a Novartis company

Short Title

Clinical Biocompatibility Evaluation of Contact Lens Coatings

Long Title

Clinical Biocompatibility Evaluation of Contact Lens Coatings

Protocol Number:	CLY935-E002 / NCT03034928
Study Phase:	N/A
Sponsor Name and Address:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099
Investigational Product:	Monthly contact lens with Coating 1 [redacted] Monthly contact lens with Coating 2 [redacted]
US IND# / EudraCT	N/A
Indication Studied:	Contact lens wear
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, 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 Sponsor.

Principal Investigator:

Signature Date

Name: <May be entered into the document or written/typed in later>

Address:

1 SYNOPSIS

Sponsor:	Alcon Research, Ltd. 6201 South Freeway Fort Worth, Texas 76134-2099	**Protocol Number:** CLY935-E002
Investigational Product:	Monthly contact lens with Coating 1 [redacted] Monthly contact lens with Coating 2 [redacted]	**Study Phase:** ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☒ N/A

Active Ingredient:	N/A
Protocol Title:	Clinical Biocompatibility Evaluation of Contact Lens Coatings
Investigator(s)/ No. of Sites:	Approximately 2
Center Location(s)/	US
No. of Subjects	Required to complete: 32 Planned to enroll: approximately 35
Duration of Treatment:	2 hours (-15 min / +1 hr) exposure per crossover period
Study Population:	Volunteer subjects aged 18 or over who are soft contact lens wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and at least 8 hours per day.
Objective(s):	The primary objective is to evaluate corneal staining observed after 2 hours of wear with coated monthly lenses against PureVision™ lenses, all pre-cycled with OPTI-FREE® RepleniSH® multi-purpose disinfection solution.
Methodology:	Double-masked, randomized, contralateral, crossover, active controlled study
Treatments:	**Test Lenses:** Test 1 (T1) Monthly contact lens with Coating 1 [redacted] pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution Test 2 (T2) Monthly contact lens with Coating 2 [redacted] pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution

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		(Alcon Laboratories, Inc., USA)
	Route of Administration:	Test and control lenses will be dispensed for contralateral wear according to randomization. Test lenses will have investigational labeling prior to pre-cycling. Lenses will be dispensed by a qualified unmasked study staff member in such a fashion that the subject and masked site personnel do not see the lens label and remain masked to the details of the lens. Subjects will use lenses as instructed by the Investigator or delegate, [redacted]
	Duration of Treatment:	Subjects will wear a total of 2 pairs of lenses. Each pair will be worn approximately 2 hours with 2 to 8 days between pairs.
	Dosage:	Both test lens types: Parameters to be available for use in this study will be within the following ranges: Base curve: 8.0 to 9.0 mm Diameter: 13.8 to 14.6 mm Power Range: 0.00 ± 0.50 D Subjects will wear spectacles over test lenses for vision correction as needed. Replacement lenses are allowed during lens fitting only. Once lens fitting is completed, no additional lenses will be provided to the subject. Subjects will return to the investigative site the same day for lens removal.

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	Control Lens:	PureVision contact lenses (balafilcon A; Bausch & Lomb, Inc., USA) pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution
	Route of Administration:	Test and control lenses will be dispensed for contralateral wear according to randomization. Control lenses will be marketed product in original commercial blister foil packaging prior to pre-cycling. Lenses will be dispensed by a qualified unmasked study staff member in such a fashion that the subject and masked site personnel do not see the lens label and remain masked to the details of the lens. Subjects will use lenses as instructed by the Investigator or delegate, according to the instructions for use contained in the Package Insert [redacted]
	Duration of Treatment:	Subjects will wear a total of 2 pairs of lenses. Each pair will be worn approximately 2 hours with 2 to 8 days between pairs.
	Dosage:	Parameters to be available for use in this study: Base curve: 8.6 mm Diameter: 14.0 mm Power Range: 0.00 ± 0.50 D Subjects will wear spectacles over control lenses for vision correction as needed. Replacement lenses are allowed during lens fitting only. Once lens fitting is completed, no additional lenses will be provided to the subject. Subjects will return to

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the investigative site the same day for lens removal.

Subject Selection:

Inclusion Criteria:

1. Age 18 years or over.
2. Able to understand and must sign an Informed Consent document that has been approved by an Institutional Review Board.
3. Successful wearer of spherical soft contact lenses in both eyes for a minimum of 5 days per week and 8 hours per day during the past 3 months.
4. Manifest cylinder less than or equal to 1.50 D in each eye.
5. Best Corrected Visual Acuity (BCVA) 20/25 or better in each eye.
6. VA with habitual spectacles 20/40 OU or better and willing to wear spectacles as needed during the washout period and during study lens exposure.

Exclusion Criteria:

1. Any anterior segment infection, inflammation, 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 intra-ocular 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.
    - Corneal staining:
        - Type 2 (macropunctate) or greater corneal staining in any region in either eye.
        - Sum of the types of corneal staining greater than or equal to 4 across all 5 corneal regions (central, nasal, temporal, superior, inferior) in either eye.
        - Corneal staining covering ≥ 20% in any

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corneal region in either eye.

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. History of intolerance or hypersensitivity to any component of the study lenses or solutions.
10. Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment.
11. Any use of topical ocular medications and artificial tear or rewetting drops that would require instillation during contact lens wear.
12. The Investigator, his/her staff, family members of the Investigator, family members of the Investigator's staff, or individuals living in the households of the aforementioned persons may not participate in the study.
13. Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial.

Assessments:

Primary Efficacy:
Corneal staining:

- Assessed in each of 5 corneal regions (central, superior, inferior, nasal and temporal)
    - Type
        - 0 none
        - 1 micropunctate
        - 2 macropunctate
        - 3 coalesced macropunctate
        - 4 patch (≥ 1 mm)
    - Area: 0-100%
        - 1% increments from 0% to 9%
        - 10% increments from 10% to100%

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[redacted]

Safety:
Adverse events
Biomicroscopy
Device deficiencies

Endpoints:

Primary Efficacy:

- Average % area of corneal staining

[redacted]

Safety:

- Biomicroscopy findings
- Adverse events
- Device deficiencies

Statistical Methods:

Planned Analysis:

Two analysis sets will be defined, safety and full analysis sets. The safety analysis set will include all subjects/eyes exposed to any study lens evaluated in this study. The full analysis set (FAS) will include all randomized subjects who are exposed and satisfy a pre-defined set of criteria. All efficacy evaluations will be based

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upon the FAS.

The primary endpoint is the average corneal staining area, where the average is taken over five regions and expressed in percentage. Data will be presented by each test coating with the corresponding control lens worn contralaterally. Summary statistics will be provided. No hypotheses are formulated; therefore, no inferences will be made.

All data from evaluable subjects will be included in the efficacy analysis, and no imputation for missing values will be performed.

Each safety variable will be summarized descriptively. Adverse events will be classified as treatment-emergent or pre-treatment. Counts and percentages will be provided by relationship to device, and separate tables will be generated for ocular and nonocular AEs. Counts and percentages in each grade category will be presented for each biomicroscopy parameter. Device deficiencies will also be tabulated. Supporting subject listings will be provided as applicable. No inferential testing will be performed for safety analysis.

Sample Size Justification

The proposed sample size of 32 is adapted from Andrasko (2008) and allows for a balanced allocation of lens sequences.

2 OVERVIEW OF STUDY PLAN

Procedure/ Assessment	Visit 1 Screening / Baseline / Pair 1 Dispense	Visit 2 Pair 1 Follow-up 2 hrs (-15 min/+1 hr)	Visit 3 Baseline / Pair 2 Dispense (+2 to 8 days)	Visit 4 Pair 2 Follow-up / Exit 2 hrs (-15 min/+1 hr)	Unsched.
Informed Consent	✓	-	-	-	-
Demographics	✓	-	-	-	-
Medical History	✓	✓	✓	✓	✓
Concomitant Medications	✓	✓	✓	✓	✓
Inclusion/Exclusion	✓	-	-	-	-
Randomize subject	✓	-	-	-	-
Reassess corneal health	(✓)	-	✓	-	-
[redacted]					
VA w/ spectacles[1] (OD, OS, OU as needed, Snellen distance)	✓	✓	✓	✓	(✓)
Manifest refraction [1]	✓	(✓)	(✓)	(✓)	(✓)
BCVA[1] (OD, OS, Snellen distance with manifest refraction)	✓	(✓)	(✓)	(✓)	(✓)
Biomicroscopy [including Corneal Staining, per region (type, area)][2]	✓	✓	✓	✓	✓
Dispense study lenses	✓	-	✓	-	-
[redacted]					
AEs	✓	✓	✓	✓	✓

Procedure/ Assessment	**Visit 1** **Screening / Baseline / Pair 1 Dispense**	**Visit 2** **Pair 1 Follow-up** 2 hrs (-15 min/+1 hr)	**Visit 3** **Baseline / Pair 2 Dispense** (+2 to 8 days)	**Visit 4** **Pair 2 Follow-up / Exit** 2 hrs (-15 min/+1 hr)	**Unsched.**
Device deficiencies	✓	✓	✓	✓	✓
[redacted]					
Exit Form	(✓)	(✓)	(✓)	✓	(✓)

[1] Source only
[2] Primary endpoint
[redacted]
(✓) assessment performed as needed

3 ABBREVIATIONS AND GLOSSARY

3.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
BCVA	Best corrected visual acuity
CRF, eCRF	Case report form, electronic case report form
D	Diopter(s)
D/C	Discontinue
EDC	Electronic data capture
FAS	Full analysis set
FDA	US Food and Drug Administration
[redacted]	[redacted]
GCP	Good clinical practice
GPCMS	Global Product Complaint Management System
hr(s)	Hour(s)
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
MedDRA®	Medical Dictionary for Regulatory Activities
min	Minute(s)
mm	Millimeter(s)
[redacted]	[redacted]
MR	Manifest refraction
N/A	Not applicable
ODf	Right eye
OS	Left eye
OU	Both eyes
SAE	Serious adverse event
SADE	Serious adverse device effect
SiHy	Silicone hydrogel
Unsched	Unscheduled
VA	Visual acuity

3.2 Glossary of Terms

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 article). *Note: For subjects, this definition includes events related to the test article, the control article, or the procedures involved. For users or other persons, this definition is restricted to events related to the test article.*
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device (test article) or control article. *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 article or control article.*
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.*
Investigational Product	Investigational product includes test and control lenses.
Malfunction	Failure of a medical device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling of the device. The intended performance of the device refers to the intended use for which the device is labeled or marketed.
Non-serious Adverse Event	Adverse event that does not meet the criteria for 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 12 for additional SAEs.*
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Significant Non-Serious Adverse Event	A 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 12 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.*

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5 INTRODUCTION

5.1 Study Rationale and Background

The objective of this study is to evaluate surface coating candidates for a new frequent replacement (monthly) silicone hydrogel (SiHy) soft contact lens.

New SiHy materials continue to be developed possessing unique material properties and superior oxygen transmissibility over contact lenses made with conventional hydrogel materials. A new lens is being developed in an effort to maintain prolonged performance by providing a durable surface along with an inherently wettable core lens material. Frequent replacement lenses worn in a daily wear modality are removed nightly and soaked in a lens care solution for cleaning and disinfection. One consideration in the development of monthly replacement lenses is the uptake and release of lens care solution preservatives. This clinical trial is an initial assessment of biocompatibility of 2 coated lens candidates which have been pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution (Test 1 and Test 2). The primary focus of the study will be on corneal staining as a result of potential preservative uptake and release. Corneal staining will be assessed after approximately 2 hours of lens wear and compared to a control lens known to demonstrate clinical biocompatibility.

The contact lens being developed is intended for the optical correction of refractive ametropia in persons with non-diseased eyes. Plano (±0.50 D) lenses will be used for this study requiring subjects to wear spectacles for vision correction.

5.2 Known and Potential Risks

A summary of the known and potential risks and benefits associated with [redacted] and [redacted] lenses can be found in the Investigator's Brochure (IB-0150). Based upon the results from preclinical testing, [redacted] and [redacted] lenses are non-toxic and biocompatible for on-eye use. The coatings being evaluated in this study have not yet been evaluated in clinical trials. Risks are minimized through close supervision by a licensed clinician during exposure to the study lenses. The potential harms associated with on-eye exposure to the new lens materials include a toxicity response, blurred vision, and ocular discomfort. In general, the risks with [redacted] and [redacted] lenses are anticipated to be similar to other marketed daily wear contact lenses. Subjects should be advised of the following warnings and precautions that have been identified for the [redacted] and [redacted] lenses based upon clinical experience with marketed contact lenses:

- Serious eye injury, scarring of the cornea, and loss of vision may result from problems associated with wearing contact lenses and using lens care products.

- Eye problems, including corneal ulcers, can develop rapidly and lead to loss of vision.
- Noncompliance with lens wear instructions may increase the risk of developing a serious eye infection.
- Smoking and/or swimming increases the risk of corneal ulcers with contact lens wear, especially when lenses are worn overnight or while sleeping.
- The risk of ulcerative keratitis has been shown to be greater among users who wear their lenses overnight compared to those who do not wear them overnight.

The risks with contact lens wear are increased with a pre-existing or active ocular infection or inflammation, improper lens fit, and noncompliance with regimen. The [redacted] and [redacted] lenses are for daily wear use and subjects who sleep in lenses and/or fail to follow the instructions for replacing their contact lens could experience an eye infection of the cornea or injury. An improperly fitted contact lens may affect corneal curvature and result in vision fluctuations upon lens removal. A corneal ulcer could develop rapidly and lead to loss of vision. The compatibility of [redacted] and [redacted] lenses with lens care solutions has not been tested clinically; biocompatibility or any associated clinical effects are unknown.

Potential serious complications with contact lens wear are usually accompanied by one or more of the following signs or symptoms:

- Moderate to severe eye pain not relieved by removing the lens
- Foreign body sensation
- Excessive tearing/ocular secretions
- Hyperemia
- Burning, stinging, or itching
- Comfort is less compared to when the lens was first placed on the eye
- Poor visual acuity/blurred vision
- Feeling of dryness

Subjects should be instructed to remove the lenses if any one of the above signs or symptoms is noticed. A serious condition such as a corneal ulcer, infection, or iritis may be present, and may progress rapidly. Less serious reactions such as abrasions, infiltrates, and bacterial conjunctivitis must be managed to avoid more serious complications.

5.3 Potential Benefits

While contact lenses with optical power may offer improved peripheral vision and the convenience of not wearing spectacles, this study will use plano (±0.50 D) lenses and the subject must wear spectacles for vision correction. By participating in this study subjects will contribute to the development of advanced contact lenses for improving successful contact lens wear. There is no intended clinical benefit to the subject.

6 ETHICS

This clinical study will be conducted in accordance with the principles of the Declaration of Helsinki, and in compliance with the International Council for Harmonization (ICH) E6 Good Clinical Practice (GCP) Consolidated Guideline and other regulations as applicable. The Investigator and all clinical study staff will conduct the clinical study in compliance with the protocol. The Investigator will ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience.

Before clinical study initiation, this protocol, the informed consent form (and assent form, if applicable), any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an Independent Ethics Committee/Institutional Review Board (IEC/IRB). The Investigator must provide documentation of the IEC/IRB approval to the 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 IEC/IRB must be provided with a copy of the Investigator's Brochure, any periodic safety updates, and all other information as required by local regulation and/or the IEC/IRB. At the end of the study, the Investigator will notify the IEC/IRB about the study's completion. The IEC/IRB also will be notified if the study is terminated prematurely. Finally, the Investigator will report to the IEC/IRB on the progress of the study at intervals stipulated by the IEC/IRB.

Voluntary informed consent will be obtained from every subject prior to the initiation of any screening or other study-related procedures. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or delegate, will 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 will 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 investigational product, 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 will be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also will be told that their records may be accessed by appropriate

authorities and Sponsor-designated personnel. The Investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject.

7 PROTOCOL AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by the Sponsor and must be approved by the IEC/IRB prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.

8 SUBJECT POPULATION

The study population includes approximately 35 subjects to be enrolled at approximately 2 sites. To participate in the study, a subject must be 18 years or older and a successful wearer of spherical soft contact lenses in a daily wear modality during the past 3 months for a minimum of 5 days per week and 8 hours per day. The complete inclusion and exclusion criteria are presented in Section 1. The expected duration of subject participation in the study is 3 to 9 days (4 visits on 2 study days).

9 TREATMENTS ADMINISTERED

Upon entry into the study, subjects will be assigned numbers in the appropriate numerical sequence by designated staff at each investigational site. Qualifying subjects will be randomized in a 1:1:1:1 manner to one of the following lens sequences, where each pair consists of a test and a control lens:

- Test 1 (OD)/ Control (OS) → Control (OD)/ Test 2 (OS)
- Test 2 (OD)/ Control (OS) → Control (OD)/ Test 1 (OS)
- Control (OD)/ Test 1 (OS) → Test 2 (OD)/ Control (OS)
- Control (OD)/ Test 2 (OS) → Test 1 (OD)/ Control (OS)

Throughout the study, the Investigator will be responsible for the accounting of all study contact lenses and will ensure that the study contact lenses are not used in any unauthorized manner.

9.1 Identity of Study Treatments

Test Lenses: Monthly contact lens with Coating 1 [redacted] pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution (Test 1)

Monthly contact lens with Coating 2 [redacted] pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution (Test 2)

Control Lenses: PureVision contact lenses pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution (Control)

Both test lenses [redacted] will be provided in blister foil packaging with investigational labeling, which includes at a minimum the following: power, base curve, diameter, lot number, expiration date, and investigational use statement. Prior to commencement of the study, the Investigator will receive sets of [redacted] and [redacted] lenses for pre-cycling, fitting and dispensing.

PureVision is a marketed product. Lenses for the study will be provided in original blister foil packaging with commercial labeling, which includes at a minimum: brand name, material, manufacturer, power, base curve, diameter, lot number and expiration date. Prior to commencement of the study, the Investigator will receive a set of PureVision lenses for pre-cycling, fitting and dispensing.

9.2 Usage

This study is a contralateral crossover study and qualifying subjects will wear 2 pairs of study lenses according to the randomized lens sequence assignment. All lenses will be pre-cycled in OptiFree RepleniSH multi-purpose disinfection solution. [redacted] Each pair of study lenses (one test and one control) will be dispensed to the subject for contralateral wear, to be worn for 2 hours (-15 min / +1 hour) and then collected from the subject. Wear time is defined as time from lens insertion to lens removal. Test and control lenses will only be available in 0.00 D ± 0.50 D, so while wearing study lenses subjects will wear habitual spectacles as needed for vision correction. Subjects will be instructed not to use topical ocular medications or lubricating drops during study lens wear.

Subjects will be instructed not to wear any contact lenses for a washout period comprising the day prior to and day of study visits. Subjects may wear their habitual contact lenses between visit days except for during the washout period.

Subjects will use and care for the study lenses as instructed by the Investigator or delegate, [redacted]

9.3 Accountability Procedures

Upon receipt of the investigational product (test and control lenses), the Investigator or delegate will conduct an inventory. Designated study staff will provide the study lenses to the subjects in accordance with their sequentially assigned subject numbers and the randomization schedule. During the study, the Investigator must maintain records of study lens dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. At the conclusion of the study, the Investigator will be responsible for returning all lidding foils, used and unused study lenses, and used and unused study supplies, unless otherwise instructed by the Sponsor.

9.4 Subject Confidentiality and Methods Used to Minimize Bias

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the Investigator must keep an enrollment log with confidential identifying information that corresponds to the subject numbers and initials of each study participant. At the end of the clinical study, the Sponsor will collect a copy of the enrollment log without any identifying subject information. All documents submitted to the

Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information should be transmitted to the Sponsor.

The intent of masking is to limit the occurrence of conscious and unconscious bias in the conduct and interpretation of the clinical study. Bias could arise from the influence that the knowledge of a specific treatment assignment may have on the recruitment and allocation of subjects, their subsequent care, the assessment of end points, the handling of withdrawals, and so on. The essential aim of masking, therefore, is to prevent identification of the treatments by the Investigator, subject, and others associated with the conduct of the study until all such opportunities for bias have passed.

This study is double-masked, with subjects randomized to use Test 1, Test 2, and Control in the assigned eyes and lens sequence. The Investigators, Investigators' staff (other than unmasked study coordinators), subjects, and Sponsor personnel (other than the Lead Clinical Site Manager, site monitors and unmasked data managers) involved in reporting, obtaining, and/or reviewing the clinical evaluations will not be aware of the specific treatment being administered. This level of masking will be maintained throughout the conduct of the study.

Subjects will be assigned lens sequence in numerical order; the randomization schedule will be blocked to ensure a balance of study lens sequence allocations within investigational sites. The randomization scheme will be generated and maintained by the Sponsor. Individual subjects may be unmasked only once all study data have been verified and validated and the database has been locked. 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 lens sequence assignment for a specific subject.

10 STUDY PROCEDURES

10.1 Outline of Study

This double-masked, randomized, contralateral, crossover, active controlled study will evaluate 2 surface coating candidates in subjects at least 18 years of age who are experienced wearers of spherical soft contact lenses and qualified according to all inclusion and exclusion criteria. Approximately 35 subjects will be enrolled and qualifying subjects will be randomized to wear 2 pair of study lenses and will attend 4 visits occurring on 2 different study days (2 visits per day, approximately 2 hours of wear time per lens pair). Visits 1 and 2 (Pair 1 dispense and follow-up) occur on the same study day and 2 to 8 days later Visits 3 and 4 (Pair 2 dispense and follow-up) occur. Subjects must not wear contact lenses for a washout period that includes the day of and day prior to study visits.

10.2 Visits and Examinations

Study lenses must be pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfection solution prior to dispensing. [redacted]

10.2.1 Visit 1 (Day 1) – Screening/Baseline/Pair 1 Dispense

1	Explain the purpose and nature of the study, and have the subject read, sign, and date the IRB-approved informed consent document (ICF). Additionally, have the individual obtaining consent from the subject and a witness, if applicable, sign and date the informed consent document. Provide a photocopy of the signed document to the subject and place the original signed document in the subject's chart. After signing the ICF, a subject will be assigned a subject number by the EDC system. A signed ICF defines the point of enrollment.
2	Confirm the subject has not worn contact lenses on the day of and the day prior to the visit. If lenses have been worn, reschedule Visit 1 to allow for the washout period.
3	Obtain demographic information and medical history, 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. [redacted]

4	Perform Snellen VA with habitual spectacles. • OD, OS, OU, distance only [redacted] *Note: Distance VA with habitual spectacles must be 20/40 OU or better for the subject to qualify for the study.*
5	Perform a manifest refraction.
6	Perform Snellen BCVA with manifest refraction. • OD, OS, distance only *Note: Distance BCVA must be 20/25 or better in each eye for the subject to qualify for the study.*
7	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area) • Conjunctival staining • Corneal vascularization • Corneal epithelial edema • Corneal stromal edema • Conjunctival compression/indention • Chemosis • Palpebral conjunctival observations • Corneal infiltrates • Other findings

8	Review inclusion/exclusion criteria to determine if subject qualifies for participation in the study. • If subject qualifies, continue to randomization (step 9) • If a subject qualifies according to all criteria except for unacceptable corneal staining, they will be permitted to return within 7 days to be reassessed. The Investigator will determine if it is permissible for the subject to use preservative-free lubricating drops prior to returning for reassessment. The use of preservative-free eye drops should not be considered a treatment, but rather a palliative measure to reduce corneal staining, and as such should not trigger an adverse event. If upon reassessment corneal staining remains unacceptable, exit subject from study as a screen failure. • If a subject does not qualify according to any criterion other than unacceptable corneal staining, exit subject from study as a screen failure.
9	Based on the randomized lens sequence assignment, have the subject insert Pair 1 study lenses, being careful to maintain the correct OD and OS lens assignments. • *Keep all lidding foils of lenses used during lens fit process for study lens accountability.* • *Follow procedures to maintain masking.*

[redacted]

13	Assess and record any AEs and device deficiencies reported or observed during the study visit. *Note: AEs and device deficiencies must be recorded for all enrolled subjects from the time of signature of informed consent including those that screen fail.*
14	Dispense study lenses for approximately 2 hours of wear and instruct the subject to refrain from using any topical ocular medications or eye drops until they remove lenses at Visit 2.
15	Schedule Visit 2 to take place 2 hours (-15 min/+1 hour) after Visit 1.
[redacted]	

10.2.2 Visit 2 [Day 1, 2 hours (-15 min/+1 hour)] – Pair 1 Follow-up

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any adverse events or device deficiencies that are observed or reported, including those associated with changes in concomitant medication dosing.
3	Review subject compliance with lens wear and adjunct product usage.
[redacted]	
6	Have subject remove study lenses. [redacted]
[redacted]	

8	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area) • Conjunctival staining • Corneal vascularization • Corneal epithelial edema • Corneal stromal edema • Conjunctival compression/indention • Chemosis • Palpebral conjunctival observations • Corneal infiltrates • Other findings
9	Perform Snellen VA with habitual spectacles. • OD, OS, OU as needed, distance only *Note: If this VA with spectacle correction shows a decrease of 2 lines or more versus Visit 1 baseline VA with spectacle correction, then BCVA with MR is required to confirm a potential loss in VA for AE reporting requirements (see Section 12).*
10	Schedule Visit 3 to take place 2 to 8 days after Visit 2. Remind subjects not to wear contact lenses on the day of or prior to Visit 3.

10.2.3 Visit 3 (+ 2 to 8 Days) –Baseline/Pair 2 Dispense

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any adverse events or device deficiencies that are observed or reported, including those associated with changes in concomitant medication dosing.
3	Review subject compliance with washout period. If lenses have been worn, reschedule Visit 3 to allow for the washout period.

4	Perform Snellen VA with habitual spectacles. • OD, OS, distance only *Note: If this VA with spectacle correction shows a decrease of 2 lines or more versus Visit 1 baseline VA with spectacle correction, then BCVA with MR is required to confirm a potential loss in VA for AE reporting requirements (see Section 12).*
5	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area) • Conjunctival staining • Corneal vascularization • Corneal epithelial edema • Corneal stromal edema • Conjunctival compression/indention • Chemosis • Palpebral conjunctival observations • Corneal infiltrates • Other findings
6	Review exclusion criteria (#5) related to corneal staining. • If subject fulfills criteria, go to step 7. • If subject shows unacceptable corneal staining, they will be permitted to return within 7 days to be reassessed. The Investigator will determine if it is permissible for the subject to use preservative-free lubricating drops prior to returning for reassessment. The use of preservative-free eye drops should not be considered a treatment, but rather a palliative measure to reduce corneal staining, and as such should not trigger an adverse event. If upon reassessment corneal staining remains unacceptable, discontinue the subject from the trial.

7	Based on the randomized lens sequence assignment, have the subject insert the Pair 2 study lenses to be evaluated, being careful to maintain the correct OD and OS lens assignments. *Note: Keep all lidding foils of lenses used during lens fit process for study lens accountability.*
[redacted]	
11	Dispense study lenses for approximately 2 hours of wear and instruct the subject to refrain from using any topical ocular medications or eye drops until they remove lenses at Visit 4.
12	Schedule Visit 4 to take place 2 hours (-15 min/+1 hour) after Visit 3.

10.2.4 Visit 4 [same day as Visit 3, 2 hours (-15 min/+1 hour)] – Pair 2 Follow-up / Exit

1	Obtain information on any changes in medical health and/or the use of concomitant medications.
2	Record any adverse events or device deficiencies that are observed or reported, including those associated with changes in concomitant medication dosing.

3	Review subject compliance with lens wear and adjunct product usage.
[redacted]	
6	Have subject remove study lenses. [redacted]
[redacted]	
8	Perform slit-lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area) • Conjunctival staining • Corneal vascularization • Corneal epithelial edema • Corneal stromal edema • Conjunctival compression/indention • Chemosis • Palpebral conjunctival observations • Corneal infiltrates • Other findings
9	Perform Snellen VA with habitual spectacles. • OD, OS, distance only *Note: If this VA with spectacle correction shows a decrease of 2 lines or more versus Visit 1 baseline VA with spectacle correction, then BCVA with MR is required to confirm a potential loss in VA for AE reporting requirements (see Section 12).*
10	Exit the subject from the study.

10.3 Unscheduled Visits

Any visit that occurs between the regularly scheduled visits must be documented in the Unscheduled Visit pages of the Case Report Form (CRF). During all unscheduled visits, the following procedures should be conducted: update medical history and concomitant medications, VA with spectacle correction [redacted] biomicroscopy [redacted], assess and collect any AEs or device deficiencies.

If the subject is discontinuing at the unscheduled visit, all exit procedures must be completed (as possible) and the CRFs for Exit should be completed rather than the CRFs for an Unscheduled Visit.

10.4 Discontinued Subjects

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

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

Any subject who exits early from the study must undergo all procedures outlined at Visit 4, as applicable. Additionally, the Exit Form must be completed and the reason for discontinuation must be identified.

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

10.5 Clinical Study Termination

If the clinical study is prematurely terminated or suspended, the Sponsor will inform the Investigator and the regulatory authorities of the termination/ suspension and the reason(s) for the termination/suspension. The Investigator should promptly notify the IEC/IRB of the termination or suspension and of the reasons. The Sponsor reserves the right to close the

investigational site or terminate the study in its entirety at any time, for reasonable cause. Reasons for the closure of an investigational site or termination of a study may include:

- Successful completion of the study
- The study's enrollment goals are met
- The Investigator fails to comply with the protocol or GCP guidelines
- Safety concerns
- Sufficient data suggesting lack of efficacy
- Inadequate recruitment of subjects by the Investigator

The Investigator also may terminate the study at his/her site for reasonable cause. If the Sponsor terminates the study for safety reasons, it will immediately notify the Investigator(s) by telephone and subsequently will provide written confirmation of and instructions for study termination.

10.6 Enrollment Stopping Criteria

Prior experience with first time exposure of new contact lens materials indicates the following potential findings:

- Severe, persistent burning/stinging – onset within seconds following lens insertion
- Severe lens awareness/discomfort or blurred vision with IP due to very poor surface wetting – onset: minutes to hours following lens insertion.

In order to protect subject safety, the following stopping criteria are established for this clinical study:

> IF approximately 20% of subjects (7 subjects) experience findings described above following contact lens wear and the event(s) are deemed to be related to study lens wear, THEN enrollment of additional subjects will be stopped across sites and a root-cause analysis of the events will be conducted.

The Investigator must report the above findings to the Sponsor immediately by telephone (refer to Alcon contact list [redacted]. If the Sponsor stops enrollment in the study due to the above criteria, it will immediately notify the Investigator(s) by telephone. The Investigator should promptly notify the IEC/IRB of the implementation of stopping rules and reason(s).

Enrollment may be resumed upon determination of causality by the Sponsor Medical Expert or an independent medical expert and applicable IRB requirements completed.

11 ANALYSIS PLAN

Continuous variables will be summarized for the observed values using the number of observations, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized with counts and percentages from each category.

11.1 Subject Evaluability

The final subject evaluability will be determined prior to breaking the code for masked treatment assignment and locking the database.

11.2 Analysis Data Sets

11.2.1 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 lens evaluated in this study. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lens received.

11.2.2 Full Analysis Set

The FAS will include all randomized subjects who satisfy the following criteria:

- Exposed to any study lens
- No biomicroscopy findings at screening as described in exclusion criterion # 5
- No current or history of pathological dry eye in either eye (exclusion criterion #6)
- No current or history of herpetic keratitis in either eye (exclusion criterion #7).
- No eye injury in either eye within twelve weeks immediately prior to enrollment for this trial (exclusion criterion #8).
- No history of intolerance or hypersensitivity to any component of the study lenses or solutions (exclusion criterion #9).

These critical deviation criteria will be identified in the Deviations and Evaluability Plan.

11.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on safety and full analysis sets, by lens sequence group.

11.4 Efficacy Analyses

This study defines one primary endpoint and [redacted]. The FAS will serve as the primary set for all efficacy analyses.

11.4.1 Primary Efficacy

The primary objective of this study is to evaluate corneal staining observed after 2 hours of wear with the following lenses: Test 1, Test 2, and Control.

The corresponding efficacy endpoint is the average of corneal staining areas observed (expressed as a percent) taken over the 5 regions: central, superior, nasal, inferior, and temporal.

11.4.1.1 Statistical Hypotheses

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

A test coating will be considered successful if $X_{Ti} < (X_C+3)$ where X_{Ti} and X_C are the observed average percent area of corneal staining for Test i (i=1, 2) and Control, respective.

11.4.1.2 Analysis Methods

Summary statistics will be provided. Data for the control lens will be separated into those collected with Test 1 worn on the contralateral eye and those collected with Test 2 worn on the contralateral eye.

11.4.2 Secondary Efficacy

No secondary efficacy objective/endpoint has been identified for this study.

11.4.2.1 Statistical Hypotheses

Not applicable.

11.4.2.2 Analysis Methods

Not applicable.

11.5 Handling of Missing Data

All data obtained in evaluable subjects/eyes will be included in the analysis.

11.6 Multiplicity

No multiplicity adjustment needs to be considered for the efficacy variables as no inferences will be made.

11.7 Safety Analysis

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

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by MedDRA Preferred Terms. In addition to an overall presentation of AEs, reports will be generated for significant non-serious AEs, and serious AEs. AEs leading to study discontinuation will be identified. Individual subject listings will be provided, as necessary.

Pre-treatment and between-treatment-period AEs will be presented, with subject listings, separated from treatment-emergent AEs. A pre-treatment AE is an event that occurs after signing informed consent but prior to exposure to a study lens. A between-treatment-period AE is an event that occurs after last exposure to Period 1 study lens but prior to exposure to Period 2 study lens.

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 (Visit 1 for Period 1 and Visit 3 for Period 2) to any subsequent visit will be presented. A supportive listing will be generated which will include all biomicroscopy data from the affected period for these eyes experiencing the increase, with the following variables: lens, Investigator, subject, age, sex, visit, eye, parameter, baseline value, and value at the visit.

Two listings (prior to exposure of study lenses, 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.

11.8 Health Economics

Not applicable.

11.9 Interim Analyses

Not applicable.

11.10 Sample Size Justification

No inferential testing is planned for this study; therefore, sample size/power calculation is not relevant. The proposed sample size of 32 is adapted from Andrasko (2008), which recruited 30 successful hydrogel contact lens wearers for each of the lens-solution biocompatibility studies, and allows for a balance allocation of lens sequences.

12 ADVERSE EVENTS

12.1 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, figures and descriptions below for categories of AEs and SAEs.

Note: Figures provide abbreviated descriptions; refer to sections below for full definitions.

Figure 12–1 Categorization of All Adverse Events

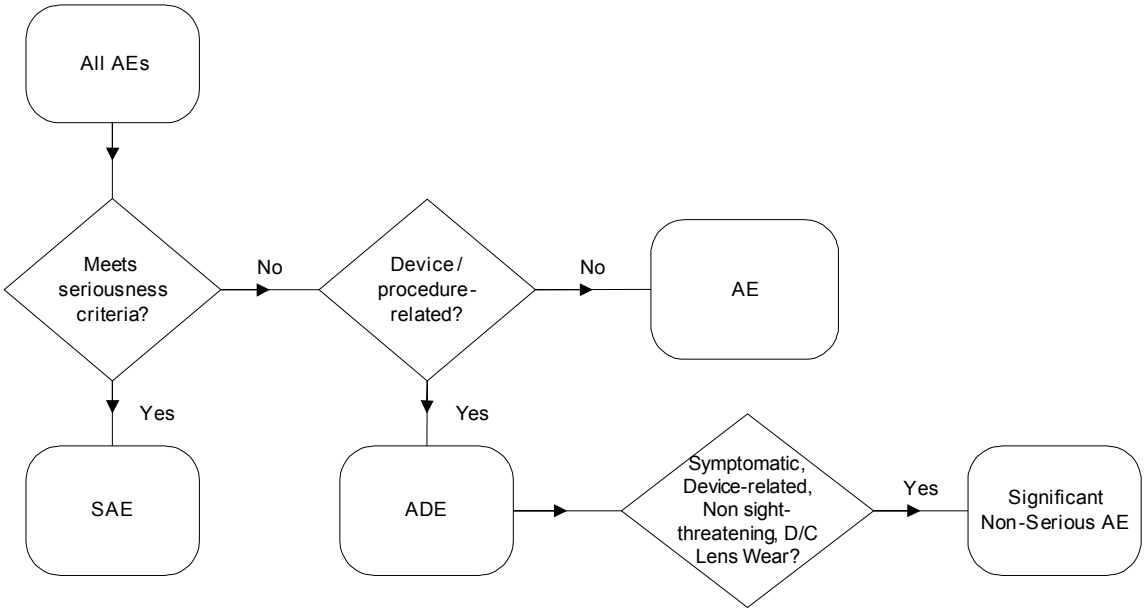
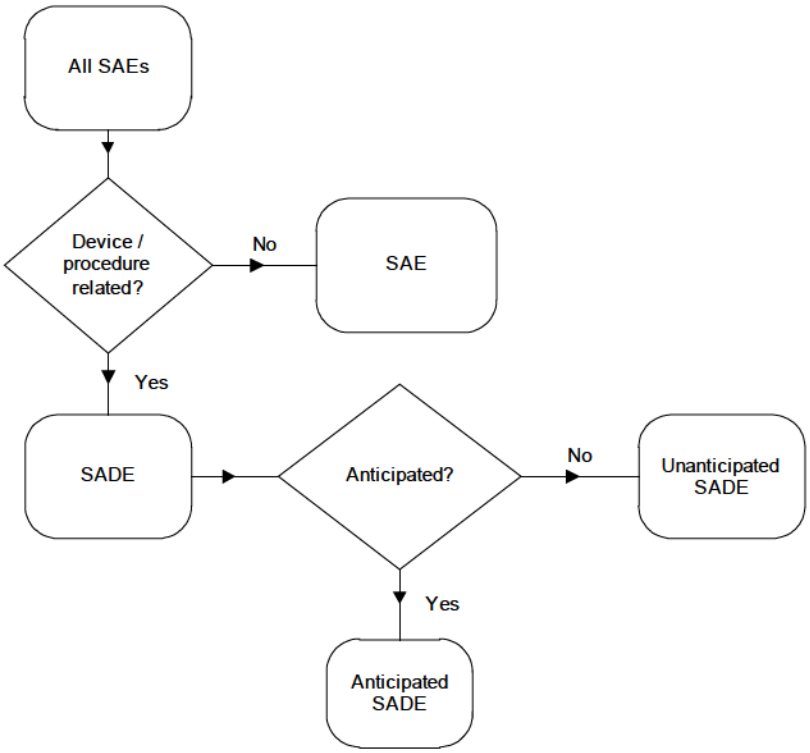


Figure 12-2 Categorization of All Serious Adverse Events



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 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
- Dense coalescent corneal staining, (eg, corneal abrasion or foreign body track) or patch staining.*
- 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 [redacted]

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 and Contact Lens Care Products.

** This criterion will be applied to non solution-related corneal staining. The presence of solution-related corneal staining is an expected occurrence in this study and the type and area of the corneal staining will be documented in the Case Report Form on a different grading scale as noted in Section 1 Synopsis/Assessments. Therefore, corneal staining that is*

predominately solution-related (in the opinion of the investigator) will not be documented as adverse event.

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

12.2 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.

12.3 Procedures for Recording and Reporting AEs and SAEs

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. Refer to Section 12.5 of this protocol [redacted] for additional information on returning product.
- 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 faxed or emailed to the Study Sponsor at

MSUS.safety@alcon.com according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Any AEs and device deficiencies for non-study marketed devices/products will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the device's/product's manufacturer as per local requirements.

Study Sponsor representatives may be contacted for any protocol related question 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.

12.4 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 event is mild if the subject is aware of, but can easily tolerate the sign or symptom.
Moderate	An event is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.
Severe	An event 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.

12.5 Return Product Analysis

[redacted]

Alcon products associated with device deficiencies and/or product related AEs should be returned and must include the Complaint number which will be provided by Study Sponsor after the case is entered in the Study Sponsor's Global Product Complaint Management System (GPCMS). [redacted]

12.6 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 of this protocol for masking procedure). 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.

12.7 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 postmarket 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.

12.8 Pregnancy in the Clinical Trial

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.

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the CRFs exist and are accessible for verification by the site monitor. If electronic records are maintained, the method of verification must be determined in advance of starting the study. At a minimum, source documents should include the following information for each subject:

Subject identification (name, sex, race/ethnicity)
Documentation of subject eligibility
Date of informed consent
Dates of visits
Documentation that protocol specific procedures were performed
Results of study parameters, as required by the protocol
Trial medication 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 trial 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.

CRFs will be provided to the sites (paper or electronic); only designated individuals may complete the CRFs. The CRFs will be submitted at regular intervals based upon the clinical trial visit schedule. It is expected that all data reported will have corresponding entries in the source documents and that the Principal Investigator will review the reported data and certify that the CRFs are accurate and complete. No subject identifiers should be recorded on the CRFs beyond subject number, and demographic information.

13.2 Data Review and Clarifications

The CRF data will be reviewed against the subject's source data by the study monitors to ensure completeness and accuracy. After monitoring has occurred at the clinical sites and the CRFs have been submitted, additional data clarifications and/or additions may be needed. Data clarifications and/or additions are documented and are part of each subject's CRFs.

13.3 Regulatory Documentation and Records Retention

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

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

14 PUBLICATION PLAN

The results of this study will not be submitted or offered for publication.

15 REFERENCES

Andrasko G, Ryen K. Corneal staining and comfort observed with traditional and silicone hydrogel lenses and multipurpose solution combinations. Optometry. 2008;79(8):444-54.

16 APPENDIX

None

Date/Time (mm/dd/yyyy GMT):	Signed by:	Justification:
12/08/2016 21:09:59	[redacted]	[redacted]
12/08/2016 21:14:20	[redacted]	[redacted]
12/08/2016 23:28:25	[redacted]	[redacted]