be discontinued at sponsor discretion. Habitual daily disposable multifocal soft contact lens wearers will also be allowed to participate and can constitute up to approximately 20% of the total subject population.

This protocol allows enrollment of the following vulnerable population(s), with associated justification for each population:

Elderly – Presbyopia and associated gradual loss of accommodation is part of the aging process and worsens with increasing age. Multifocal contact lenses are a commonly used correction option for this condition. The contact lens under study is intended to alleviate this condition. Therefore, it is appropriate and necessary to include elderly subjects in this clinical trial to gain data regarding the safety and effectiveness of the [redacted] MF contact lenses in this population.

8.1 Inclusion Criteria

Written informed consent must be obtained before any study specific assessment is performed. Upon signing informed consent, the subject is considered enrolled in the study.

Subjects eligible for inclusion in this study must fulfill **all** of the following criteria:

1. Subject must be able to understand and sign an IRB/IEC approved Informed Consent form.
2. Willing and able to attend all scheduled study visits as required per protocol.
3. Subject must be at least 40 years of age.
4. Subject must be willing to stop wearing their habitual contact lenses and be willing to not wear glasses during study lens wear for the duration of study participation.

5. Current wearer of daily disposable and biweekly/monthly replacement multifocal soft contact lenses (including AOHG MF) in both eyes for a minimum of 5 days per week and 8 hours per day during the past 3 months.

6. Manifest cylinder ≤ 0.75 D in each eye.

7. BCVA distance (as determined by manifest refraction at screening) 20/25 or better in each eye with a spherical refractive error between -1.00 and - 4.00 D, and requiring a near ADD of LO, MED or HI (ADD of +0.75 D to +2.50 D) in each eye.

   Note: Study lens parameters available in this study are:

   - *LO ADD with -1.25 D to -4.00 D (in 0.25 D steps)*
   - *MED ADD with -1.00 D to -4.00D (in 0.25 D steps)*
   - *HI ADD with -1.50 D to -3.00 D (in 0.25 D steps)*

8. Subject willing to wear the study contact lenses as defined for the full duration of the study.

9. Subject must possess spectacles and be willing to wear habitual spectacles for vision correction when study lenses are not worn, during wash out period and as directed by PI.

8.2 Exclusion Criteria

Subjects fulfilling **any** of the following criteria are not eligible for participation in this study.

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 planning 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, and/or any infiltrate.

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 12 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. Currently pregnant or lactating, as stated by subject.
11. Any history of amblyopia, strabismus or binocular vision abnormalities.
12. Any use of topical ocular medications and artificial tear or rewetting drops that would require instillation during contact lens wear.
13. 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.
14. Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial.
15. Monovision contact lens wearers and wearers of contact lens in one eye only.
16. 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.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s): [redacted] MF (LID210464)

Comparator Product(s) (If applicable):	AOHG MF

Table 9–1 Test Product

Test Product	[redacted] Multifocal contact lenses ([redacted] MF) LID210464
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	The investigational frequent replacement multifocal contact lens is indicated for the optical correction of presbyopia with or without refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may require a reading addition of +3.00 diopters (D) or less and who may have up to approximately 1.50 diopters (D) of astigmatism that does not interfere with visual acuity.

Product description and parameters available for this study	• Material: lehfilcon A
	• Water content: 55% (targeted)
	• Power range:
	  ○ LO ADD with -1.25 D to -4.00 D (in 0.25 D steps) spherical power as available
	  ○ MED ADD with -1.00 D to -4.00D (in 0.25 D steps) spherical power as available
	  ○ HI ADD with -1.50 D to -3.00 D (in 0.25 D steps) spherical power as available
	• Base curve (mm): 8.4 mm (targeted)
	• Diameter (mm): 14.2 mm (targeted)

Formulation	Refer to IB

Usage	• Wear:
	  ○ Daily Wear
	  ○ Bilateral
	• Replacement period: 30-day replacement
	• Exposure: At least 8 hours per day, 5 days per week, over a 4-week period.

	• Lens Care: Cleaned and disinfected with CLEAR CARE Cleaning & Disinfecting Solution after each use • 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.
Number/Amount of product to be provided to the subject	• Subjects will insert study lenses at Visit 2 and Visit 3 at the site. • No spare lenses will be provided to the subject.
Packaging description	Blister foil pack
Labeling description	• Lens Foil label includes at a minimum: - material name and identifier - base curve - diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational device statement - sponsor information • Provided in ~15 lenses per power per package, identified with the following at a minimum: - a color coded label stating the protocol number - LID number - power - an investigational use only statement - Handling unit
Training and/or experience	No additional training or experience is required to administer the test product.

requirements for device	
Storage conditions	Lenses are to be stored at room temperature
Supply	• Lenses supplied by the sponsor • CLEAR CARE Cleaning & Disinfecting Solution supplied by sponsor to be provided to the subject • LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.

Table 9–2 Comparator Product

Comparator Product(s)	AIR OPTIX plus HydraGlyde Multifocal contact lenses (AOHG MF)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for Use	These comparator multifocal soft contact lenses are indicated for the optical correction of presbyopia, with or without refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may require a reading addition of +3.00 diopters (D) or less and who may have up to approximately 1.50 diopters (D) of astigmatism that does not interfere with visual acuity.
Product description and parameters available for this study	• Material: lotrafilcon B • Water content: 33% • Power range: Limited lens parameters will be available for use in this study: o LO ADD with -1.25 D to -4.00 D (in 0.25 D steps) spherical power as available o MED ADD with -1.00 D to -4.00 D (in 0.25 D steps) spherical power as available o HI ADD with -1.50 D to -3.00 D (in 0.25 D steps) spherical power as available • Base curve (mm): 8.6 mm

	• Diameter (mm):14.2 mm
Formulation	Refer to package insert

Usage	• Wear:
	  o Daily Wear
	  o Bilateral
	• Replacement period: 30-day replacement
	• Exposure: At least 8 hours per day, 5 days per week, over a 4-week period.
	• Lens Care: Cleaned and disinfected with CLEAR CARE Cleaning & Disinfecting Solution after each use
	• 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.

Number/Amount of Product to be Provided to the subject	• Each site will procure their own comparator lenses. • Subjects will insert study lenses at Visit 2 and Visit 3 at the site. • No spare lenses will be provided to the subject.
Packaging description	Commercial packaging
Labeling description	Commercial foil
Training and/or experience requirements for device	No additional training or experience is required to administer the comparator product.
Storage conditions	Lenses are to be stored at room temperature
Supply	• Each site will procure their own comparator lenses. • CLEAR CARE Cleaning & Disinfecting Solution supplied by sponsor to be provided to the subject • LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.

9.2 Other Medical Device or Medication Specified for Use During the Study

No other medical devices or medications are required to be used in conjunction with the treatments during the clinical study.

9.3 Treatment Assignment / Randomization

Subjects will be randomized in a 1:1 ratio to receive treatment in crossover sequence test product then comparator product or comparator product then test product, respectively.

Sequence	EDC/randomization integration system	Lens Name
Sequence 1	LID210464/AOHG MF	[redacted] MF/AOHG MF
Sequence 2	AOHG MF/LID210464	AOHG MF/[redacted] MF

[redacted]

Only after signing the ICF, a subject will be assigned a subject number by the electronic data capture system.

A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the randomization system. The randomization list will be generated and maintained by the study sponsor.

At Visit 1, all eligible subjects will be randomized via the EDC/randomization integration system to one of the treatments (lens sequences). The investigator's delegate will access the respective system after confirming that the subject meets all the eligibility criteria. A randomization number will be automatically assigned to the subject according to the subject randomization list but will not be communicated to the site user. The EDC/randomization integration system will inform the site user of the treatment (lens sequence) assignment to be dispensed to the subject. The same randomization assignment will be followed for lens fitting.

9.4 Treatment Masking

This study is double-masked, with subjects randomized to use [redacted] MF or AOHG MF contact lenses for the duration of the 30 day treatment period. [redacted]

[redacted]

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.

Masked study personnel must avoid seeking information that may compromise masking.

In the event of a medical emergency where the knowledge of subject treatment is required, an individual investigator will have the ability to unmask the treatment assignment for a specific subject after contacting an appropriate study sponsor representative if time allows.

9.5 Accountability Procedures

Upon receipt of the IPs, the investigator or delegate must conduct an inventory. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. All IPs sent to the investigator must be accounted for by study sponsor personnel, and in no case be used in an unauthorized situation.

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, unless otherwise directed by the sponsor. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

The investigator is responsible for proper disposition of all unused IPs at the conclusion of the study, according to the instructions provided in the MOP.

9.6 Changes to Concomitant Medications, Treatments/Procedures

After the subject is enrolled into the study, the investigator must instruct the subject to notify the study site about:

- Any new medications
- Alterations in dose or dose schedules for current medications
- Any medical procedure or hospitalization that occurred or is planned
- Any nondrug therapies (including physical therapy and blood transfusions)

The investigator must document this information in the subject's case history source documents.

10 STUDY PROCEDURES AND ASSESSMENTS

10.1 Informed Consent and Screening

The investigator or delegate must explain the purpose and nature of the study, and have the subject read, sign, and date the IRB/IEC-approved informed consent document. The subject must sign the ICF BEFORE any study-specific procedures or assessments can be performed, including study-specific screening procedures. Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the informed consent document.

The investigator or delegate must provide a copy of the signed document to the subject and place the original signed document in the subject's chart, or provide documentation as required by local regulations.

10.2 Description of Study Procedures and Assessments

Study-specific procedures and assessments described here may include standard of care; other standard of care procedures performed in the clinical management of the subject are not excluded.

Detailed descriptions of assessments and procedures are provided in the MOP. The investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified site personnel.

10.2.1 Demographics

Obtain demographic information including age, race, ethnicity, and sex.

10.2.2 Medical History and Concomitant Medication

Collect medical history information for the past year, including information on all medications used within the past 30 days. Include herbal therapies, vitamins, and all over-the-counter as well as prescription medications. Throughout the subject's participation, obtain information on any changes in medical health and/or the use of concomitant medications.

Targeted Medical History and Concomitant Medications will be collected in the eCRF as outlined in the MOP.

10.2.3 Lens Fitting

During Visit 1, the investigator should determine if a subject meets the qualification of Inclusion Criteria #7 based upon their habitual contact lens prescription and screening manifest refraction, indicating that a subject could be fit within the available study lens parameters. In this trial, lens fitting assessments are performed after screening and confirmation of Inclusion/Exclusion criteria, and after a subject is randomized. If a subject meets Inclusion Criteria #7 during screening, but at the time of lens fitting, is determined by the PI to be unable to wear study lenses in the available parameters (for both test and comparator), the subject should be discontinued from the study as an Early Exit, and not categorized as a screen failure.

10.2.4 Investigational Product Compliance

Review subject compliance with the IP usage and adjunct product usage and collect all used and unused study IPs and other products that were dispensed.

10.2.5 Adverse Event Collection: Safety Assessment

Assess and record any adverse events that are observed or reported since the previous visit, including those associated with changes in concomitant medication dosing.

10.2.6 Slit Lamp Biomicroscopy: Safety Assessment

SLE of the cornea, iris/anterior chamber and lens must be performed in both eyes before instillation of any diagnostic eye drops.

10.2.7 Device Deficiencies: Safety Assessment

Assess and record any Device Deficiencies that are reported or observed since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11.

10.3 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visit and the visit is conducted by study personnel, this visit must be documented as an Unscheduled Visit. If the subject seeks medical attention outside the clinic (for example, at an Emergency Room) or at the clinic but is seen by nonstudy personnel, the investigator is to capture adverse event-related information on the Adverse Event form upon becoming aware.

During all unscheduled visits, the investigator must conduct the following procedures:

- Collect Adverse Event information, as applicable
- Collect device deficiency information, as applicable
- Record changes in medical condition or concomitant medication
- Perform Slit Lamp Biomicroscopy exam

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

If during an Unscheduled Visit the subject is discontinuing the IP or discontinuing from the study, the investigator must conduct Exit procedures according to Table 3–1 Schedule of Study Procedures and Assessments and Section 10.4.3, as possible. Do not complete an Unscheduled Visit if a subject is exiting between scheduled study visits. An Early Exit Visit should be completed instead.

Unplanned Lens Replacement is to be used only 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.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent and prior to randomization to product/dispense of study product.

The investigator must document the reason for screen failure in the subject's case history source documents.

Subject numbers must not be re-used.

10.4.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the investigator after signing informed consent and after randomization.

Subject numbers of discontinued subjects must not be re-used (i.e., subject replacement is not allowed).

Subjects may discontinue from study or study treatment at any time for any reason. Subjects may also be discontinued from study treatment at any time if, in the opinion of the investigator, continued treatment poses a risk to their health.

If a subject discontinues from study treatment, every effort must be made to keep the subject in the study and to continue with the study assessments as specified in the schedule of study procedures and assessments until the final visit.

For subjects discontinuing from the study, the investigator must complete all Exit procedures according to Table 3–1 Schedule of Study Procedures and Assessments and Section 10.4.3, if the subject is willing and able, and if in the opinion of the investigator it is safe for the subject to do so.

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.

10.4.3 Schedule of Procedures and Assessments for Subjects Discontinued from Investigational Product

Other than screen failures, if a subject discontinues from the study, the subject should undergo an Early Exit Visit, as possible. Refer to Table 3–1.

10.5 Clinical Study Termination

The study sponsor reserves the right to suspend or close the investigational site or suspend or terminate the study in its entirety at any time.

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.
- The investigator must:
    - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
    - Provide subjects with recommendations for poststudy treatment options as needed.

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

Breaking of the masked treatment codes will be done after locking the database.

10.5.1 Follow-Up of Subjects After Study Participation Has Ended

Following this study, the subject will return to their eye care professional for their routine eye care.

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 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 11-1 Categorization of All Adverse Events

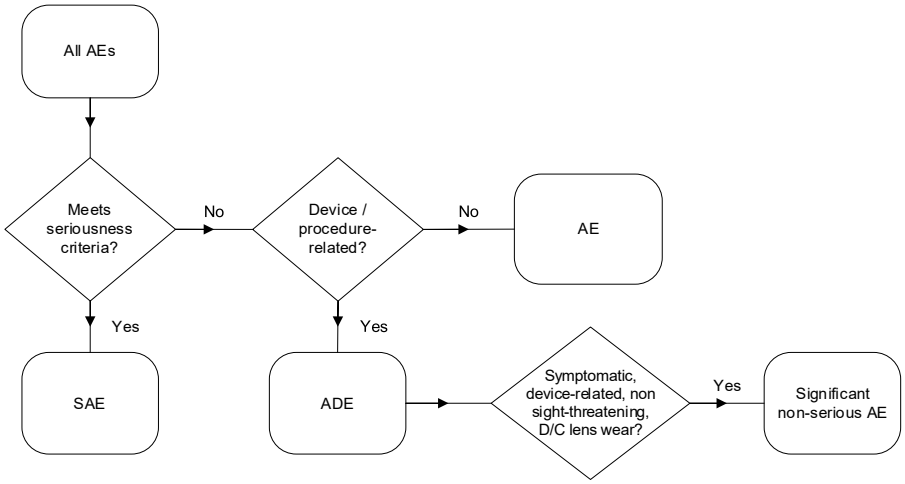
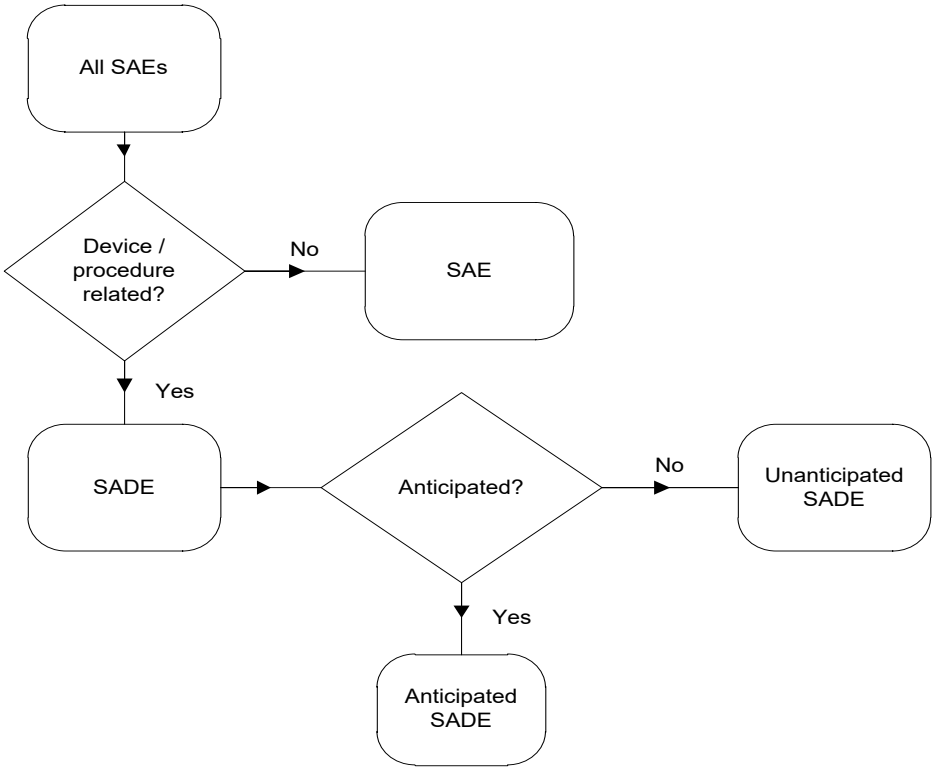


Figure 11-2 Categorization of All Serious Adverse Events



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 at distance (e.g., with manifest refraction or habitual correction) from enrollment visit that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting ≥50% of corneal surface area

Significant Non-Serious Adverse Events

A significant non-serious AE is a device-related, non-sight threatening adverse event 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 Non-Serious Adverse Event:

- Peripheral non-progressive non-infectious 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 at distance (e.g., with manifest refraction or habitual correction) from enrollment visit that persists for 2 or more weeks
- Neovascularization score greater than or equal to grade 2 (Refer to MOP for grading scales)

The above events are based on 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

11.2 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?”

In addition, changes in *any protocol-specific parameters and/or questionnaire (e.g., biomicroscopy findings, subjective ratings 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.

11.3 Procedures for Recording and Reporting

AEs are collected from the time of informed consent Any pre-existing 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.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- 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 non-operational, 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 non-study marketed devices/products (i.e., CLEAR CARE Cleaning & Disinfecting Solution, will be considered and processed as spontaneous (following the post-market 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 and their contact information is provided in the Manual of Procedures that accompanies this protocol.

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 on 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 is upgraded from non-serious to serious or from unrelated to related.

11.4 Return Product Analysis

Study sponsor representatives and their contact information are provided in the MOP that accompanies this protocol.

Alcon study 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 (GPCMS).

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study [redacted]
If the treatment assignment needs to be unmasked in the interest of subject safety, the Investigator is encouraged to contact an appropriate study sponsor representative prior to unmasking the information if there is sufficient time. Dependent upon the individual circumstances (i.e., medical emergency), the assignment may be unmasked prior to contact with the study sponsor. The study sponsor must be informed of all cases in which the treatment assignment was unmasked and of the circumstances involved. Additionally, the study sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting requirements.

11.6 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 discontinuation, 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 3 months after subject completed the study should be documented and available upon the study sponsor's request.

All complaints received after this time period will be considered and processed as spontaneous (following the post-market vigilance procedures) 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.

11.7 Pregnancy in the Clinical Study

Pregnancy should be included in the corresponding eCRF if 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.

12 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.

12.1 Subject Evaluability

Final subject evaluability must be determined prior to breaking the code for masked treatment (lens sequence) assignment and locking the database, based upon the Deviations and Evaluability Plan.

12.2 Analysis Sets

12.2.1 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], any AE or device deficiency occurring after Informed Consent and prior to the initial exposure to the study lenses (test or comparator) under evaluation in this clinical protocol will be listed as pre-treatment.

For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding lens sequence.

12.2.2 Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study, except for lenses used for lens fitting at Visit 1.

12.2.3 Per Protocol Analysis Set

The per protocol (PP) analysis set is a subset of FAS and excludes all data/subjects that have met any of the critical deviation or evaluability criteria identified in the Deviation and Evaluability Plan.

12.3 Demographic and Baseline Characteristics

Demographic information will be summarized by lens sequence and overall. Frequencies and percentages will be presented for categorical variables such as sex, age group, race, and ethnicity. Number of observations, mean, SD, median, minimum, and maximum will be presented for continuous variables such as age.

12.4 Effectiveness Analyses

This study defines 1 primary, 2 [redacted] endpoint. Unless otherwise specified, effectiveness evaluations will use the FAS as the primary analysis set, [redacted]

[redacted]

[redacted]

[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate noninferiority in visual acuity at distance when wearing [redacted] MF contact lenses compared to AOHG MF contact lenses, after 30 days of wear.

The primary endpoint is binocular HC/HI VA at distance (4 m or 3 m) at Day 30. This VA is collected with study lenses, on the logMAR scale.

12.4.1.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.05 for noninferiority:

H_0: $\mu_{(T)} - \mu_{(C)} \geq 0.05$
H_a: $\mu_{(T)} - \mu_{(C)} < 0.05$

where $\mu_{(T)}$ and $\mu_{(C)}$ denote the mean distance binocular HC/HI VA at Day 30 for [redacted] MF and AOHG MF, respectively, on the logMAR scale.

12.4.1.2 Analysis Methods

A mixed effects repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, visit, lens by visit interaction, period, sequence, and habitual lens stratum. Within-subject correlation due to the crossover design will also be accounted for in the model. Lens difference ([redacted] MF minus AOHG MF) and the corresponding one-sided 95% upper confidence limit will be computed at Day 30. Noninferiority in distance VA will be declared if upper confidence limit is less than 0.05.

[redacted]

[redacted]

12.6 Safety Analyses

The safety endpoints are:

- AEs
- Biomicroscopy findings
- Device Deficiencies

There are no safety hypotheses planned in this study. The focus of the safety analysis will be a comprehensive descriptive assessment of occurrence of adverse events as well as the other listed parameters.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. 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 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 IP.

Each biomicroscopy parameter will be tabulated by its grade. For each biomicroscopy parameter, counts 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 those eyes experiencing the increase.

Two listings for device deficiencies, prior to exposure to study contact lenses and treatment-emergent, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be conducted for the safety analyses.

12.7 Interim Analyses and Reporting

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

12.8 Sample Size Justification

[redacted]

Sample size required for [redacted] the primary effectiveness a[redacted], at 90% power and one-sided α=0.05, is summarized below:

Endpoint	SD (Paired Difference)	N/Sequence (NI margin = 0.05)
Distance VA	0.0845	13/Sequence
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

The investigator must ensure that the subject's identity is kept confidential 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. The study sponsor may collect a copy of the enrollment log ***without any directly identifying subject information***.

The study sponsor may share patient-level data collected in this trial with qualified researchers to help facilitate product development or enhancements in research that is not directly related to the study objectives. The Informed Consent explains this to the study subject.

13.2 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 CRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Site 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 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 CRF are consistent with the original source data.

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

13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, 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 CRF.

13.4 Sponsor and Monitoring Responsibilities

The study sponsor will select principal investigators that are qualified by education, training, and experience to assume responsibility for the proper conduct of this clinical trial. For this study, the principal investigator and sub investigators must be eye care professionals appropriately licensed to diagnose and treat subjects with the condition under study.

The study sponsor is financially funding this clinical trial and will compensate the investigator and/or the Institution(s) at which the study is conducted in accordance with a signed clinical trial agreement.

The study sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals according to the study monitoring plan. The clinical investigation will be monitored to ensure that the rights and well-being of the subjects are protected, the reported data are accurate, complete, and verifiable from the source documents, and the study is conducted in compliance with the current approved protocol (and amendments[s], if applicable), with current GCP, and with applicable regulatory requirements.

The site may not screen subjects or perform the informed consent process on any subject until it receives a notification from an appropriate study sponsor representative that the site may commence conducting study activities. Monitoring will be conducted periodically while the clinical study is ongoing. Monitoring methods may include site visits, telephone, written and fax correspondence. Close-out visits will take place after the last visit of the last subject at the site.

A coordinating investigator may be identified by the study sponsor to review and endorse the final study report. In cases where a coordinating investigator is engaged, the study sponsor will select the coordinating investigator based upon their experience, qualifications, active study participation, and their willingness and availability to take on this role.

13.5 Regulatory Documentation and Records Retention

The investigator is required to maintain up-to-date, complete regulatory documentation as indicated by the study sponsor and the investigator's files will be reviewed as part of the ongoing study monitoring. Financial information is to be kept separately.

Additionally, the investigator must keep study records and source documents consistent with the terms of the clinical study agreement with the study sponsor. If the investigator retires, relocates, or for any other reason withdraws from responsibility of keeping the study records, then the study sponsor must be notified, and suitable arrangements made for retention of study records and source documents needed to comply with national and international regulations.

13.6 Quality Assurance and Quality Control

The study sponsor will secure agreement from all involved parties to ensure direct access to all study related sites, source data and documents, and reports for the purpose of monitoring and auditing by the study sponsor, and inspection by domestic and foreign regulatory authorities. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly. Agreements made by the study sponsor with the investigator/institution and any other parties involved in the clinical study will be provided in writing as part of the protocol or as a separate agreement.

14 ETHICS

Investigations are conducted in compliance with Good Clinical Practices; international and national regulations, laws and guidelines; ISO 14155; the conditions of approval imposed by reviewing IRBs/IECs or regulatory authorities; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki.

- The SOPs of the study sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations shall apply.
- Notifications and timelines for reporting protocol deviations should be based upon applicable Ethics Committee requirements.

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. The investigator is not allowed to deviate from the protocol except to protect the rights, safety, and well-being of human subjects under emergency circumstances. Emergency deviations may proceed without prior approval of the sponsor and the IRB/EC, but shall be documented and reported to the sponsor and the IRB/EC as soon as possible. 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. Failure to implement identified corrective and preventative actions may result in site closure by the sponsor. Use of waivers to deviate from the clinical protocol is prohibited.

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

Voluntary informed consent must be obtained in writing from every subject. The obtaining of consent shall be documented before any procedure specific to the clinical investigation is applied to the subject.

The investigator must have a defined process for obtaining the required consent. Specifically, the investigator, or their 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 and the study, 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 (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

The investigator must have a defined process in case a subject would like to withdraw their consent (s). The investigator is the designated contact point for any such withdrawals.

The investigator must have a defined process in case a subject would like to exercise any of their rights under applicable Data Protection laws. The investigator is the designated contact point for any such requests.

The study sponsor assures that the key design elements of this protocol will be registered on www.clinicaltrials.gov if required by current regulations and, if applicable, other public databases as required by local country regulations. In addition, results of this study will be made publicly available on www.clinicaltrials.gov regardless of outcome if required by current regulations and, if applicable, in other public databases as required by local country regulations.

15 REFERENCES

15.1 Regulations and Standards

The following references 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
- EN ISO 14155:2020 - Clinical investigation of medical devices for human subjects - Good Clinical Practice
- 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
- The California Bill of Rights, if applicable

15.2 Scientific and Other References

Not applicable. There are no references.