Title

Clinical Performance of a Silicone Hydrogel Following Six Nights of Extended Wear

Protocol Number:	CLL949-C005 / NCT03614130
Development Stage of Project:	[redacted]
Sponsor Name and Address:	Alcon Research, [redacted] 6201 South Freeway Fort Worth, Texas 76134-2099
Test Product:	[redacted] soft contact lenses
Investigator Agreement:	I have read the clinical study described herein, and recognize its confidentiality. I agree to conduct this study in accordance with the ethical principles contained within the Declaration of Helsinki, and the described study in compliance with the protocol and any conditions of approval imposed by the Institutional Review Board and/or the FDA, Good Clinical Practice (GCP), ISO 14155, and all applicable regulatory requirements including 21 CFR Parts 50 (Protection of Human Subjects), 54 (Financial Disclosure), 56 (Institutional Review Boards), and 812 (Investigational Device Exemptions). Additionally, I will comply with all procedures for data recording and reporting, will permit monitoring, auditing, and inspection of my research center, and will retain all records until notified by the Study Sponsor.
Principal Investigator:	
	Signature Date
Name and professional position:	[May be entered into the document or written/typed in later]
Address:	

[redacted]

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1 GLOSSARY OF TERMS

Names of test product	Throughout this document, the test product will be referred to as [redacted]
Name of Control Product(s)	Biofinity® (comfilcon A) soft contact lenses, referred to as Biofinity
Adverse Device Effect	Adverse event related to the use of an investigational medical device (test product) or control product. *Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation; any malfunction; and use error or intentional misuse of the test product or control product.*
Adverse Event	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device (test product). *Note: For subjects, this definition includes events related to the test product, the control product, or the procedures involved. For users or other persons, this definition is restricted to events related to the test product.* Requirements for reporting Adverse Events in the study can be found in Section 11.
Anticipated Serious Adverse Device Effect	Serious adverse device effect which by its nature, incidence, severity, or outcome has been identified in the risk management file.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequate labeling.* Requirements for reporting Device Deficiencies in the study can be found in Section 11.

Enrolled Subject	Any subject who signs an informed consent form for participation in the study.
Interventional Clinical Trial	A research trial that prospectively assigns, whether randomly or not, human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, and/or a research trial in which diagnostic or monitoring procedures beyond standard of care are conducted and generate outcomes for use in analysis of data.
Investigational Product	Is defined as a preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or control product in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or when used to gain further information about the authorized form.
Malfunction	Failure of a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical investigation plan.
Non-serious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Randomized Subjects	Any subject who is assigned a randomized treatment.
Serious Adverse Device Effect (SADE)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Serious Adverse Event (SAE)	Adverse event that led to any of the following: • Death. • A serious deterioration in the health of the subject that either resulted in:

	a. a life-threatening illness or injury. *Note: Life-threatening means that the individual was at immediate risk of death from the event as it occurred, ie, it does not include an event which hypothetically might have caused death had it occurred in a more severe form.* *b.* any potentially sight-threatening event or permanent impairment to a body structure or a body function. c. in-patient hospitalization or prolonged hospitalization. *Note: Planned hospitalization for a pre-existing condition, without serious deterioration in health, is not considered a serious adverse event. In general, hospitalization signifies that the individual remained at the hospital or emergency ward for observation and/or treatment (usually involving an overnight stay) that would not have been appropriate in the physician's office or an out-patient setting. Complications that occur during hospitalization are adverse events. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred, the event should be considered serious.* *d.* a medical or surgical intervention to prevent a) or b). *e.* any indirect harm as a consequence of incorrect diagnostic test results when used within manufacturer's instructions for use. • Fetal distress, fetal death, or a congenital abnormality or birth defect.

	Refer to Section 11 for additional SAEs.
Significant Non-Serious Adverse Event	Is a symptomatic, device-related, non-sight threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. *Refer to Section 11 for additional Significant Non-Serious AEs.*
Unanticipated Serious Adverse Device Effect (USADE)	Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the risk management file.
Use Error	Act or omission of an act that results in a different medical device response than intended by manufacturer or expected by user. *Note: This definition includes slips, lapses, and mistakes. An unexpected physiological response of the subject does not in itself constitute a use error.*

2 LIST OF ACRONYMS AND ABBREVIATIONS

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

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
[redacted]	[redacted]
Biofinity	Biofinity (comfilcon A) soft contact lenses
CFR	Code of Federal Regulations
[redacted]	[redacted]
CRF	Case report form
CSM	Clinical site manager
CTT	Clinical trial team
D	Diopter(s)
D/C	Discontinue
eCRF	Electronic case report form
EDC	Electronic data capture
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
IB	Investigator's brochure
ICF	Informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IP	Investigational product
IRB	Institutional review board
IRT	Interactive response technology
ISO	International Organization for Standardization
[redacted]	[redacted]
LCSM	Lead clinical site manager
LID	Lens identification
logMAR	Logarithm of the minimum angle of resolution
mm	Millimeter
MOP	Manual of procedures
n	Number
N/A	Not applicable
OD	Right eye
OS	Left eye
SAE	Serious adverse event
SADE	Serious adverse device effect
SD	Standard deviation
SiHy	Silicone hydrogel
SLE	Slit-lamp examination

Abbreviation	Definition
SOP	Standard operating procedure
[redacted]	[redacted]
US / USA	United States of America
USADE	Unanticipated serious adverse device effect
VA	Visual acuity
vs	Versus

3 PROTOCOL SUMMARY

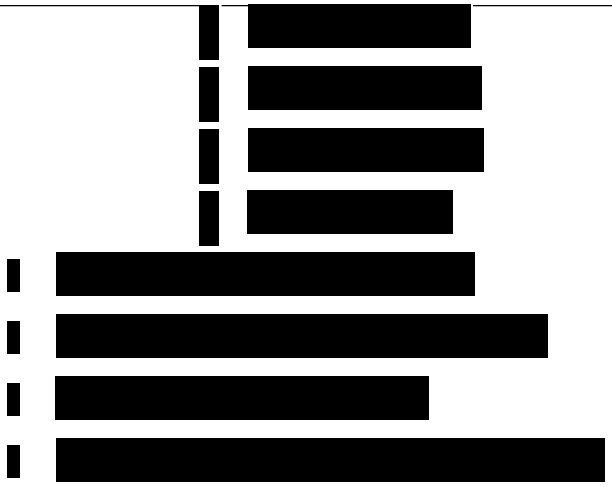
This will be a prospective, randomized, controlled, double-masked, contralateral wear clinical trial.

Approximately 2 sites in the US will enroll approximately 22 subjects. Subjects will be randomized to wear the test [redacted] lens in one eye and the control Biofinity lens in the other eye. Subjects will be expected to attend 3 visits: Baseline/Dispense, 1-Day Follow-up, and 1-Week Follow-up/Exit.

Following randomization during the Baseline/Dispense Visit, study lenses will be dispensed to the subject. All study lenses are to be worn overnight for approximately 6 nights. Subjects will be expected to wear the study lenses continuously in an extended wear modality. [redacted]

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: [redacted] soft contact lenses Control Product: Biofinity (comfilcon A) soft contact lenses
Purpose and rationale	The purpose of this clinical study is to evaluate the on-eye performance of the investigational [redacted] lens compared to the commercially available Biofinity lens following 1 week of extended wear.
Objective	The primary objective is to assess [redacted] performance of the [redacted] soft contact lens when worn in an extended wear modality (ie, up to 6 nights of continuous wear) as compared to Biofinity soft contact lens.
Endpoints	Primary Effectiveness • Distance VA (Snellen)

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessments	Effectiveness • VA (Snellen distance) with IP [redacted]

	[redacted]  Safety • AEs • Biomicroscopy • Device deficiencies
Study Design	This will be a prospective, randomized, controlled, double-masked, contralateral clinical trial. Subject participation in the study will be approximately 1 week with approximately six nights of extended wear.
Subject population	Volunteer subjects aged 18 or over who are soft contact lens wearers, excluding Biofinity habitual wearers, have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and in an extended wear modality a minimum of 1 night per week. [redacted] Pregnant and breastfeeding women are excluded from this study.
Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Successful wear of spherical soft contact lenses in both eyes during the past 3 months for a minimum of 5 days per week and in an extended wear modality a minimum of 1 night per week. • Best corrected VA 20/25 or better in each eye.

Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	• Current Biofinity lens wearer.
Data analysis and sample size justification	No formal hypotheses are formulated for the primary effectiveness endpoint of VA; hence no inferential testing will be performed. Descriptive summary statistics will be provided on the Snellen categories as well as the converted logMAR values. [redacted]
Key words	[redacted] Biofinity, extended wear, 6 nights
[redacted]	

Table 3–1 Schedule of Study Procedures and Assessments

Procedure/ Assessment	**Visit 1, Day 1: Baseline/Dispense**	**Visit 2, Day 2: 1-Day Follow-up** 24 hours after Visit 1 (±4 hours)	**Visit 3, Week 1: 1-Week Follow-up/Exit** 7 days (-1 day) of lens wear	**Unsched Visit**
			Ideally subjects should be seen within 4 hours of awakening.	
Informed Consent	✓	-	-	-
Demographics	✓	-	-	-
Medical History	✓	-	-	-
Concomitant Medications	✓	(✓)	(✓)	(✓)
Inclusion/ Exclusion	✓	-	-	-

Procedure/ Assessment	**Visit 1, Day 1: Baseline/Dispense**	**Visit 2, Day 2: 1-Day Follow-up** 24 hours after Visit 1 (±4 hours)	**Visit 3, Week 1: 1-Week Follow-up/Exit** 7 days (-1 day) of lens wear	**Unsched Visit**
Habitual lens (brand, power)	✓	-	-	-
VA w/ habitual correction (OD, OS, Snellen distance)*	✓	-	✓	(✓)
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Biomicroscopy	✓	✓‡	✓‡ ✓ at Exit	✓
Dispense study lenses	✓	-	-	-
VA w/ study lenses (OD, OS, Snellen distance)	✓	✓	✓	✓
[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	Visit 1, Day 1: Baseline/Dispense	Visit 2, Day 2: 1-Day Follow-up 24 hours after Visit 1 (±4 hours)	Visit 3, Week 1: 1-Week Follow-up/Exit 7 days (-1 day) of lens wear	Unsched Visit
[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]
AEs	✓	✓	✓	✓
Device deficiencies	✓	✓	✓	✓
Exit Form	(✓)	(✓)	(✓)	(✓)

*source only
[redacted]
†Biomicroscopy with contact lenses still on-eye (not to include corneal staining)
(✓) assessment performed as necessary [redacted]

4 PROTOCOL AMENDMENTS

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

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

[redacted]

[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]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]

[redacted]	[redacted]
	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

5 INTRODUCTION

5.1 Rationale and Background

[redacted]

[redacted]

[redacted]

In this clinical trial, the performance of the investigational [redacted] lens will be compared to the commercially available Biofinity lens in a contralateral design with approximately 1 week (including approximately 6 nights of extended wear) of exposure. The intended use of this contact lens is for vision correction. Therefore, the objective measurement of VA is planned as the primary variable for the comparison with the Biofinity lens. [redacted]

5.2 Purpose of the Study

The purpose of this clinical study is to evaluate the on-eye performance of the investigational [redacted] lens compared to the commercially available Biofinity lens following approximately 6 nights of extended wear. At the end of the study, a clinical study report will be prepared in accordance with applicable regulatory requirements and standards.

[redacted].

5.3 Risks and Benefits

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

Biofinity lenses are for up to 6 nights/7 days of continuous wear. Further details on any known potential risks and benefits can be found in the package insert.

A summary of the known potential risks and benefits associated with [redacted] can be found in the IB. [redacted]

[redacted] In general, the risks with [redacted] are anticipated to be similar to other marketed weekly/monthly soft contact lenses.

[redacted]

Refer to the IB for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective

The primary objective is to assess [redacted] the [redacted] soft contact lens when worn in an extended wear modality (ie, up to 6 nights of continuous wear) as compared to Biofinity soft contact lens.

6.2 Secondary Objective

Not Applicable.

[redacted]

6.4 Safety Objective

Table 6–2 Safety Objective

Objective	Endpoints
[redacted] evaluation of performance and safety profile of the test lens.	AEs Device deficiencies Biomicroscopy findings

7 INVESTIGATIONAL PLAN

7.1 Study Design

This will be a prospective, randomized, controlled, double-masked, contralateral wear clinical trial.

Approximately 2 sites in the US will enroll approximately 22 subjects. Subjects will be randomized to wear the test [redacted] lens in one eye and the control Biofinity lens in the other eye. Subjects will be expected to attend 3 visits: Baseline/Dispense, 1-Day Follow-up, and a 1-Week Follow-up/Exit.

Following randomization during the Baseline/Dispense Visit, study lenses will be dispensed to the subject. All study contact lenses are to be worn overnight for approximately 6 nights. Subjects will be expected to wear the study lenses continuously in an extended wear modality. [redacted]

The study is expected to take approximately 6 weeks for completion.

7.2 Rationale for Study Design

[redacted]

The purpose of this extended wear [redacted] clinical study is to [redacted] develop [redacted] clinical information for safety and efficacy variables such as VA, [redacted]

[redacted]

[redacted]er establish proof of principle for extended wear in this novel silicone hydrogel lens.

7.4 Rationale for Choice of Control Product

Biofinity was chosen as the control product [redacted] to compare to [redacted] with regard to effectiveness and safety. Both [redacted] and Biofinity are silicone hydrogel lenses[redacted]d for [redacted] continuous wear. The Biofinity lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes.

7.5 Data Monitoring Committee

Not applicable.

8 STUDY POPULATION

The study population consists of adult male and female subjects (aged 18 or over), with non-diseased eyes, who require optical correction for refractive ametropia. It is aimed to enroll approximately 22 subjects in approximately 2 US sites. Estimated time needed to recruit subjects for the study is approximately 3 weeks. The intended study population consists of volunteer subjects aged 18 or over who are soft contact lens wearers, excluding Biofinity habitual wearers, who have at least 3 months of contact lens wearing experience, and who wear their habitual lenses at least 5 days per week and in an extended wear modality. [redacted]

8.1 Inclusion Criteria

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

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

1.	Subject must be at least 18 years of age and able to understand and sign an IRB/IEC approved Informed Consent form.
2.	Willing to attend all scheduled study visits as required per protocol.
3.	Successful wear of spherical soft contact lenses in both eyes during the past 3 months for a minimum of 5 days per week and in an extended wear modality a

	minimum of 1 night per week.
[redacted]	[redacted]
5.	Best spectacle corrected visual acuity 20/25 or better in each eye.
[redacted]	[redacted]

8.2 Exclusion Criteria

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

1.	Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the Investigator.
2.	Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the Investigator.
3.	History of ocular or intraocular surgery, including refractive surgery which contact lens extended wear could be contraindicated, as determined by the Investigator and/or history of irregular cornea.
4.	Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher; or presence of corneal infiltrate(s).
5.	Current or history of pathologically dry eye in either eye that, in the opinion of the Investigator, would preclude contact lens wear.
6.	Current or history of herpetic keratitis in either eye.
7.	Eye injury in either eye within twelve weeks immediately prior to enrollment for this trial.
8.	Current or history of intolerance, hypersensitivity or allergy to any component of the study products.
9.	Current Biofinity lens wearer.
10.	Any use of topical ocular medications and artificial tear or rewetting drops that

	would require instillation during contact lens wear.
11.	Currently pregnant or breast-feeding.
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.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Products

Replacement lenses will not be provided to the subject. In the event a lens needs to be replaced, the subject must return to the site for a replacement lens.

Test Product: [redacted] soft contact lenses

Control Product: Biofinity (comfilcon A) soft contact lenses

Table 9–1 Test Product

Test Product	[redacted] soft contact lenses (LID011121) [redacted]
Manufacturer	Alcon Laboratories, [redacted] 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended purpose in the current study	The intended use of this contact lens is for vision correction.
Product description	[redacted]

and parameters available for this study	[redacted]
Formulation	Silicone Hydrogel. Additional details can be found in the IB.
Usage	• Wear: o Extended Wear – ~6 nights o Contralateral • Exposure: ~1 week • [redacted] • Additional details can be found in the Manual of Procedures
Number/Amount of product to be provided to the subject	One lens per eye will be dispensed to the subject on Visit 1.
Packaging description	Blister foil pack
Labeling description	• Lens Foil label includes: - material name and/or identifier - base curve - diameter - manufacturing protocol number - packing solution - power - lot number - expiration date - content statement - investigational device statement - Sponsor information • Provided in boxes of up to 8 lenses per power per box, identified with the following: - a color coded label stating the protocol number - material identifier - power

	- an investigational use only statement - tracking number
Storage conditions	Stored at room temperature.
Supply	All study lenses will be provided to the site. The site will dispense the study lenses to the subject at Visit 1.

Table 9–2 Control Product

Control Product	Biofinity (comfilcon A) soft contact lenses (Biofinity)
Manufacturer	CooperVision®
Indication for Use	The intended use of this contact lens is for vision correction.
Product description and parameters available for this study	• Material: comfilcon A • Water content: 48% • [redacted] • Base curve: 8.6 mm • Diameter: 14.0 mm
Formulation	Silicone Hydrogel. Additional details can be found in the Biofinity package insert.
Usage	• Wear: o Extended Wear – ~6 nights o Contralateral • Exposure: ~1 week • [redacted] • Additional details can be found in the Manual of Procedures
Number/Amount of Product to be Provided to the subject	One lens per eye will be dispensed to the subject on Visit 1.
Packaging description	Blister foil pack in commercial packaging
Labeling description	• Lens Foil label includes: - material name

	- base curve - diameter - packing solution - power - lot number - expiration date - content statement - Manufacturer information - Country of origin
Storage conditions	Stored at room temperature.
Supply	[redacted]. The site will dispense the study lenses to the subject at Visit 1.

[redacted]

9.3 Treatment Assignment / Randomization

Subjects will be randomized in a 1:1 ratio to receive treatment with [redacted] or Biofinity in one eye and the other lens in the fellow eye, as indicated below:

Sequence 1: [redacted] (OD) / Biofinity (OS)

Sequence 2: Biofinity (OD) / [redacted] (OS)

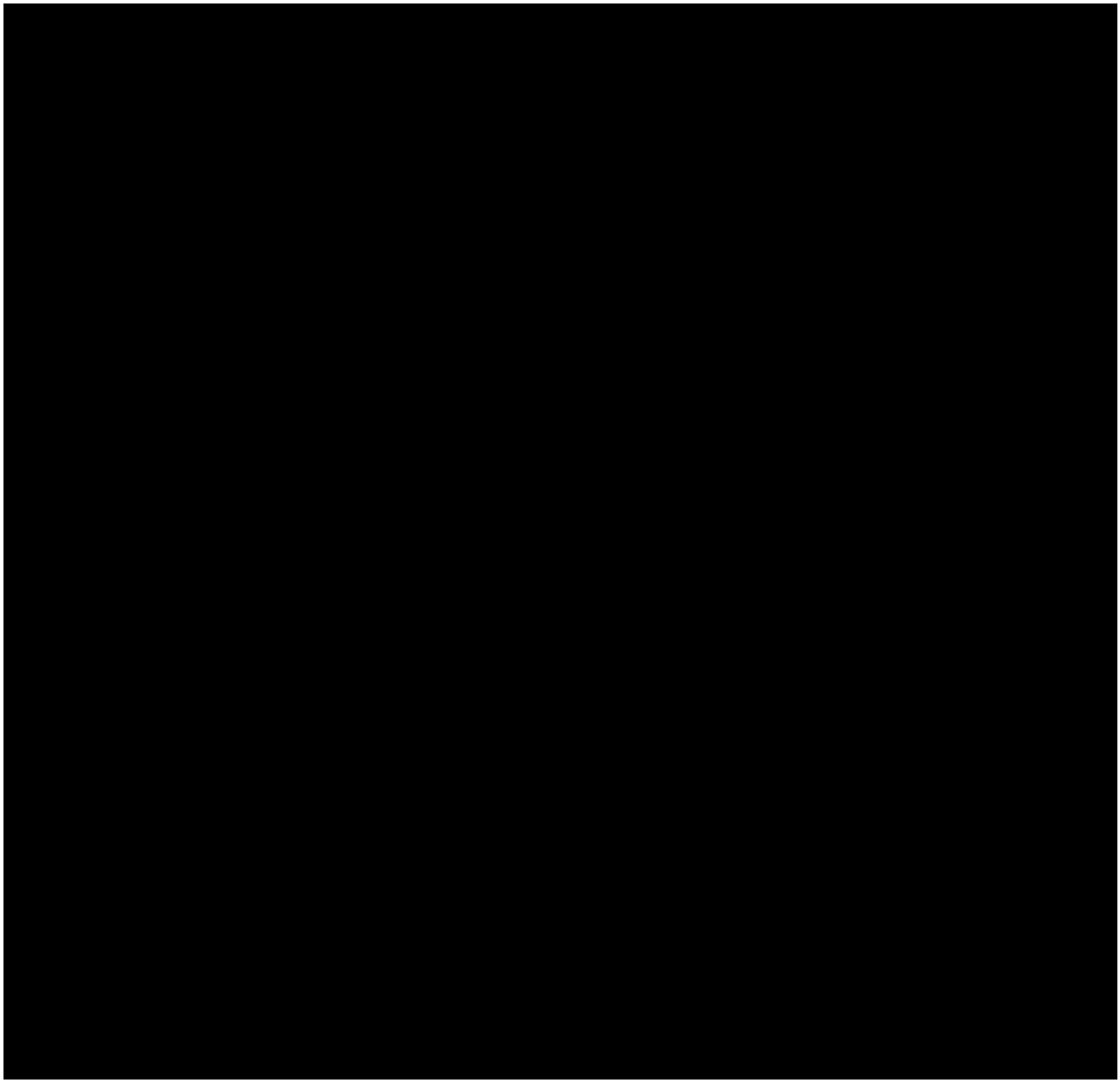
Only after signing the ICF, a subject will be assigned a subject number by the electronic data capture system.

A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned a treatment (lens sequence) according to the randomization list [redacted]. The randomization list will be generated and maintained by the Study Sponsor.

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

9.4 Treatment masking

This study is double-masked, with subjects randomized to use [redacted] and Biofinity in either eye for the duration of the treatment period.



[redacted] Unmasking will occur only after all planned study data have been validated, and the database locked.

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

In the event of a medical emergency where the knowledge of subject treatment is required, an individual Investigator will have the ability to unmask the treatment assignment for a specific subject after contacting an appropriate Study Sponsor representative if time allows. Unmasking must be done according to the instructions provided for the study IRT system.

9.5 Accountability Procedures

Upon receipt of the IP, the Investigator or delegate must conduct an inventory. [redacted] Throughout the study, the Investigator or delegate must maintain records of IP dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. All IPs sent to the Investigator must be

accounted for by Study Sponsor personnel, and in no case be used in an unauthorized situation.

It is the Investigator's responsibility to ensure that:

- All study products are accounted for and not used in any unauthorized manner
- All used foils and unused supplies are returned by each subject
- All unused products (supplied by the Study Sponsor) are available for return to the Study Sponsor, as directed
- Any study lenses associated with a device deficiency or with any product-related adverse event (ie, ADE or SADE) are returned to the Study Sponsor for investigation, unless otherwise directed by the Sponsor. Refer to Section 11 of this protocol for additional information on the reporting of device deficiencies and AEs and the return of study products associated with these events.

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

9.6 Changes to concomitant medications, treatments / procedures

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

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

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

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

10 STUDY PROCEDURES AND ASSESSMENTS

Visit	Window
Visit 1, Day 1: Baseline/Dispense	N/A
Visit 2, Day 2: 1-Day Follow-Up	24 hours (±4 hours) after Visit 1
Visit 3, 1 Week: 1-Week Follow-Up/Exit	7 days (-1 day) of lens wear following insertion

Unscheduled Visits and Early Termination Visits are allowed, if necessary.

At the Baseline/Dispense Visit, study lenses will be dispensed contralaterally to the subject. All study lenses will be worn in an extended wear modality for approximately 6 nights. Problem lenses (if any) will not be discarded but collected by the subject and returned to the investigational site. [redacted]. VA will be measured at all visits, and any decrease of two or more lines from the Dispense Visit to any follow-up visits should be explained by the Investigator. [redacted]

10.1 Informed Consent and Screening

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

10.2 Description of Study Procedures and Assessments

10.2.1 Demographics

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

10.2.2 Medical History

Collect medical history information, including information on all medications used within the past 30 days. Include herbal therapies, vitamins, and all over-the-counter as well as

prescription medications. Throughout the subject's participation, obtain information on any changes in medical health and/or the use of concomitant medications.

10.2.3 Investigational Product compliance

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

10.2.4 Adverse Event Collection: Safety Assessment

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

10.2.5 Slit-Lamp Biomicroscopy: Safety Assessment

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

10.2.6 Device Deficiencies: Safety Assessment

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

[redacted]

10.3 Unscheduled Visits

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

- Collect Adverse Event information
- Record changes in medical condition or concomitant medication
- Collect Device Deficiency information, as applicable
- Assess and record VAs
- Perform biomicroscopy (assessments with or without lenses, as applicable)

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

If during an Unscheduled Visit the subject is discontinuing the IP or discontinuing from the study, the Investigator must conduct Exit procedures according to Table 3-1, Schedule of Study Procedures and Assessments, as possible.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent, not meeting the inclusion/exclusion criteria, and prior to randomization to product/dispense of study product.

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

Subject numbers must not be re-used.

10.4.2 Discontinuations

Discontinued subjects are individuals who voluntarily withdraw or are withdrawn from the study by the Investigator after signing the informed consent, including screen failures.

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

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

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

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

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

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

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

10.5 Clinical Study Termination

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

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

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

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

10.5.1 Follow-up of subjects after study participation has ended

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

11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

11.1 General Information

An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test article). Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 11–1 Categorization of All Adverse Events

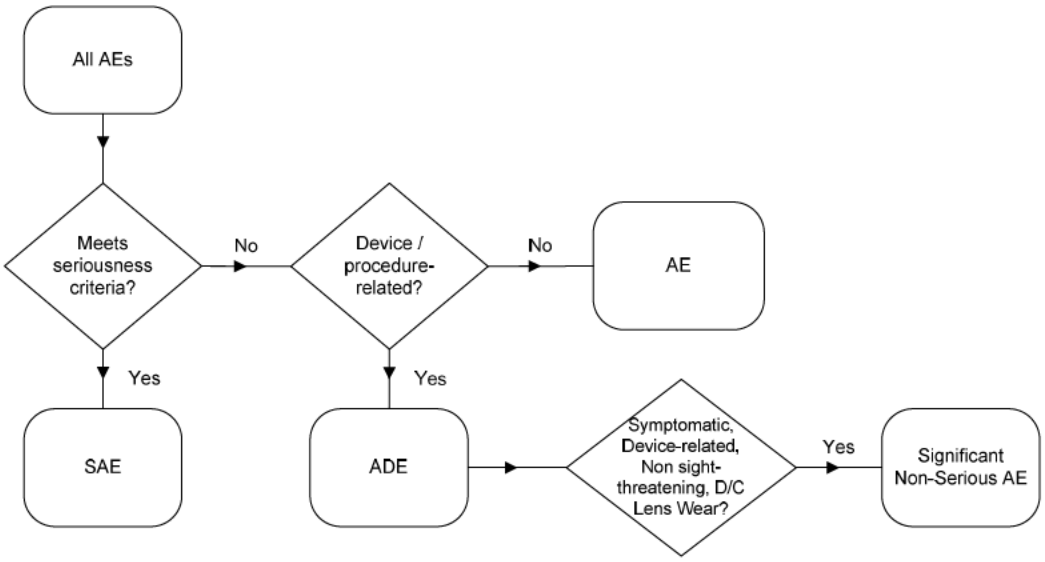
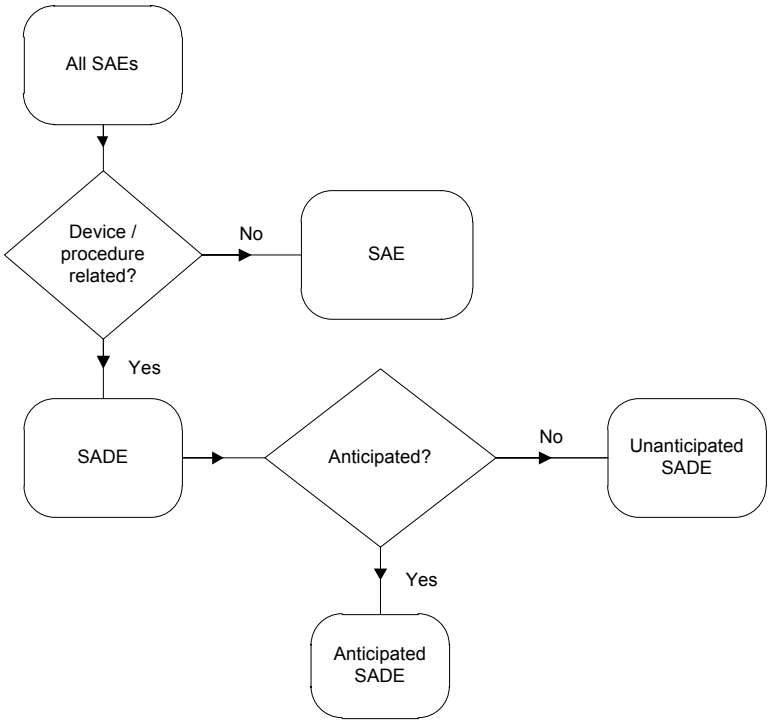


Figure 11-2 Categorization of All Serious Adverse Events



Serious Adverse Events

In addition to reporting all AEs (serious and non-serious) meeting the definitions, the Investigator must report any occurrence of the following as an SAE:

- An ocular infection including a presumed infectious ulcer with any of the following characteristics*:
    - Central or paracentral location
    - Penetration of Bowman's membrane
    - Infiltrates > 2 mm diameter
    - Iritis
    - Increase in intraocular pressure
    - Culture positive for microorganisms
    - Increasing size or severity at subsequent visits
- Any central or paracentral corneal event (such as neovascularization) that results in permanent opacification
- Hypopyon

- Hyphema
- Neovascularization within the central 6 mm of the cornea
- Permanent vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting ≥ 50% of corneal surface area

*NOTE: Culture samples (from the subject's eyes, lenses, etc) must be taken [*as described in the MOP; and documented in the narrative section(s) of the corresponding ADE-SAE eCRF*], for any suspected ocular infection, including infiltrates with overlying epithelial defect.

Significant Non-Serious Adverse Events

A significant non-serious AE is a device-related, non-sight threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. In addition, the Investigator must report any occurrence of the following as a Significant Non- Serious Adverse Event:

- Peripheral non-progressive non-infectious ulcers
- All symptomatic corneal infiltrative events
- Corneal staining score greater than or equal to Grade 3 (Refer to MOP for grading scales)
- Temporary vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that persists for 2 or more weeks
- Neovascularization score greater than or equal to Grade 2 (Refer to MOP for grading scales)

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

Device Deficiencies

A device deficiency is inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. A device deficiency may or may not be associated with patient harm (ie, ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The Investigator should determine the applicable category listed in the Device Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. Examples of device deficiencies include the following:

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

11.2 Monitoring for Adverse Events

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

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

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

11.3 Procedures for Recording and Reporting

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

In addition, temporary lens awareness or visual changes during the fitting process are not considered AEs if the Investigator assesses that the symptom(s) can reasonably resolve within the anticipated adaptation period.

- ADEs or SAEs are documented on the *Serious Adverse Event and Adverse Device Effect* eCRF within 24 hours of the Investigator's or site's awareness.
- Device deficiencies are documented on the *Device Deficiency* eCRF within 24 hours of the Investigator's or site's awareness.

- A printed copy of the completed *Serious Adverse Event and Adverse Device Effect* and/or *Device Deficiency* eCRF must be included with product returns.
- Additional relevant information after initial reporting must be entered into the eCRF as soon as the data become available.
- Document any changes to concomitant medications on the appropriate eCRFs.
- Document all relevant information from Discharge Summary, Autopsy Report, Certificate of Death, etc, if applicable, in narrative section of the *Serious Adverse Event and Adverse Device Effect* eCRF.

[redacted]

Study Sponsor representatives may be contacted for any protocol related question and their contact information is provided in the MOP that accompanies this protocol.

Further, depending upon the nature of the AE or device deficiency being reported, the Study Sponsor may request copies of applicable portions of the subject's medical records. The Investigator must also report all AEs and device deficiencies that could have led to a SADE according to the requirements of regulatory authorities or IRB/IEC.

Intensity and Causality Assessments

Where appropriate, the Investigator must assess the intensity (severity) of the AE based upon medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

Mild	An AE is mild if the subject is aware of but can easily tolerate the sign or symptom.

Moderate An AE is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.

Severe An AE is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

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

Causality

Related An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.

Not Related An AE classified as not related may either be definitely unrelated or simply unlikely to be related (ie, there are other more likely causes for the AE).

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

Additionally, the Study Sponsor shall immediately conduct an evaluation of any unanticipated adverse device effect, including anticipated adverse events that occur in unanticipated severity or frequency. The results of this evaluation will be reported to the FDA, the IRB and participating Investigators within 10 working days upon receiving notification of the effect.

11.4 Return product analysis

Investigational product associated with device deficiencies and/or product related AEs [ie, ADE or SADE] will be returned for investigation as detailed in the MOP.

11.5 Unmasking of the Study Treatment

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

11.6 Follow-Up of Subjects with Adverse Events

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

The Investigator should provide the Study Sponsor with any new safety information (which includes new AEs and changes to previously reported AEs) that may affect the safety evaluation of the device. For AEs that are unresolved/ ongoing at time of subject exit from study, any additional information received at follow-up should be documented in the eCRFs up to study completion (ie, database lock).

Any additional data received up to 1 month after subject discontinuation or exit must be documented and available upon the Study Sponsor's request. All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements, as applicable.

The Investigator should also report complaints on non-Alcon products directly to the manufacturer as per the manufacturer's instructions or local regulatory requirements.

11.7 Pregnancy in the Clinical Study

Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case–by-case basis. Should a woman become pregnant during study participation, the pregnancy will be documented on the Medical history eCRF.

12 ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, standard deviation (SD), median, minimum and maximum. Categorical variables will be summarized with counts and percentages from each category. Any deviations to the analysis plan will be updated during the course of the study as part of a protocol amendment or will be detailed in the clinical study report.

12.1 Subject Evaluability

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

12.2 Analysis Sets

Only 1 analysis set will be defined, namely the safety analysis set. It will include all eyes exposed to any study lenses evaluated in this study.

Eyes will be analyzed based upon the lens exposed at the time of the clinical assessment.

12.3 Demographic and Baseline Characteristics

Demographic information and habitual lens information will be presented by lens sequence and overall.

12.4 Effectiveness Analyses

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to assess [redacted] performance of the [redacted] soft contact lens when worn in an extended wear modality (ie, up to 6 nights of continuous wear) as compared to Biofinity soft contact lens.

The primary endpoint is VA with study lenses, collected by eye.

12.4.1.1 Statistical Hypotheses

No hypothesis testing of the primary effectiveness endpoint is planned.

12.4.1.2 Analysis Methods

Summary statistics will be provided.

[redacted]

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

[redacted]

12.5 Handling of Missing Data

All data obtained in evaluable subjects/eyes will be used. No imputation for missing values will be carried out.

12.6 Safety Analyses

The safety endpoints are:

- AEs
- Biomicroscopy
- Device Deficiencies

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

Descriptive summaries (counts and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. A listing containing details of the AEs will also be provided.

Each biomicroscopy parameter will be tabulated by its grade.

Frequency for each device deficiency category will be presented and a supporting listing will be provided.

[redacted]

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

The Investigator must ensure that the subject's anonymity is maintained throughout the course of the study. In particular, the Investigator must keep an enrollment log with confidential identifying information that corresponds to the subject numbers and initials of each study participant. At the end of the clinical study, the Study Sponsor will collect a copy of the enrollment log ***without any identifying subject information***. All documents submitted to the Study Sponsor will identify the subjects exclusively by number and demographic information. No other personally identifying information will be transmitted to the Study Sponsor.

[redacted]

[redacted]

13.2 Completion of Source Documents and Case Report Forms

The nature and location of all source documents will be identified to ensure that original data required to complete the CRFs exist and are accessible for verification by the site monitor, and all discrepancies shall be appropriately documented via the query resolution process. Site monitors are appointed by the Study Sponsor and are independent of study site staff.

If electronic records are maintained, the method of verification must be determined in advance of starting the study.

At a minimum, source documents include the following information for each subject:

- Subject identification (name, sex, race/ethnicity)
- Documentation of subject eligibility
- Date of informed consent
- Dates of visits
- Documentation that protocol specific procedures were performed
- Results of study parameters, as required by the protocol
- IP accountability records
- Documentation of AEs and other safety parameters (if applicable)
- Records regarding medical histories and the use of concomitant therapies prior to and during the study
- Date of study completion and reason for early discontinuation, if applicable

It is required that the author of an entry in the source documents be identifiable. Direct access to source documentation (medical records) must be allowed for the purpose of verifying that the data recorded on the CRF are consistent with the original source data.

Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The Principal Investigator is responsible for reviewing and certifying that the CRFs are accurate and complete. [redacted]

13.3 Data Review and Clarifications

A review of CRF data to the subject's source data will be completed by the site monitor to ensure completeness and accuracy. After the CRFs have been completed, additional data clarifications and/or additions may be needed as a result of the data cleaning process. Data clarifications are documented and are part of each subject's CRF.

13.4 Sponsor and Monitoring Responsibilities

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

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

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

[redacted]

[redacted]

13.5 Regulatory Documentation and Records Retention

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

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

13.6 Quality Assurance and Quality Control

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

14 ETHICS

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

- The Declaration of Helsinki, and in compliance with the ICH E6 GCP Consolidated Guideline, ISO 14155:2011, and the applicable US FDA 21 CFR Regulations.
- SOPs of the Study Sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations.

- Notifications and timelines for reporting protocol deviations should be based upon applicable Ethics Committee requirements

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

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

Voluntary informed consent must be obtained in writing from every subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject. The Investigator must have a defined process for obtaining consent. Specifically, the Investigator, or their delegate, must explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the Investigator, and if required by local regulation, other qualified personnel. The Investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and Sponsor-designated

personnel. The Investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

15 REFERENCES

15.1 References applicable for all clinical studies

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

15.1.1 US references applicable for clinical studies

- 21 CFR Part 11 - Electronic Records; Electronic Signatures
- 21 CFR Part 50 - Protection of Human Subjects
- 21 CFR Part 56 - Institutional Review Boards
- 21 CFR Part 812 - Investigational Device Exemptions
- 21 CFR Part 54 - Financial Disclosure by Clinical Investigators
- The California Bill of Rights

15.2 References for this clinical study

Not applicable. There are no references.

[redacted]
