Title

Performance Assessment of a Modified Daily Disposable Contact Lens

Protocol Number:	CLP691-C002 / NCT03762668
Development Stage of Project:	Development
Sponsor Name and Address:	Alcon Research, Ltd. and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	Modified delefilcon A Contact Lens

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:

Table of Contents

List of Tables

List of Figures

1 GLOSSARY OF TERMS

Names of test product(s)	Modified delefilcon A Contact Lens (MDACL)
Name of Control Product(s)	Delefilcon A Contact Lens (DACL)
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device (test product) or control 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 of the test product or control product.*
Adverse Event (AE)	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). *Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product.* Requirements for reporting Adverse Events in the study can be found in Section 11.
Anticipated Serious Adverse Device Effect (ASADE)	Serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the risk management file.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.* 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.
Interventional Clinical Trial	A research trial that prospectively assigns, whether randomly or not, human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, and/or a research trial in which diagnostic or monitoring procedures beyond standard of care are conducted and generate outcomes for use in analysis of data.
Investigational Product	Is defined as a preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or control 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 a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Product Complaints	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 Subjects	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 that either resulted in: 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, ie, 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. c. in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.*

	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, or a congenital abnormality or birth defect. *Refer to Section 11 for additional SAEs.*
Serious Public Health Threat	Any event type which results in imminent risk of death, serious deterioration in state of health, or serious illness that requires prompt remedial action. This would include: Events that are of significant and unexpected nature such that they become alarming as a potential public health hazard, eg, human immunodeficiency virus (HIV) or Bird Flu.
Significant Non-Serious Adverse Event	Is 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 Non-Serious AEs.*
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 management file.
Use Error	Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. *Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.*

2 LIST OF ACRONYMS AND ABBREVIATIONS

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

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CI	Confidence intervals
CRF	Case report form
D	Diopter
D/C	Discontinue
DAILIES TOTAL1, DT1 or DT1 Contact Lens	DAILIES TOTAL1 Water Gradient silicon hydrogel daily disposable Contact Lenses
DACL	Delefilcon A Contact Lens (DACL)
DEP	Deviations and evaluability plan
eCRF	Electronic case report form
EDC	Electronic data capture
EN	European Standard
EOD	End of Day
FAS	Full analysis set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
HDE	Humanitarian device exemption
[redacted]	[redacted]
HIV	Human immunodeficiency virus
IB	Investigator's brochure
ICF	Informed consent form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IP	Investigational product
IRB	Institutional review board
IRT	Interactive response technology
ISO	International Organization for Standardization
LID	Lens identification
LogMAR	Logarithm of the minimum angle of resolution
MDACL	Modified delefilcon A Contact Lens
mm	Millimeter
MOP	Manual of procedures
N/A	Not applicable

Abbreviation	Definition
OD	Right eye
OS	Left eye
OU	Both eyes
PP	Per protocol
RMF	Risk Management File
SADE	Serious adverse device effect
SAE	Serious adverse event
SiHy	Silicone hydrogel
SOP	Standard operating procedure
US	United States
USADE	Unanticipated serious adverse device effect
[redacted]	[redacted]
VA	Visual acuity

3 PROTOCOL SUMMARY

This is a prospective, multi-site, randomized, bi-lateral cross-over, double-masked study comparing 2 Daily Disposable Contact Lenses. The expected duration of subject participation in the study is approximately 2 weeks, with 3 scheduled visits. The study is expected to be completed in approximately 5 weeks.

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: Modified delefilcon A Contact Lens (MDACL) (LID016029) Control Product: Delefilcon A Contact Lens (DACL) (LID006961)
Purpose and rationale	To demonstrate noninferiority of VA [redacted] of MDACL compared to the current DACL. [redacted]
Objective(s)	The primary objective is to demonstrate that VA with MDACL is noninferior to that with the current DACL. [redacted]
Endpoint(s)	Primary Effectiveness • High Contrast Distance VA (LogMAR) [redacted]

	[redacted] Safety • Adverse Events • Biomicroscopy findings • Device deficiencies
Assessment(s)	Effectiveness • High Contrast Distance VA (LogMAR) [redacted] Safety • Adverse Events • Biomicroscopy • Device deficiencies

Study Design	This study will be a prospective, randomized, double-masked, bi-lateral crossover of two weeks in duration, with 1-week exposure to both test and control lenses. Follow-up visits are planned after 1 week wearing of each device.
Subject population	Adapted DT1 contact lens wearers with normal eyes [redacted] willing and able to be fit with the study lenses and comply with the visit and wearing schedule. Planned to enroll: ~60 Target to complete: 54
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	Volunteer subjects aged 18 or older who are current wearers of commercial DAILIES TOTAL1 Contact Lenses in both eyes. Wearers must have at least 3 months wearing experience in their current DT1 correction, with a minimum wearing time of 5 days per week and 8 hours per day.
Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	• Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator. • History of refractive surgery or irregular cornea. • Ocular or intraocular surgery within the previous 12 months (excluding placement of punctal plugs) or during the study. • Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher in either eye. • Current or history of herpetic keratitis in either eye. • Eye injury in either eye within 12 weeks immediately prior to enrollment for this trial. • 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. • Monocular subjects (only one eye with functional vision).

Data analysis and sample size justification

To address the primary [redacted] effectiveness endpoints, planned analyses are summarized below:

Endpoint	Comparison	Statistical Method
Primary		
High contrast distance VA (logMAR)	MDACL vs. DACL Noninferiority (margin = 0.05)	Mixed effect repeated measures model
[redacted]		

A sequential gatekeeping strategy will be implemented to control multiplicity, thereby controlling the overall type I error at one-sided 0.05.

No inferential testing will be carried out for safety endpoints.

Sample size calculation for primary [redacted] effectiveness endpoints is summarized below:

Endpoint	Assumptions	Power	N per sequence
Primary			
Distance VA	Paired differences SD = 0.0383	80% (one-sided $\alpha = 0.05$)	4
[redacted]			

Key words Contact lens, vision correction, visual acuity, high contrast, [redacted]

Associated materials Not applicable

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Visit 1	Visit 2		Visit 3	Unscheduled Visit	Early Exit
	Day 1 Baseline / Dispense Lens 1	Day 7 (± 2 days) Follow-up Lens 1 / Dispense Lens 2		Day 7 (± 2 days) Follow-up Lens 2 / Exit		
Informed Consent	✓	-	-	-	-	-
Demographics	✓	-	-	-	-	-
Medical/Ocular History	✓	-	-	-	-	-
Concomitant Medications	✓	(✓)	-	(✓)	(✓)	(✓)
Inclusion/Exclusion	✓	-	-	-	-	-
VA w/ habitual correction (logMAR distance)*	✓	-	-	-	(✓)	✓
Manifest refraction*	✓	(✓)	(✓)	(✓)	(✓)	(✓)
BCVA (logMAR distance with manifest refraction)*	✓	(✓)	(✓)	(✓)	(✓)	(✓)
AEs (Both reported and observed)	✓	✓		✓	✓	✓
Biomicroscopy	✓	✓		✓	✓	✓
Device deficiencies	✓	✓		✓	✓	✓
Randomize subject	✓	-	-	-	-	-
IP Dispense	✓	-	✓	-	-	-
High contrast VA w/IP (logMAR distance)	✓	✓	✓	✓	(✓)	(✓)
[redacted]						
[redacted]						
[redacted]						
[redacted]						

Procedure/ Assessment	Visit 1	Visit 2		Visit 3	Unscheduled Visit	Early Exit
	Day 1 Baseline / Dispense Lens 1	Day 7 (± 2 days) Follow-up Lens 1 / Dispense Lens 2		Day 7 (± 2 days) Follow-up Lens 2 / Exit		
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Exit Form	(✓)	(✓)	(✓)	(✓)	(✓)	✓

[redacted]

* Source only

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.

4.1 Amendments

There are no amendments. This is the first version of the protocol.

5 INTRODUCTION

5.1 Rationale and Background

[redacted]

5.2 Purpose of the Study

The purpose of the study is demonstrate noninferiority of VA [redacted] of MDACL compared to the current DACL.

[redacted]

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

[redacted]

5.3 Risks and Benefits

The benefits specific to the DACL include:

Refractive Benefits:

- Correction of ametropia
- Improved peripheral (side) vision

Comfort Benefits:

- Sustained comfort with contact lens over wearing period
- Freedom from spectacles including comfort

Ocular Health Benefits:

- Alternative to invasive refractive surgery
- Non-permanent device application
- Highest oxygen transmissibility compared to currently marketed daily disposable contact lenses

Lifestyle Benefits:

- Convenience of daily disposable modality (no need for lens cleaning, disinfection, storage, and conditioning)
- Perceived improvement in cosmetic appearance

Risks:

Potential hazardous situations associated with the use of DACL Soft Contact Lens Family have been analyzed in accordance with European Standard (EN) International Organization for Standardization (ISO) 14971:2012 and managed in such a way that all associated risks have been reduced to or maintained at acceptable levels. During the risk assessment, no new hazards were introduced.

Harm is defined as physical injury or damage to the health of people, or damage to property or environment. The Risk Management File [redacted] identifies 19 types of harms such as:

Negligible harms that may be associated with temporary user discomfort:

- Blurred vision
- Eye redness
- Ocular discomfort
- Visual disturbance – minor
- Pain-no intervention required

Moderate harms that may cause injury or impairment requiring professional medical intervention:

- Allergic response-hypersensitivity
- Corneal abrasion
- Inflammation

Serious harms that may cause injury or impairment with partial loss of function despite professional medical intervention:

- Decreased vision-permanent (Severe)
- Microbial infection – serious
- Ulcerative keratitis (corneal ulcer) – non-infectious

Refer to the IB-0164, Investigator's Brochure for MDACL for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

The primary objective is to demonstrate that visual acuity with MDACL is noninferior to that with DACL.

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
Demonstrate noninferiority of MDACL when compared to the current DACL, in evaluating VA	High Contrast VA with IP (logMAR distance) at each study Visit.

6.2 Secondary Objective(s)

Not applicable

[redacted]

6.4 Safety Objective(s)

Table 6–3 [redacted]

Objective(s)	Endpoint(s)
Describe the safety profile of the investigational products	• Adverse Events (AEs) • Biomicroscopy findings • Device Deficiencies (DDs)

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is an interventional, prospective, multi-site, randomized, bi-lateral cross-over, double-masked study comparing 2 Daily Disposable Contact Lenses. The expected duration of subject participation in the study is approximately 2 weeks, with 3 scheduled visits. The study is expected to be completed in approximately 5 weeks.

7.2 Rationale for Study Design

[redacted]

7.2.1 Purpose and Timing of Interim Analyses and Resulting Design Adaptations

Not applicable

7.3 Rationale for Duration of Treatment/Follow-Up

One week of exposure to each product is sufficient [redacted] Both, test and control lenses have the same wearing modality (daily disposable) [redacted]

7.4 Data Monitoring Committee

Not applicable

8 STUDY POPULATION

The study population consists of male and female subjects aged or older. . It is aimed to enroll (consent) approximately 60 subjects in approximately 5 sites within the US, with a target of approximately 12 subjects with a maximum of 18 subjects per site per site. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 2 weeks.

8.1 Inclusion Criteria

1. Subject must be at least 18 years of age
2. Subject must be able to understand and sign an IRB/IEC approved Informed Consent form
3. Current wearers of commercial DAILIES TOTAL1 in both eyes. Wearers must have at least 3 months wearing experience in their current DAILIES TOTAL1 correction, with a minimum wearing time of 5 days per week and 8 hours per day.

[redacted]

5. Manifest cylinder ≤ 0.75 D in each eye (at Screening)
6. BCVA 20/25 or better in each eye (as determined by manifest refraction at screening)
7. Subject must be willing and able to attend all scheduled study visits as required per protocol

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.

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 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.
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. 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 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. Monocular subjects (only one eye with functional vision).

Women of childbearing potential or women who are pregnant at the time of study entry are not excluded from participation. Pregnancy should be included in the Medical History section of the eCRF when a pregnant woman enters the study or 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.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product: MDACL

Control Product (If applicable): DACL

Table 9–1 Test Product

Test Product	MDACL
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway

	Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	delefilcon A spherical soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes with 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: delefilcon A • LID Number: LID016029 [redacted]
Formulation	Please see the IB-0164
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Daily Disposable • Exposure: At least 8 hours per day, 5 days per week, over the study treatment duration (7±2 days) • Lens Care: N/A
Number/Amount of product to be provided to the subject	Lenses will be provided in packages of (10) lenses per power, identified with the following: • a color coded label stating the protocol number • material identifier or LID Number • power • an investigational use only statement • tracking number
Packaging description	Blister foil pack
Labeling description	Blister foil label includes at a minimum: • Lens Foil label includes: - material name or identifier - base curve

	- diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information
Storage conditions	Lenses should be stored at room temperature.
Supply	Test product will be shipped to the site by Alcon.

Table 9–2 Control Product

Control Product(s)	DACL
Manufacturer	Alcon
Indication for Use	delefilcon A spherical soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes with 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: delefilcon A • LID Number: LID006961 • Water content: 33% [redacted] • Base curve (mm): 8.5 • Diameter (mm): 14.1
Formulation	Please see the package insert
Usage	• Wear: o Daily Wear o Bilateral • Replacement period: Daily Disposable

	• Exposure: At least 8 hours per day, 5 days per week, over the study treatment duration (7±2 days) • Lens Care: N/A
Number/Amount of Product to be Provided to the subject	• Lenses will be provided in packages of (10) lenses per power, identified with the following: - a color coded label stating the protocol number - material identifier or LID Number - power - an investigational use only statement - tracking number
Packaging description	Blister foil pack
Labeling description	Blister foil label includes at a minimum: • Lens Foil label includes: - material name or identifier - base curve - diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information
Storage conditions	Lenses should be stored at room temperature.
Supply	Test product will be shipped to the site by Alcon.

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 (lens) in crossover sequence MDACL then DACL or DACL then MDACL, respectively.

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 iMedidata BALANCE 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/IRT integration system to one of the lens treatment sequences. The Investigator or 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/IRT integration system will inform the site user of the treatment sequence assignment to be dispensed to the subject.

9.4 Treatment masking

This study is double-masked, with subjects randomized to use MDACL and DACL (in a crossover fashion) for approximately 7 days for each period.

Table 9–3 Unmasked Individuals Associated with the Study

Unmasked Individual	Extent of Unmasking	Rationale
Clinical Site Monitor, Clinical Operations Lead, Randomization Specialist, Clinical Data Manager	Unmasked monitor for IP accountability purposes, unmasked Investigator for IP administration.	Knowledge of subject treatment is required in the event of a medical emergency.

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. Unmasked study personnel must not disseminate information that is potentially unmasking to any masked personnel. The masked and unmasked site personnel must coordinate all study activities as necessary to protect masking and minimize bias during the study.

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. Unmasking must be done according to the instructions provided for the study IRT system.

9.5 Accountability Procedures

Upon receipt of the IPs, the Investigator or delegate must conduct an inventory. During the study, unmasked designated study staff must provide the IPs to the subjects in accordance with their randomization assignment. Throughout the study, the Investigator or delegate must maintain records of IP dispensation and collection for each subject. 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.

It is the Investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner
- All used foils and unused supplies are returned by each subject
- 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 (ie, 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 non-drug 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

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. Collect at Visit 1.

10.2.2 Medical History

Collect medical history information, 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. Collect at Visit 1.

10.2.3 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.

10.2.4 Habitual VA Assessment (logMAR)

Perform logMAR high contrast VA, distance only, OD and OS, with habitual correction (at Visit 1 and upon exit). Capture data in source only.

10.2.5 Manifest Refraction

Perform manifest refraction. Required for Visit 1. Assessment should also be performed at any other study visit if necessary [redacted]

10.2.6 BCVA (logMAR)

Perform high contrast distance BCVA (logMAR) with manifest refraction, OD and OS. Required for Visit 1. Assessment should be performed at any other study visit if necessary [redacted]

10.2.7 Adverse Event Collection

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

10.2.8 Slit-Lamp Biomicroscopy

Slip-lamp examination of the cornea, adnexa and anterior segment of the eye must be performed, OD and OS, before instillation of any diagnostic eye drops.

10.2.9 Device Deficiencies

Assess and record any Device Deficiencies that are reported or observed at each study visit, including those associated with changes in concomitant medication dosing since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11. Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent, regardless of subject enrollment status (screen failure or randomized).

10.2.10 High Contrast VA Assessment (logMAR)

Perform logMAR VA, distance only, OD and OS, with IP at all scheduled study visits.

[redacted]

10.3 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visits, this visit must be documented as an Unscheduled Visit. During all unscheduled visits, the Investigator must conduct, at a minimum, the following procedures:

- Collect adverse event information
- Record changes in medical condition or concomitant medication
- Assess and record VAs
- Collect device deficiencies information
- Perform biomicroscopy

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.

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 the informed consent, including screen failures.

Subject numbers of discontinued subjects must not be re-used.

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.

For subjects discontinuing from the study, the Investigator must complete all Exit procedures according to Table 3-1 Schedule of Study Procedures and Assessments, 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

Not applicable

10.5 Clinical Study Termination

The Study Sponsor reserves the right to close the investigational site 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 post-study treatment options as needed.

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

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 article). Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 11–1 Categorization of All Adverse Events

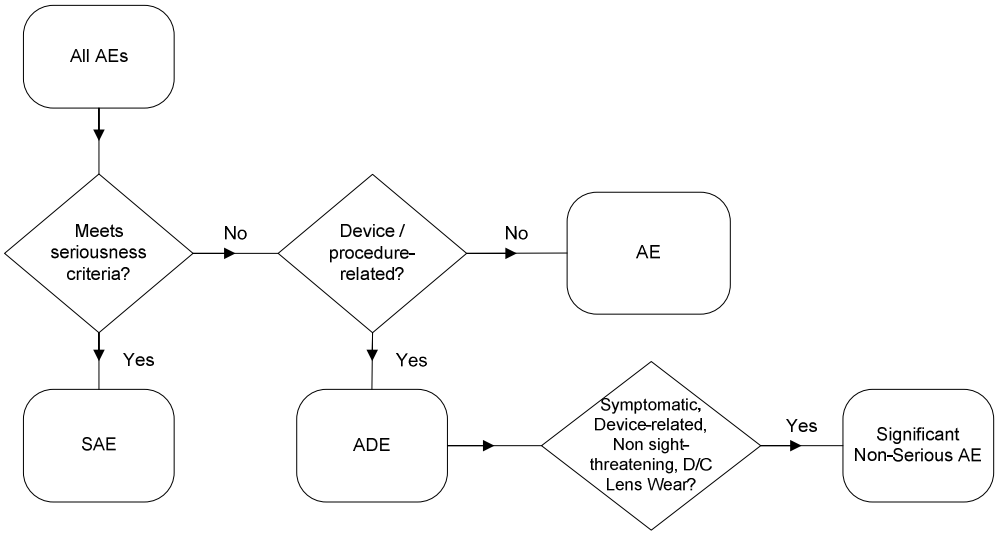
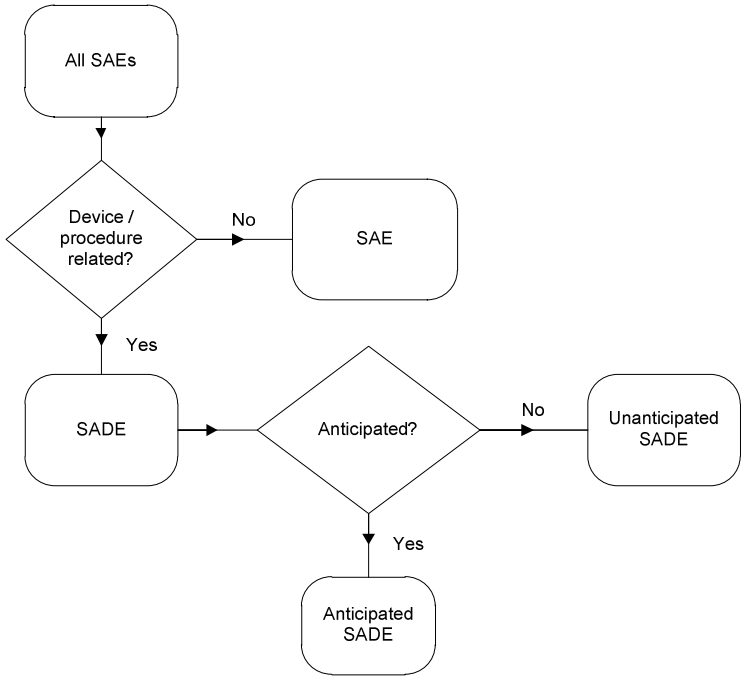


Figure 11–2 Categorization of All Serious Adverse Events



Serious Adverse Events

In addition to reporting all AEs (serious and non-serious) 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 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) [Grading scale is based on ISO 11980:2012 unless specified differently in MOP]
- 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 (Refer to MOP for grading scales) [Grading scale is based on ISO 11980:2012 unless specified differently in MOP]

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 subject harm (ie, 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 subject harm separately. Examples of device deficiencies include the following:

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

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:

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

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.

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 (ie, 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 control articles 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 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 (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.

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 (ie, 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 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), as applicable.

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study (see Section 9.4). If the treatment code needs to be broken 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 (ie, medical emergency), the code may be broken prior to contact with the Study Sponsor. 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.

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 subject exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (ie, database lock).

Any additional data received up to 3 months 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 (following the postmarket

vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

11.7 Pregnancy in the Clinical Study

Women of childbearing potential or women who are pregnant at the time of study entry are not excluded from participation. Pregnancy should be included in the Medical History section of the eCRF when a pregnant woman enters the study or 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 (SD), median, minimum, and maximum, as well as confidence intervals (CIs) or confidence limits where applicable. Categorical variables will be summarized with counts and percentages from each category. Any deviations to the 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 lens sequence assignment and locking the database, based upon the Deviations and Evaluability Plan (DEP).

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. 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.

12.2.3 Per Protocol Analysis Set

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

12.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized by lens sequence and overall. Counts 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, [redacted] effectiveness endpoints. All effectiveness evaluations will use the FAS as the primary analysis set.
[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to demonstrate that the high contrast visual acuity with Test is noninferior to that with Control. The primary endpoint is high contrast distance VA with study lenses, collected in logMAR, for each eye.

12.4.1.1 Statistical Hypotheses

The null and alternative hypotheses are formulated in terms of the predefined margin of 0.05 in logMAR 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 high contrast distance VA, in logMAR, for Test and Control, respectively.

12.4.1.2 Analysis Methods

A mixed effect repeated measures model will be utilized to test these hypotheses. The model will include terms for lens, visit, lens by visit interaction, period, and sequence.
Within-subject correlation due to the crossover will also be accounted for in the model. Lens

difference (Test minus Control) and the corresponding one-sided 95% upper confidence limit will be computed. Noninferiority in VA will be declared if upper confidence limit is less than 0.05.

[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 (counts 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 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 of study lenses and treatment-emergent, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be done for safety analysis.

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]

To demonstrate noninferiority (margin=0.05 logMAR) as a one-tailed hypothesis with α=0.05, and using a standard deviation of 0.0383 for paired differences, 80% power can be attained with a sample size of 8 (4 per sequence group).

To demonstrate noninferiority (margin=0.75) as a one-tailed hypothesis with α=0.05, and using a standard deviation of 2.17 for paired differences, 80% power can be attained with a sample size of 54 (27 per sequence group).

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

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. At the end of the clinical study, the Study Sponsor will collect a copy

of the enrollment log ***without any identifying subject information***. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

The Study Sponsor may release anonymized study data to external researchers for purposes of future research directly related to the study objectives, or future research that is beyond the scope of the current study objectives. The Informed Consent Form explains this to study subjects. Anonymization means that all identifiable information will be removed from the dataset and all links to the subjects in the study will be removed. Anonymization of the data will maintain confidentiality of the subjects who participate in the study so that they cannot be identified by external researchers. The anonymized data set will contain records from all of the subjects in the current study, but the anonymization process might change the data set in some ways, so external researchers will be informed that they might not be able to duplicate some of the results from this study.

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 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

This clinical study must be conducted in accordance with the ethical principles contained within:

- The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.
- SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.
- 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. 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. 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 Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. 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 and the process 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 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 Study Sponsor assures that the key design elements of this protocol will be registered on www.clinicaltrials.gov as 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 as required by current regulations and, if applicable, in other public databases as required by local country regulations.

15 REFERENCES

15.1 References applicable for all clinical studies

- ISO 11980:2012 Ophthalmic optics - Contact lenses and contact lens care products - Guidance for clinical investigations
- ISO 14155:2011 Clinical investigation of medical devices for human subjects - Good clinical practice

15.1.1 US references applicable for clinical studies

- 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

15.2 References for this clinical study

Not applicable. There are no references.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]