Device Protocol for CLY935-E007

Title: Clinical Biocompatibility of Three Daily Wear Monthly Replacement Silicone Hydrogel Contact Lenses with Two Multi-purpose Disinfecting Solution Combinations

Protocol Number:	CLY935-E007 /NCT04789382
Sponsor Name and Address:	Alcon Research, LLC and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product(s):	LID018869

Investigator Agreement:

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

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

Principal Investigator:

Signature Date

Name and professional position:

Address:

1 PROTOCOL SYNOPSIS

Trial Sponsor	Alcon 6201 South Freeway Fort Worth, Texas 76134-2099
Name of Test Product(s)	Test Product 1 (Test1): LID018869 pre-cycled with OPTI-FREE® RepleniSH® multi-purpose disinfecting solution (RepleniSH) Test Product 2 (Test2): LID018869 pre-cycled with Biotrue® multi-purpose solution (Biotrue)
Name of Control Product(s)	Control Product 1 (Control1): Biofinity® pre-cycled with RepleniSH Control Product 2 (Control2): PureVision® (PV) pre-cycled with Biotrue
Title of Trial	Clinical Biocompatibility of Three Daily Wear Monthly Replacement Silicone Hydrogel Contact Lenses with Two Multipurpose Disinfecting Solution Combinations
Protocol Number	CLY935-E007
Number of Sites Country	~2 US
Clinical Investigation Type	☐ Early Feasibility ☒ Traditional Feasibility ☐ Pivotal (pre-market monadic claims) ☐ Post Market Interventional / Confirmatory ☐ Post Market Non-Interventional / Observational
Planned Duration of Exposure	~ 4 hrs total (test and control, excluding washout): Test1: 2 hrs [redacted] Test2: 2 hrs [redacted] Control1: 2 hrs [redacted] Control2: 2 hrs [redacted]
Number of Subjects	Target to complete: 32
	Planned to enroll: ~36
Study Population	Volunteer subjects aged 18 or over who are habitual spherical 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 of this study is to evaluate corneal

	staining observed after 2 hours of wear with LID018869 [redacted] against both PureVision, pre-cycled with Biotrue, and Biofinity lenses, pre-cycled with RepleniSH.
Endpoints	Primary Effectiveness • Average % area of corneal staining [redacted] Safety • Adverse Events (AEs) • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness • Corneal staining in each of the 5 corneal regions (central, superior, inferior, nasal and temporal) o Type (Grade 0-4) o Area (0 -100%) • VA (Snellen distance) with habitual correction • Manifest refraction [redacted]

	[redacted] Safety • AEs • Biomicroscopy • Device deficiencies	
Study Design	☒ Prospective ☐ Single group ☐ Parallel group ☒ Crossover (MPDS) ☐ Other	☐ Single-masked (trial subject) ☐ Single-masked (Investigator) ☒ Double-masked ☐ Open-label ☐ Other
	☒ Contralateral (lenses) ☐ Bilateral ☐ Monocular lens wear	☒ Randomized

Lens Assignment	Subjects will be randomized in a 1:1:1:1 manner to receive one of 4 regimen sequences with lens and MPDS combinations:
	Sequence 1: LID018869+RepleniSH (OD)/Biofinity+RepleniSH (OS)//PV+Biotrue (OD)/LID018869+Biotrue (OS)
	Sequence 2: Biofinity+RepleniSH (OD)/LID018869+RepleniSH (OS)//LID018869+Biotrue (OD)/PV+Biotrue (OS)
	Sequence 3: LID018869+Biotrue (OD)/PV+Biotrue (OS)//Biofinity+RepleniSH (OD)/LID018869+RepleniSH (OS)
	Sequence 4: PV+Biotrue (OD)/LID018869+Biotrue (OS)//LID018869+RepleniSH (OD)/Biofinity+RepleniSH (OS)	

Test Product 1 Details	Primary component/material	[redacted] lenses; pre-cycled with RepleniSH
	[redacted]	[redacted]
	LID Number	LID018869
	Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
	[redacted]	[redacted]
Test Product 2 Details	Primary	[redacted] lenses; pre-

	component/material	cycled with Biotrue
	[redacted]	[redacted]
	LID Number	LID018869
	Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
	[redacted]	[redacted]
Control Product 1 Details	Primary component/material	comfilcon A lenses; pre-cycled with RepleniSH
	Product Name	Biofinity
	Manufacturer	CooperVision
	[redacted]	[redacted]
Control Product 2 Details	Primary component/material	balafilcon A lenses; pre-cycled with Biotrue
	Product Name	PureVision
	Manufacturer	Bausch [redacted]
	Other	-0.50 D
Inclusion Criteria	1. Subject must be at least 18 years of age. 2. Subject must be able to understand and must sign an ICF that has been approved by an IRB. 3. Successful wear of spherical soft contact lenses in both eyes for a minimum of 5 days per week and 8 hours per day during the past 3 months. 4. Manifest cylinder ≤ 1.50 D in each eye. 5. BCVA (distance with manifest refraction) better than or equal to 20/25 Snellen in each eye. 6. Subject must be willing to stop wearing their habitual contact lenses for the duration of study lens exposure and during the washout period. [redacted]	
Exclusion Criteria	1. Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator.	

	2. Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the Investigator. 3. History of refractive surgery or plan to have refractive surgery during the study or irregular cornea in either eye. [redacted] 6. Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear. [redacted] 11. Any use of topical ocular medications and artificial tear or rewetting drops that would require instillation during contact lens wear. [redacted]

Associated Materials	[redacted]

Table 1-1 Schedule of Study Procedures and Assessments

Schedule of Study Procedures and Assessments

Procedure/ Assessment	PRESCREENING	Visit 1[µ] Screen/ Baseline/ Pair 1 Exposure	Visit 2 Pair 1 Follow-up 2 hrs [redacted]	Washout[µ] (the day of and day prior to Visit 3)	Visit 3 Baseline/ Pair 2 Exposure [redacted]	Visit 4 Pair 2 Follow-up 2 hrs [redacted] Exit^	Early Exit	USV
Washout Consent*	X							
Informed Consent		X						
Demographics		X						
Medical History*		X	X		X	X	X	X
Concomitant Medications*		X	X		X	X	X	X
Habitual lens (brand, power*, lens care)		X						
Review compliance*			X		X	X	X	(X)
VA w/ habitual spectacles (OD, OS, Snellen distance)*		X	X		X	X	X	(X)
VA w/ habitual spectacles OU*		X						
Manifest refraction*		X	(X)		(X)	(X)	(X)	(X)
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Biomicroscopy [including Corneal Staining, per region (type, area)]		X[∞]	X		X[∞]	X	X	(X)

Procedure/ Assessment	PRESCREENING	Visit 1[µ] Screen/ Baseline/ Pair 1 Exposure	Visit 2 Pair 1 Follow-up 2 hrs [redacted]	Washout[µ] (the day of and day prior to Visit 3)	Visit 3 Baseline/ Pair 2 Exposure [redacted]	Visit 4 Pair 2 Follow-up 2 hrs [redacted] Exit^	Early Exit	USV
Inclusion/Exclusion		X						
Randomization		X						
Dispense pre-cycled study lenses		X			X			(X)
[redacted]		[redacted]			[redacted]			
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]

Procedure/ Assessment	PRESCREENING	Visit 1[µ] Screen/ Baseline/ Pair 1 Exposure	Visit 2 Pair 1 Follow-up 2 hrs [redacted]	Washout[µ] (the day of and day prior to Visit 3)	Visit 3 Baseline/ Pair 2 Exposure [redacted]	Visit 4 Pair 2 Follow-up 2 hrs [redacted] Exit[^]	Early Exit	USV
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]			[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
AEs		X	X		X	X	X	X
Device deficiencies		X	X		X	X	X	X
Exit Form		(X)	(X)		(X)	X	X	(X)

[redacted]

1.1 Abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
Biotrue	Biotrue multi-purpose solution
CFR	Code of Federal Regulations
CIP	Clinical investigation plan
Control1	Biofinity® pre-cycled with RepleniSH
Control2	PureVision® (PV) pre-cycled with Biotrue
[redacted]	[redacted]
eCRF	Electronic case report form
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
hr(s)	Hour(s)
IB	Investigator's brochure
ICF	Informed consent form
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
LID	Lens identification
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
MPDS	Multi-purpose disinfecting solution
N/A	Not applicable
OD	Right eye
OS	Left eye
OU	Both eyes
PV	PureVision
RepleniSH	OPTI-FREE RepleniSH multipurpose disinfecting solution
SAE	Serious adverse event
SADE	Serious adverse device effect
Test1	LID018869 pre-cycled with OPTI-FREE RepleniSH multi-purpose disinfecting solution (RepleniSH)
Test2	LID018869 pre-cycled with Biotrue multi-purpose solution (Biotrue)
US/USA	United States
USADE	Unanticipated serious adverse device effect
USV	Unscheduled visit
VA	Visual acuity

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3 INTRODUCTION

3.1 Study Rationale and Purpose

[redacted]

The purpose of this study is to evaluate biocompatibility of an investigational contact lens [redacted] compared to marketed contact lenses (PureVision/Biofinity) which have been pre-cycled in OPTI-FREE RepleniSH multi-purpose disinfecting solution (RepleniSH) and/or Biotrue multi-purpose solution (Biotrue). The primary endpoint (average % area of corneal staining) was selected to fulfill the primary objective of the study. [redacted]

[redacted]

RepleniSH was chosen as a representative solution containing the Polyquarterium-1 preservative and Biotrue was chosen as a representative solution containing the polyaminopropyl biguanide (PHMB) preservative.

[redacted]

3.2 Trial Objective

The primary objective of this study is to evaluate corneal staining observed after 2 hours of wear with LID018869 [redacted] against both PureVision, pre-cycled with Biotrue, and Biofinity lenses, pre-cycled with RepleniSH.

3.3 Risks and Benefits

[redacted] There is no intended clinical benefit to the subject. Material properties and design characteristics of the contact lens in development are features consistent with successful contact lens wear.

Based upon non-clinical testing, the new contact lens in development is assessed to be non-toxic and biocompatible for on-eye use.

A summary of the known potential risks and benefits associated with the new contact lens in development can be found in the Investigator's Brochure. [redacted].

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

3.4 Subject Population

The study population includes approximately 36 volunteer subjects to be enrolled at approximately 2 sites, with approximately 18-36 subjects enrolled per site. The study population will consist of subjects with normal eyes (other than the need for optical correction for refractive ametropia) and who are adapted, existing wearers of soft contact lenses in both eyes.

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

Rescreening of subjects after screen failure is not allowed in this study.

3.5 Outline of Study

This will be a single-site, prospective, randomized, double-masked, contralateral crossover study comparing 3 contact lenses pre-cycled in two different MPDS. The expected duration of subject participation in the study is approximately up to 1 week, with 2 study visit days. The study is expected to be completed in approximately 1.5 months.

4 TREATMENTS ADMINISTERED

Subjects will be randomized in a 1:1:1:1 manner to receive one of 4 regimen sequences with lens and MPDS combinations:

Sequence 1: LID018869+RepleniSH (OD)/Biofinity+RepleniSH (OS)//PV+Biotrue (OD)/LID018869+Biotrue (OS)

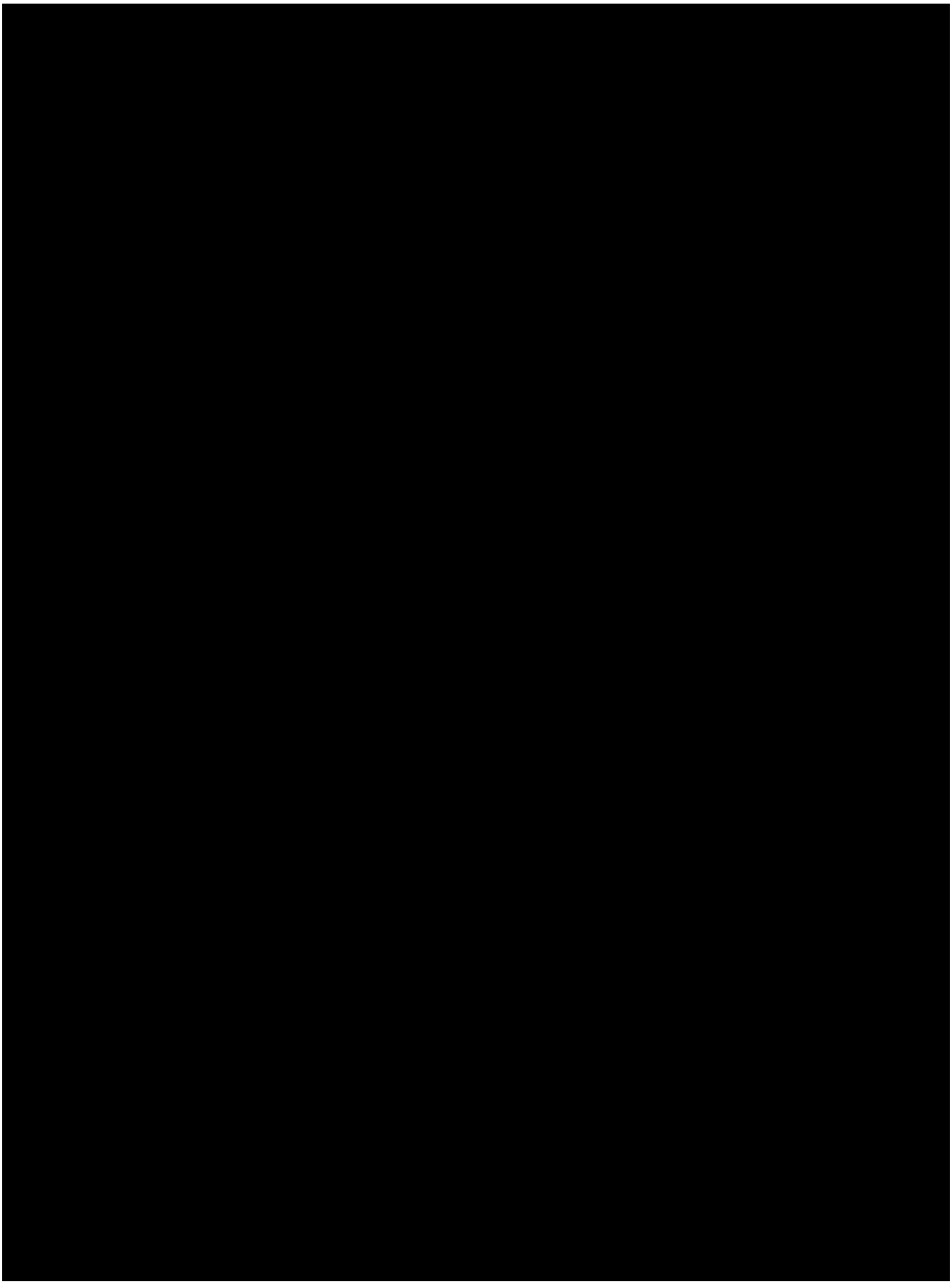
Sequence 2: Biofinity+RepleniSH (OD)/LID018869+RepleniSH (OS)//LID018869+Biotrue (OD)/PV+Biotrue (OS)

Sequence 3: LID018869+Biotrue (OD)/PV+Biotrue (OS)//Biofinity+RepleniSH (OD)/LID018869+RepleniSH (OS)

Sequence 4: PV+Biotrue (OD)/LID018869+Biotrue (OS)//LID018869+RepleniSH (OD)/Biofinity+RepleniSH (OS)

4.1 Identity of Study Treatments

DESCRIPTION OF TEST AND CONTROL PRODUCTS				
	Test Product 1	Test Product 2	Control Product 1	Control Product 2
LID Number	LID018869	LID018869	N/A	N/A
Lens identified in randomization system as:	LID018869+RepleniSH	LID018869+Biotrue	Biofinity + RepleniSH	PV+Biotrue
Lens	[redacted]		Biofinity	PureVision
Material			comfilcon A	balafilcon A
Water Content			48%	36%
Base Curve (mm)			8.6	8.6



DESCRIPTION OF TEST AND CONTROL PRODUCTS		
Usage	• Wear: o Daily Wear o Contralateral • Replacement period: N/A • Exposure: 2 hours [redacted] exposure per crossover period • Lens Care: Lenses will be pre-cycled in RepleniSH or Biotrue [redacted]	
[redacted]	[redacted]	[redacted]

4.2 Accountability Procedures

Upon receipt of the study lenses, the Investigator or delegate will conduct an inventory. Designated study staff will provide the study lenses to the subjects in accordance with their randomization schedule. [redacted]

[redacted]

5 STUDY PROCEDURES AND ASSESSMENTS

5.1 Visits and Examinations

Study lenses must be pre-cycled with RepleniSH or Biotrue prior to dispensing. [redacted]

[redacted]

[redacted]	[redacted]

5.1.2 Visit 1 (Day 1) – Screen/Baseline/Pair 1 Exposure

1.	Confirm the subject has not worn contact lenses on the visit day of and the day prior to the visit. If lenses have been worn, reschedule Visit 1 to allow for the washout period.
2.	Explain the purpose and nature of the study, and have the subject read, sign, and date the IRB-approved informed consent document. 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 informed consent document defines the point of enrollment.
3.	Obtain demographic information and medical history, including information on all medications used within the past 30 days [redacted]
4.	Perform Snellen VA with habitual spectacles • OD, OS, OU, distance only Record habitual lens information (brand, power) and lens care information (brand). [redacted]
5.	Perform a manifest refraction.

[redacted]	[redacted]
7.	Perform slit lamp biomicroscopy (without contact lenses) to evaluate the following: [redacted]
8.	Review inclusion/exclusion criteria to determine if the subject qualifies to be randomized into the study. • If subject qualifies, request randomization and continue with Step 9. [redacted] • If a subject does not qualify according to any criteria other than unacceptable corneal staining, exit subject from study as a screen failure.
9.	Based upon the randomized lens sequence assignment, have the subject insert Pair 1 study lenses, being careful to maintain the correct OD and OS lens assignments and the correct lens pre-soaking assignment. [redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[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.	Study lenses will be worn for approximately 2 hours of wear and instruct the subject 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 [redacted] after Visit 1. Instruct the subject to remain in the office before completing Visit 2.
[redacted]	[redacted]

5.1.3 Visit 2 (Day 1, 2 Hours [redacted] – Pair 1 Follow-up

1.	Obtain information on any changes in medical health and/or the use of concomitant medications.
2.	Record any device deficiencies or AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit.
3.	Review subject compliance with lens wear and adjunct product usage.

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
7.	Have subject remove study lenses.
8.	Perform slit lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area); take photos for corneal staining • Corneal staining • Conjunctival staining • Palpebral conjunctival observations • Corneal epithelial edema • Corneal stromal edema • Corneal vascularization • Conjunctival compression/indention • Chemosis • Corneal infiltrates • Other findings
[redacted]	[redacted]
10.	Schedule Visit 3 [redacted] Remind subjects not to wear contact lenses on the day prior to and of Visit 3.

5.1.4 Visit 3 [redacted] – Baseline/Pair 2 Exposure

1.	Obtain information on any changes in medical health and/or the use of concomitant medications.
2.	Record any device deficiencies or AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit(s).
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
5.	Perform slit lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area); take photos for corneal staining • Corneal staining • Conjunctival staining • Palpebral conjunctival observations • Corneal epithelial edema • Corneal stromal edema • Corneal vascularization • Conjunctival compression/indention • Chemosis • Corneal infiltrates • Other findings
[redacted]	[redacted]

7.	Based upon the randomized lens sequence assignment, have the subject insert Pair 2 study lenses, being careful to maintain the correct OD and OS lens assignments and the correct lens pre-soaking assignment.
11.	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.*
12.	Study lenses will be worn for approximately 2 hours of wear and instruct the subject refrain from using any topical ocular medications or eye drops until they remove lenses at Visit 4.
13.	Schedule Visit 4 to take place 2 hours after Visit 3. Instruct the subject to remain in the office before completing Visit 4.

5.1.5 Visit 4 (same day as Visit 3, 2 hours [redacted] – Pair 2 Follow-up/Exit

1.	Obtain information on any changes in medical health and/or the use of concomitant medications.
2.	Record any device deficiencies or AEs, including those associated with changes in concomitant medication dosing, which are observed or reported since the previous visit.
3.	Review subject compliance with lens wear and adjunct product usage.
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
7.	Have subject remove study lenses.
8.	Perform slit lamp biomicroscopy (without contact lenses) to evaluate the following: • Limbal hyperemia • Bulbar hyperemia • Corneal staining – 5 regions (type, area); take photos for corneal staining • Corneal staining • Conjunctival staining • Palpebral conjunctival observations • Corneal epithelial edema • Corneal stromal edema • Corneal vascularization • Conjunctival compression/indention • Chemosis • Corneal infiltrates • Other findings

9.	Perform Snellen VA with habitual spectacles • OD, OS, distance only
10.	Exit the subject from the study.

5.2 Unscheduled Visits

Any visit that occurs between regularly scheduled visits is an Unscheduled Visit. If a subject requires an Unscheduled Visit, he/she must be advised to return to the office wearing the study lenses, if possible (unless he/she is experiencing a sign or symptom [as indicated in Section 3.3 Risks and Benefits]).

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

If during an Unscheduled Visit the subject is discontinuing from the study, the investigator must refer to Table 1-1.

5.3 Discontinued Subjects

Discontinued subjects are those who withdraw or are withdrawn from the study after signing the informed consent, including screen failures. Subjects may discontinue from the study at any time for any reason. Subjects may also be discontinued from the study at any time if, in the opinion of the Investigator, their continued participation poses a risk to their health. Discontinued subjects will not be replaced (i.e., their subject numbers will not be 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 (excluding screen failures) must undergo all procedures outlined at Visit 4, as applicable.

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

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

5.4 Clinical Study Termination

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

If the clinical study is prematurely terminated or suspended by the Study Sponsor:

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

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

6 ANALYSIS PLAN

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

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

6.1 Subject Evaluability

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

6.2 Analysis Data Sets

6.2.1 Safety Analysis Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. As such, the Safety Analysis Set will include all subjects/eyes exposed to any study lens, whether or not presoaked in the study MPDS. For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses/regimen exposed in the corresponding regimen sequence.

6.3 Demographic and Baseline Characteristics

Demographic information (age, sex, ethnicity, race) will be summarized on the Safety Analysis Set. Baseline data pertaining to habitual lens (lens brand, lens care brand) will be summarized on the Safety Analysis Set as well.

6.4 Effectiveness Analyses

This study defines one primary effectiveness endpoint [redacted] The Safety Analysis Set will be used for all effectiveness analyses.

6.4.1 Primary Effectiveness

The primary objective of this study is to evaluate corneal staining observed after 2 hours of wear with LID018869 [redacted] against both PureVision, pre-cycled with Biotrue, and Biofinity lenses, pre-cycled with Replenish. The primary endpoint is the average of corneal staining areas observed (expressed as a percent) taken over the 5 regions: central, superior, nasal, inferior, and temporal, after 2 hours of lens wear.

6.4.1.1 Statistical Hypotheses

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

6.4.1.2 Analysis Methods

Descriptive statistics will be presented.

[redacted]

6.6 Handling of Missing Data

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

[redacted]

6.8 Safety Analysis

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

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Descriptive summaries (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.

Separate individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to study lenses/MPDS, and for AEs that occur during the washout periods.

[redacted]

No inferential testing will be done for safety analysis.

[redacted]

[redacted]

7 ADVERSE EVENTS AND DEVICE DEFICIENCIES

Terms and Definitions

Adverse Event (AE)	Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device (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.*
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device (test *product*) or control *product*. *Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the test product or control product.*
Anticipated Serious Adverse Device Effect (ASADE)	An effect, which by its nature, incidence, severity or outcome has been identified in the risk assessment.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. This definition includes device deficiencies related to the investigational medical device or the comparator*

Malfunction	Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan (CIP), or investigator's brochure (IB).
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in the health of the subject 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, i.e., it does not include an event which hypothetically might have caused death had it occurred in a more severe form.* b) any potentially sight-threatening event or permanent impairment to a body structure or a body function. c) in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered an SAE. 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. *Note: Planned hospitalization for a preexisting condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.* *Refer to Section 7.1 for additional SAEs.*
Serious Health Threat	Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons *Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.*
Significant Non-Serious Adverse Event	A symptomatic, device-related, non-sight-threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 7.1 for additional Significant 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	User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user. *Note:* *a) Use error includes the inability of the user to complete a task.* *b) Use errors can result from a mismatch between the characteristics of the user, user interface, task, or use environment.* *c) Users might be aware or unaware that a use error has occurred.*

	d) An unexpected physiological response of the patient is not by itself considered a use error. *A malfunction of a medical device that causes an unexpected result is not considered a use error.*

7.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test *product*).

Figure 7–1 Categorization of All AEs

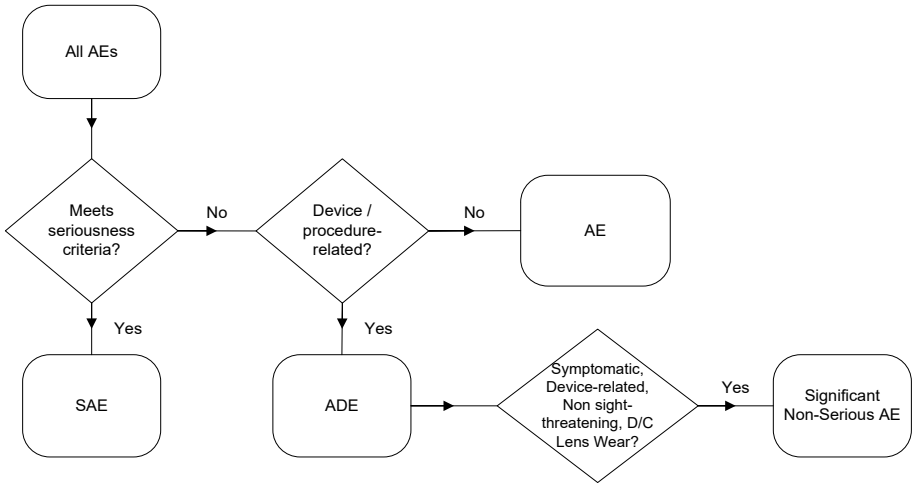
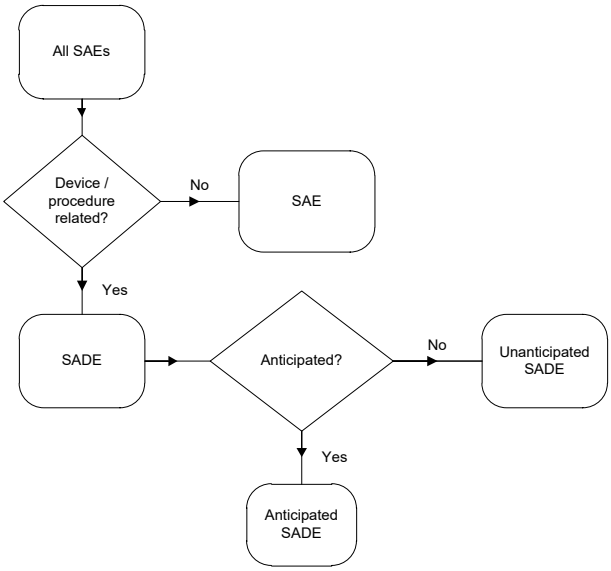


Figure 7-2 Categorization of All Serious Adverse Events



[redacted]

[redacted]

[redacted]

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

[redacted]

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (i.e., ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category listed in the

Device Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. [redacted]

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

7.2 Monitoring for Adverse Events

At each visit, after the subject has had the opportunity to spontaneously mention any problems, the Investigator should inquire about AEs by asking the standard questions:

- "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?"

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

7.3 Procedures for Recording and Reporting

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

[redacted]

[redacted]

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

[redacted]

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

[redacted].

[redacted]

[redacted]

Intensity (Severity)

[redacted]

The Study Sponsor will assess the AEs and may upgrade the Investigator's assessment of seriousness and/or causality. The Study Sponsor will notify the Investigator of any AEs that are upgraded from non-serious to serious or from unrelated to related.

[redacted]

7.5 Follow-Up of Subjects with Adverse Events

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

[redacted]

[redacted]

[redacted]

[redacted]

8 CONFIDENTIALITY, BIAS, AND MASKING

8.1 Subject Confidentiality and Methods Used to Minimize Bias

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. [redacted]

[redacted]

[redacted]

8.2 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed during the study. [redacted]

9 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

9.1 Completion of Source Documents and Case Report Forms

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

[redacted]

[redacted]

10 ETHICS AND COMPLIANCE

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

10.1 Compliance

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

10.2 Institutional Review Board (IRB)

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

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

Voluntary informed consent must be obtained from every subject (and/or legal representative, as applicable) prior to the initiation of any screening or other study-related procedures. [redacted]

[redacted]

Amendment 2

Itemized Changes:

[redacted]

12 REFERENCES

12.1 References Applicable for All Clinical Trials

- 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

12.1.1 US References Applicable for Clinical Trials

- 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

[redacted]

13 APPENDIX

N/A

Signature Page for V-CLN-0004618 v3.0

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