Title

Axis Orientation Comparison of Two Silicone Hydrogel Toric Contact Lenses

Protocol Number:	CLC127-C001 / NCT03392532
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:	AIR OPTIX plus HydraGlyde for Astigmatism soft contact lenses (LID009941)
Investigator Agreement:	I have read the clinical study described herein, and recognize its confidentiality. I agree to conduct this study in accordance with the ethical principles contained within the Declaration of Helsinki, and the described study in compliance with the protocol, Good Clinical Practice (GCP), ISO 14155, and all applicable regulatory requirements. Additionally, I will comply with all procedures for data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the Study Sponsor.
Principal Investigator:	

Signature Date

Name and professional position:

Address:

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1 GLOSSARY OF TERMS

Names of test product(s)	Throughout this document, test product will be referred to as AOHG toric
Name of Control Product(s)	AIR OPTIX® for Astigmatism soft contact lenses (AO toric)
Adverse Device Effect	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	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	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.
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.
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
AO toric	AIR OPTIX for Astigmatism soft contact lenses
AOHG toric	AIR OPTIX plus HYDRAGLYDE for Astigmatism soft contact lenses (LID009941)
BCVA	Best corrected visual acuity
CE	*Conformité Européene* or European Conformity
CFR	Code of Federal Regulations
CI	Confidence interval
CRF	Case report form
CSM	Clinical site manager
CTT	Clinical trial team
D	Diopter
D/C	Discontinue
DC	Diopters cylinder
DEP	Deviations and evaluability plan
EOBO	Polyxyethylene-polyoxybutylene
eCRF	Electronic case report form
EDC	Electronic data capture
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
IB	Investigator's brochure
ICF	Informed consent form
ICH	International Council for Harmonisation 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 of Standardization
LCSM	Lead clinical site manager
LID	Lens identification
min	Minute
mm	Millimeter
MOP	Manual of procedures
N	Number
N/A	Not applicable
OU	Both eyes
PMA	Premarket approval

Abbreviation	Definition
PP	Per protocol analysis set
pt	Point
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SLE	Slit-lamp examination
US	United States
USADE	Unanticipated serious adverse device effect
VA	Visual acuity

3 PROTOCOL SUMMARY

This is a prospective, randomized, bilateral crossover, double-masked, controlled study. The study population will include approximately 35 subjects in 1 US site, with a potential 2nd US site being added if necessary to meet the target enrollment. The study will consist of volunteer subjects with normal eyes (other than correction for refractive error) who are at least 18 years of age, are adapted wearers of soft contact lenses, and have at least 3 months of soft contact lens wearing experience.

Two pairs of toric contact lenses (AOHG toric and AO toric) will be evaluated during 1 office visit in this crossover study. Subjects will be randomly assigned in a 1:1 manner to either receive AOHG toric or AO toric lenses for use during Period 1 of the study. For Period 2, the contact lenses that were not allocated for use in Period 1 will then be assigned per the specified sequence group:

Sequence Group

1) AOHG toric → AO toric
2) AO toric → AOHG toric

Subjects will wear Pair 1 assigned study lenses bilaterally for approximately 30 min before crossing over into Pair 2 assigned study lenses bilaterally for approximately 30 min. There will be a 30 (+15) min washout period between removal of Pair 1 and insertion of Pair 2 study lenses.

The following assessments will be performed monocularly in the right and left eye for Pair 1 and Pair 2 lenses (see section 10 for details):

- Axis orientation 10 min after lens insertion

[redacted]

Once Pair 2 lenses are removed, the study exit procedures will be performed for each subject.

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: AOHG toric lenses Control Product: AO toric lenses
Purpose and rationale	The overall purpose of this non-dispense study is to evaluate the rotational characteristics of the AOHG toric lens, by assessing lens orientation as the primary variable compared to the commercially available AO toric lens.
Objective(s)	• The primary effectiveness objective of this study is to evaluate the percentage of AOHG toric lenses that orient within ± 30 degrees from the 90° axis (ideal location), 10 min after lens insertion. • [redacted] • The safety objective is to describe the safety profile of the investigational products through evaluation of adverse events (AEs), biomicroscopy findings, and device deficiencies.
Endpoint(s)	Primary Effectiveness • Percent of lenses with axis orientation within ±30 degrees from the 90° axis (ideal location), 10 min

	after lens insertion [redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessment(s)	Effectiveness • Axis orientation 10 min after lens insertion [redacted]

	[redacted] Safety • AEs • Biomicroscopy • Device Deficiencies
Study Design	This is a prospective, randomized, bilateral crossover, double-masked, controlled study. Subject participation in the study will be approximately 2 hours during 1 visit where subjects will bilaterally wear the 1st study lens from the assigned lens sequence (Pair 1) for approximately 30 min before crossing over into the 2nd study lens of the assigned lens sequence (Pair 2) bilaterally for approximately 30 min. There will be a 30 (+15) min washout period between removal of Pair 1 and insertion of Pair 2 study lenses.
Subject population	Volunteer subjects aged 18 or over who are adapted soft contact lens wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 3 days per week and at least 8 hours per day.
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Successful wear of soft contact lenses for vision correction in both eyes during the past 3 months for a minimum of 3 days per week and 8 hours per day. • Subjects must have ≥ 0.75 D corneal or manifest astigmatism. • Requiring contact lens sphere power from -0.50 to -8.00 D; cylinder power less than or equal to -2.25 DC; and for cylinder powers greater than -1.00 DC, axis should be within ± 30 ° from 90° or 180° axis (i.e., between 60° to 120° or 30° to 150° inclusive).

	• Best spectacle corrected VA 20/25 or better in each eye.
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 ocular or intraocular surgery which contact lens wear could be contraindicated, as determined by the Investigator, including refractive surgery and/or irregular cornea. • Biomicroscopy findings at baseline that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher; presence of corneal infiltrates • Current or history of herpetic keratitis in either eye. • Eye injury within 12 weeks immediately prior to enrolling in this trial. • History of intolerance or hypersensitivity to any component of the study lenses. • Any clinically significant corneal thinning disorder such as keratoglobus, keratoconus or pellucid marginal degeneration
Data analysis and sample size justification	To address the primary [redacted] effectiveness endpoints, collected 10 min after lens insertion, planned analyses are summarized below: Endpoint / Comparison / Statistical Method Primary Percentage of AOHG toric lenses orienting within ±30 degrees of the 90° axis / Threshold = 90% / Descriptive statistics [redacted] Since only one endpoint will be tested inferentially, there is no

concern for multiplicity.

No inferential testing will be carried out for safety endpoints.

Sample size calculation/interpretation for primary [redacted] effectiveness endpoints are summarized below.

Endpoint	Assumptions	Power	N
Primary			
Percentage of AOHG toric lenses orienting within ±30 degrees of the 90° axis	Not applicable	Not applicable 95% confidence interval for proportion will extend 0.10 from 0.90	30

[redacted]

Key words

- HYDRAGLYDE
- Astigmatism
- Axis orientation
- AOHG toric
- AO toric

Associated materials

No lens care products will be used. Re-wetting drops will not be permitted.

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	Baseline/ Screening	Exposure Pair 1 – Period 1	Exposure Pair 2 – Period 2	Exit
Informed Consent	✓	-	-	-
Demographics	✓	-	-	-
Medical History	✓	-	-	-
Concomitant Medications	✓	-	-	(✓)
Inclusion/Exclusion	✓	-	-	-
Habitual lens information (brand, power, axis)*	✓	-	-	-
VA w/ habitual correction (Snellen distance)*	✓	-	-	✓
Manifest refraction*	✓	-	-	-
BCVA (Snellen distance with manifest refraction)*	✓	-	-	-
[redacted]				
Biomicroscopy[#]	✓	-	-	✓
Fit study lenses	-	✓	✓	-
Axis orientation 10 (+2) min after insertion[1]	-	✓	✓	-
[redacted]				

Procedure/ Assessment	Baseline/ Screening	Exposure Pair 1 – Period 1	Exposure Pair 2 – Period 2	Exit
[redacted]				
Adverse Events	✓	✓	✓	✓
Device deficiencies	✓	✓	✓	✓
Exit Form	(✓)	(✓)	(✓)	✓

(✓) if applicable;
* Source only
[redacted]
[1] Data will be used for deriving primary effectiveness endpoint.
[redacted]
[#] PI may choose to take photograph or video of slit lamp observations

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

Soft toric contact lenses were introduced into clinical practice over 40 years ago (Holden 1975) Since then, toric lens technology has continued to grow, with improvements in design, lens formulation, and reproducibility in order to enhance vision and contact lens wear experience. Patients who do not wish to wear spectacles or undergo refractive surgery for the correction of refractive errors may opt for contact lenses. Contact lenses are often described in terms of material (eg, hydrogel, silicone hydrogel), modality (daily wear or extended wear) and replacement schedule (daily disposable, planned replacement, or conventional). All contact lenses intended to be reused must be cleaned and disinfected with solutions designed for this purpose and compatible with the lens polymer.

Alcon launched a monthly replacement lens known as AIR OPTIX for Astigmatism soft contact lenses (AO toric) in 2009. AO toric lenses are indicated for the optical correction of astigmatism of up to 6 D in people with healthy eyes with or without refractive ametropia (myopia or hyperopia). AO toric lenses are made from a fluoro-silicone hydrogel lens material consisting of 33% water and 67% lotrafilcon B. When placed on eye, the lenses glide over the cornea and serve as a refracting medium to focus light rays on the retina. These lenses use the Precision 8|4 design which helps minimize the interaction between the lens and the lower lid to provide improved comfort. The lenses also feature a patented surface treatment to help resist deposits. The lenses, immersed in phosphate buffered saline solution, are provided sterile in individual blister packs. AO toric lenses carry the European Conformity (CE)-mark and have US FDA 510(k) marketing clearance for daily wear and premarket approval (PMA) for extended wear (for up to 6 nights of continuous wear) with removal for disposal, or cleaning and disinfection.

Recently, Alcon introduced AIR OPTIX plus HYDRAGLYDE (AOHG sphere), a spherical lens, into the global markets. The AOHG sphere lens is comprised of the same lotrafilcon B material with a packaging saline that was designed to incorporate wetting agents for improved lens surface wettability, lubricity, and longer lasting lens surface moisture out of

package compared to packaging saline without any wetting agents. The goal of the AOHG toric lens project is to upgrade the packaging saline of commercial AO toric lenses (which currently consists of isotonic, sodium-phosphate buffered saline) to that currently used in the AOHG sphere lens.

This non-dispense clinical trial will evaluate the on-eye performance of the lotrafilcon B toric lens packaged in the AOHG packaging saline (AOHG toric lens).

5.2 Purpose of the Study

The overall purpose of this non-dispense study is to evaluate the rotational characteristics of the AOHG toric lens, by assessing lens orientation as the primary variable and comparing it to the commercially available AO toric lens.

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

There are no immediate plans to submit the results of this development study for publication; however, the results may be offered for publication if they are of scientific interest, or if the results relate to a product that is subsequently approved or cleared for marketing.

5.3 Risks and Benefits

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles; however, this study will only use a few select contact lens powers and subjects may require spectacles for vision correction. There is no intended clinical benefit to the subject; however, subjects will receive study visit assessments free of change (that will not substitute for a regular eye exam). Material properties and design characteristics of AOHG toric lenses are features consistent with successful contact lens wear. Based upon nonclinical data and documented rationale for applicability of test results, and clinical and market experience with similar contact lens materials and packaging saline, AOHG toric lenses are assessed to be non-toxic and biocompatible for on-eye use.

AO toric lenses are indicated for daily and extended wear (up to 6 nights) use; further details on any known potential risks and benefits can be found in the package insert.

A summary of the known potential risks and benefits associated with AOHG toric lenses can be found in the IB. Any risks to subjects in this trial are minimized by compliance with the eligibility criteria and study procedures, and through close supervision by a licensed clinician

during exposure to the study lenses. In general, the risks with AOHG toric lenses are anticipated to be similar to other marketed frequent replacement soft contact lenses.

There may also be unknown risks with the use of AOHG toric lens. During clinical exposure, qualified investigational site personnel will verify that the dispensed lenses demonstrate adequate centration and movement on the eye. In this study, the duration of the planned clinical exposure of the investigational AOHG toric lens is approximately 30 minutes. Site personnel will educate subjects on proper hygiene and lens care, handling, and compliance with use of the study contact lens, as applicable. Site personnel will advise the subjects to remove contact lenses and/or alert site staff for prompt follow-up if there are 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)

The overall objective of the study is to evaluate the rotational characteristics of the AOHG toric lens.

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
Evaluate the percentage of AOHG toric lenses that orient within ±30 degrees from the 90º axis (ideal location), 10 min after lens insertion	Percent of lenses with axis orientation within ±30 degrees from the 90° axis (ideal location), 10 min after lens insertion

6.2 Secondary Objective(s)

Not applicable

[redacted]

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

Objective(s)	Endpoint(s)
Describe the safety profile of the investigational products	• AEs • Biomicroscopy findings • Device deficiencies

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, randomized, bilateral crossover, double-masked, controlled study.

The study population will include approximately 35 subjects to be enrolled at 1-2 sites and will consist of volunteer subjects with normal eyes (other than correction for refractive error) who are at least 18 years of age, are adapted wearers of soft contact lenses, and have at least 3 months of soft contact lens wearing experience.

Subjects will be randomly assigned in a 1:1 manner to either receive AOHG toric or AO toric lenses for bilateral wear during Period 1 of the study. For Period 2, the contact lenses that were not allocated for use in Period 1 will then be assigned per the specified sequence group:

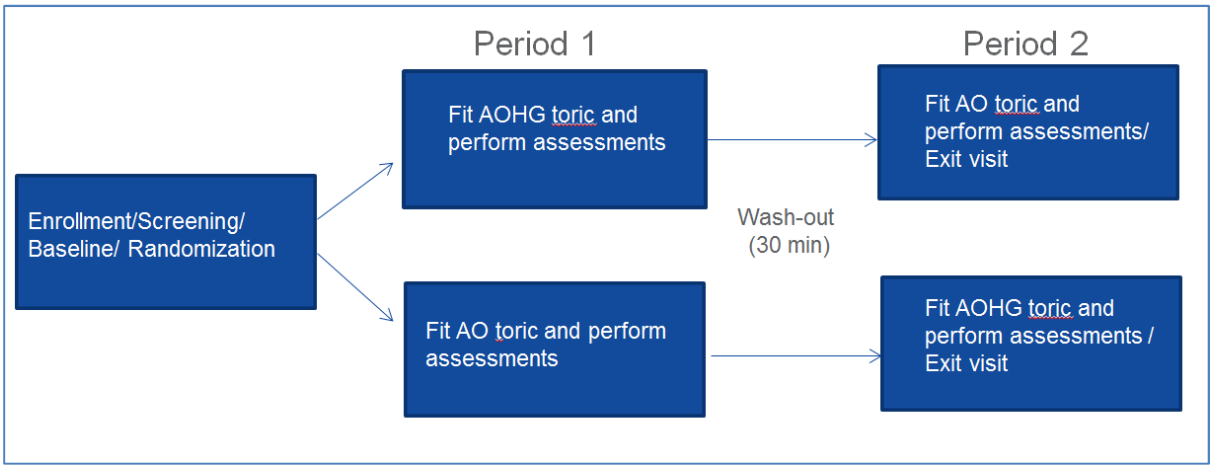
Sequence Group

1) AOHG toric → AO toric
2) AO toric → AOHG toric

Subjects will be expected to attend 1 office visit. The total expected duration of the subject's participation is approximately 2 hours with approximately 30 minutes of exposure to each study lens.

The study is expected to take approximately 4 weeks for completion. The study outline is provided in Figure 7-1 (below):

Figure 7–1 Flowchart of Study Visit



7.2 Rationale for Study Design

In this study, the on-eye performance of the investigational AOHG toric lens and the commercially available AO toric lens will be assessed in a prospective, double-masked, bilateral crossover design with approximately 30 minutes of exposure to each study lens. The study design as well as the exposure duration of study lenses is supported by the nonclinical and clinical data presented in the IB.

7.3 Rationale for Duration of Treatment/Follow-Up

The duration of exposure to the investigational products was chosen to address the objective of this study, and is aligned with AO toric fitting guidelines for initial fit assessment following lens insertion.

7.4 Rationale for Choice of Control Product

AO toric lenses were chosen as the control product to address the study objectives. Both AOHG toric and AO toric lenses are fluoro-silicone hydrogel lenses consisting of 33% water and 67% lotrafilcon B, and are prescribed for monthly wear. AO toric lenses are indicated for the optical correction of astigmatism of up to 6D or less in people with healthy eyes with or without refractive ametropia (myopia or hyperopia).

7.5 Data Monitoring Committee

Not applicable

8 STUDY POPULATION

The study population consists of adult male and female subjects (aged 18 and over) with non-diseased eyes, who require optical correction for astigmatism. It is aimed to enroll approximately 35 subjects in 1 US site, with a potential 2nd US site being added if necessary to meet target enrollment. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 4 weeks.

The intended study population consists of volunteer subjects aged 18 or over who are adapted soft contact lens wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 3 days per week and at least 8 hours per day.

Subjects must require contact lens sphere power from -0.50 to -8.00 D; cylinder power less than or equal to -2.25 DC; and for cylinder powers greater than -1.00 DC, axis should be between 60° to 120° or 30° to 150° inclusive. Because an approximately 10% screening failure rate is expected, approximately 35 subjects are expected to be enrolled to obtain a target of 30 completed subjects.

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 at least 18 years of age and must be able to understand and sign an IRB/IEC approved Informed Consent form.
2.	Willing and able to attend the single study visit as required per protocol.
3.	Successful wear of soft contact lenses for vision correction in both eyes during the past 3 months for a minimum of 3 days per week and 8 hours per day.
4.	Subjects must have ≥ 0.75 D corneal or manifest astigmatism.

5.	Requiring contact lens sphere power from -0.50 to -8.00 D; cylinder power less than or equal to -2.25 DC; and for cylinder powers greater than -1.00 DC, axis should be within ± 30 ° from 90° or 180° axis (i.e., between 60° to 120° or 30° to 150° inclusive).
6.	Distortion-free keratometric readings at baseline.
7.	Best spectacle corrected visual acuity 20/25 or better in each eye.

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 ocular or intraocular surgery, including refractive surgery which contact lens wear could be contraindicated, as determined by the Investigator and/or irregular cornea.
4.	Biomicroscopy findings at baseline that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher; presence of corneal infiltrates
5.	Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear.
6.	Current or history of herpetic keratitis in either eye.
7.	Eye injury within 12 weeks immediately prior to enrolling in this trial.
8.	History of intolerance or hypersensitivity to any component of the study lenses.
9.	Any clinically significant corneal thinning disorder such as keratoglobus, keratoconus or pellucid marginal degeneration
10.	Enrollment of site staff or family/household members of the site staff who are listed on the study personnel log as having a role in the execution of this study.
11.	Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial.

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): AIR OPTIX plus HYDRAGLYDE for Astigmatism soft contact lenses

Control Product(s): AIR OPTIX for Astigmatism soft contact lenses

Table 9–1 Test Product

Test Product	AIR OPTIX plus HYDRAGLYDE for Astigmatism soft contact lenses (AOHG toric) - LID009941
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	The intended use of this contact lens is for vision correction. Limited parameters are available for use in this non-dispensing study in accordance with the study objective.

Product description and parameters available for this study	• Material: lotrafilcon B
	• Water content: 33%
	• Power range:
	  o Sphere: -1.00 D, -3.00 D and -5.00 D
	  o Cylinder: -1.25 DC
	  o Axis availability: 90 & 180
	• Base curve (mm): 8.7 mm (target)
	• Diameter (mm): 14.5 mm (target)
	• Other: Additional details can be found in the IB

Formulation	Silicone Hydrogel. Additional details can be found in the IB for AOHG toric.

Usage	• Wear:
	  ○ Daily Wear for this study
	  ○ Bilateral
	• Replacement period: N/A for this non-dispense study
	• Exposure: Approximately 30 minutes
	• Lens Care: N/A
	• Additional details can be found in the MOP

Number/Amount of product to be provided to the subject	One pair of test study lenses will be provided to the subject at a single visit to be worn for in-office use only. The test lenses will be removed after approximately 30 minutes of lens wear. The test lenses will not be dispensed to subject to take home. Replacement lenses are allowed only if there is a device deficiency (eg, torn lens).
Packaging description	Blister containing phosphate buffered saline solution with wetting agents

Labeling description	• Lens Foil label includes:
	  - 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 boxes of 40 lenses per power per box, identified with the following:
	  - a color coded label stating the protocol number
	  - material identifier
	  - power
	  - an investigational use only statement
	  - tracking number

Storage conditions	Stored at room temperature.
Additional information	N/A
Supply	Refer to the MOP for a detailed description

Table 9–2 Control Product

Control Product(s)	AIR OPTIX for Astigmatism soft contact lenses (AO toric)
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for Use	The intended use of this contact lens is for vision correction. Limited parameters are available for use in this non-dispensing study in accordance with the study objective.

Product description and parameters available for this study	• Material: lotrafilcon B
	• Water content: 33%
	• Power range:
	  ○ Sphere: -1.00 D, -3.00 D and -5.00 D
	  ○ Cylinder: -1.25 DC
	  ○ Axis availability: 90 & 180
	• Base curve (mm): 8.7 mm (target)
	• Diameter (mm): 14.5 mm (target)
	• Other: Additional details can be found in the IB

Formulation	Silicone Hydrogel. Additional details can be found in the IB for AO toric.

Usage	• Wear:
	  ○ Daily Wear for this study
	  ○ Bilateral
	• Replacement period: N/A for this non-dispense study

	• Exposure: Approximately 30 minutes • Lens Care: N/A • Additional details can be found in the MOP
Number/Amount of Product to be Provided to the subject	One pair of control study lenses will be provided to the subject at a single visit to be worn for in-office use only. The control lenses will be removed after approximately 30 minutes of lens wear. The control lenses will not be dispensed to subject to take home. Replacement lenses are allowed only if there is a device deficiency (eg, torn lens).
Packaging description	Blister containing phosphate buffered saline solution with wetting agents
Labeling description	• Lens Foil label includes: - material name and identifier - base curve - diameter - packing solution - power - lot number - expiration date - content statement - Sponsor information • Provided in boxes of 6 lenses per power per box, identified with the following: - a color coded label stating the protocol number - material identifier - power - an investigational use only statement - tracking number
Storage conditions	Stored at room temperature.
Additional identifying information	N/A
Supply	Refer to the MOP for a detailed description.

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 investigational products during the clinical study.

9.3 Treatment Assignment / Randomization

Subjects will be randomized in a 1:1 ratio to receive treatment in crossover sequence AOHG toric then AO toric or AO toric then AOHG toric, 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 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 assignment to be dispensed to the subject.

9.4 Treatment masking

This study is double-masked, with subjects randomized to use AOHG toric and AO toric lenses (in a crossover fashion) for the duration of the approximately 30 minute treatment period for each lens pair. All study team members (at the site and the Study Sponsor) are masked to the assigned sequence with the exception of those mentioned in Table 9-3.

Table 9–3 Unmasked Individuals Associated with the Study

Unmasked Individual	Extent of Unmasking	Rationale
Unmasked Study Coordinator(s)	The Unmasked Study Coordinator(s) will manage IP inventory, as well as IP administration. This individual will have access to IP supply,	The Unmasked Study Coordinator(s) will be unmasked to allow for processing of IP shipment, storage, and dispensing, as

Unmasked Individual	Extent of Unmasking	Rationale
	accountability logs, and other documents or supplies pertaining to IP. The unmasked coordinator will also assist with device deficiency and adverse event reporting.	well as accountability for all IP.
LCSM	The LCSM will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP. This individual assists with masked and unmasked data reviews.	The LCSM will be unmasked to allow for oversight of the CSM, in conjunction with all IP accountability tasks.
CSM	CSM will have access to IP supply, accountability logs, and other documents or supplies pertaining to IP accountability. This individual monitors unmasked and masked study data.	The CSM will be unmasked to allow for performance of IP accountability, management of device deficiencies and related AE lens returns, and any other IP related tasks.
Unmasked Data Manager(s)	The Unmasked Data Manager(s) will have access to restricted fields in RAVE that would contain unmasking data.	The Unmasked Data Manager(s) will be unmasked to allow for review of all restricted data.
IRT Manager	The IRT manager will be unmasked to allow for system programming, testing, and to allow for technical oversight of the system.	The IRT manager is unmasked to all aspects of the trial for system development purposes.
Randomization Specialist	The Randomization Specialist will be unmasked to allow for generation of the randomization list and uploading of that list into the IRT system.	Generates and therefore has full knowledge of treatment codes but otherwise is operationally not associated with the CTT or any decision making aspects related to clinical trial design, execution, or reporting.

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 retained by designated unmasked staff
- 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

Changes in concomitant treatments during Visit 1 are not allowed unless needed for the proper medical care and treatment of the subject for a specific medical condition.

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

Subjects will be expected to attend only 1 office visit which includes 2 different study periods, 30 minutes each. Subjects will wear Pair 1 assigned study lenses bilaterally for approximately 30 min before crossing over into Pair 2 assigned study lenses bilaterally for approximately 30 min. There will be a 30 minute (+15 min) washout period between removal of Pair 1 and insertion of Pair 2 study lenses.

All study procedures and assessments will be conducted during the 1 office visit before subject is exited at the end of the single visit.

During Period 1, the study procedures will be conducted in the following order:

- Subjects will insert the first pair of lenses in the randomized sequence, being instructed to always begin with the right lens.
- [redacted]
- [redacted]
- The following assessments will then be performed monocularly in the right and left eye:

- Axis orientation 10 min after lens insertion.

The procedures described above will be repeated for the second pair of study lenses in the randomized sequence for Period 2.

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.

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.

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.

10.2.4 Adverse Event Collection: Safety Assessment

Assess and record any adverse events that are observed or reported, including those associated with changes in concomitant medication dosing since signature of informed consent.

10.2.5 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.

10.2.6 Device Deficiencies: Safety Assessment

Assess and record any Device Deficiencies that are reported or observed, including those associated with changes in concomitant medication dosing since enrollment. Requirements for reporting device deficiencies in the study can be found in Section 11.

10.2.7 Additional Study Assessments: Effectiveness and Safety Assessments

The following are additional study assessments. Refer to the MOP for further details.

- BCVA (Snellen distance with manifest refraction)
- [redacted]
- Axis orientation
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

10.3 Unscheduled Visits

This is a single visit study during which the subject will be enrolled, screened, randomized, exposed to study products, and exited during the same study visit. No unscheduled visits are expected for this study.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent, not meeting inclusion/exclusion criteria, and prior to randomization to product/dispense (exposure) of study product will be considered a screen failure.

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

Other than screen failures, if a subject discontinues from the study the subject should undergo an Early Exit visit. Refer to Table 3-1, Schedule of Study Procedures and assessments.

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(s) 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.

An 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

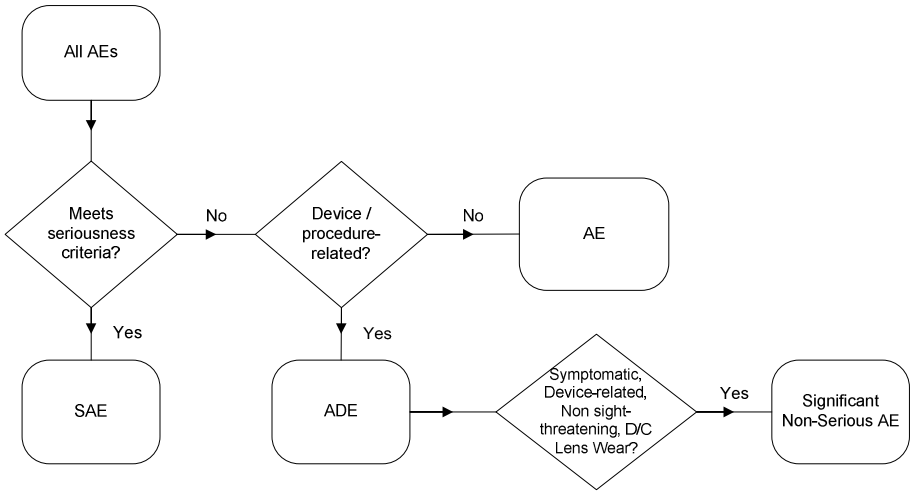
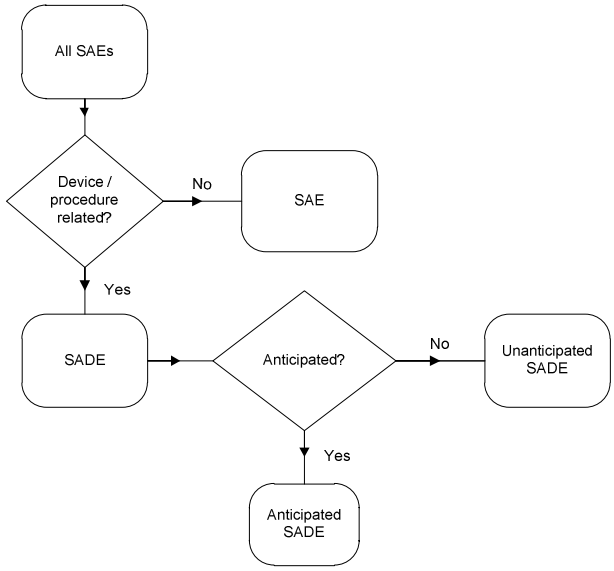


Figure 11-2 Categorization of All Serious Adverse



Specific Events Relevant to this Protocol

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 timepoints
- 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 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 upon ISO 11980:2012 unless specified differently in MOP]
- Temporary vision loss as defined by loss of 2 or more lines of BCVA from enrollment 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 upon ISO 11980:2012 unless specified differently in MOP]

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

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (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 patient 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 the study 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 enrolling in the study?"
- "Have there been any changes in the medicines you take since enrolling in the study?"

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 to [redacted] 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 upon medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

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

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

Causality

Related	An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study

procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.

Not Related — An AE classified as not related may either be definitely unrelated or simply unlikely to be related (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 must 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 (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 1 month after subject discontinuation or exit must be documented and available upon the Study Sponsor's request. All complaints received after this time period will be considered and processed as spontaneous (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

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. 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 (CI) 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.

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. N, 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. Supportive analyses of the primary [redacted] effectiveness endpoints will be conducted using the PP Analysis Set only if the number of subjects excluded from the PP Analysis Set exceeds 5% of the FAS.

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary endpoint is the percent of AOHG toric with axis orientation within ±30 degrees from the 90° axis (ideal location), 10 min after lens insertion. This percentage is calculated for the binary variable derived based on axis location of each lens, as defined below:

> Yes – if the absolute difference between the axis location and 90 is less than or equal to 30 (ie, lens axis located between the 60° and 120° axis inclusive)
>
> No – otherwise

12.4.1.1 Statistical Hypotheses

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

12.4.1.2 Analysis Methods

Frequency and percentage of lenses classified as 'Yes' will be provided for AOHG toric and AO toric, and a two-sided CI will be calculated.

A threshold of 90% (as a minimum) has been established for this endpoint based upon historical data. Therefore, percent of 'Yes' for AOHG toric lenses will be compared numerically to 90%.

[redacted]

12.5 Handling of Missing Data

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for the primary [redacted] effectiveness analyses.

12.6 Safety Analyses

The safety endpoints are:

- Adverse events
- Biomicroscopy Finding
- 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 non-serious 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 (Baseline / Screening assessment time point during Visit 1) to subsequent assessment at the Exit will be presented. A supportive listing will be generated which will include all biomicroscopy data from all assessment time points for these eyes experiencing the increase.

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

No inferential testing will be done for safety analysis.

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

Although inferential testing is not planned for the primary effectiveness endpoint, expected precision of the observed results is provided. A two-sided 95% confidence interval for a single proportion will extend approximately 0.10 from the observed value when the expected proportion is 0.90, with a sample size of 30.

[redacted]

[redacted]

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.

Additionally, Alcon may have an expert Alcon Observer present during the planned study visit to make technical observations during the visit. The assessments made by the sponsor representative(s) will be considered optional and will not impact subject evaluability. The Investigator and the Alcon Observer(s) will make and record their observations separately.

The Alcon Observer must be supervised by the Investigator or designee to ensure the Alcon Observer’s presence or activities do not bias the outcome of the study, affect the quality of the research data, and/or compromise the rights and welfare of the subject. The Alcon Observer will not intervene with the standard of care provided to study subjects or make safety-related decisions or assessments. The activities of Alcon Observer(s) will be described in the ICF.

The Alcon Observer(s) will perform a technical assessment through the biomicroscope of each treatment pair of contact lenses, on some or all subjects, using the investigative site’s biomicroscope (slit-lamp). The Alcon Observer will remain masked to the investigational product until after database lock. The Alcon Observer will record general observations related to lens fit and surface characteristics made during the slit-lamp examination onto a eCRF in a separate database with access only provided to internal Alcon personnel.

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 IB, package insert for AO toric, 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

Holden BA. The principles and practice of correcting astigmatism with soft contact lenses. Aust J Optom. 1975 Aug;58:279-99.

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
11/17/2017 19:45:30	[redacted]	[redacted]
11/17/2017 19:51:36	[redacted]	[redacted]
11/17/2017 20:04:07	[redacted]	[redacted]
11/17/2017 20:37:29	[redacted]	[redacted]