Clinical Assessment of a Daily Disposable Soft Silicone Hydrogel Contact Lens

STUDY ID

CLU484-P003

PROTOCOL

NCT06044948

Device Protocol for CLU484-P003

Title: Clinical Assessment of a Daily Disposable Soft Silicone Hydrogel Contact Lens

Protocol Number:	CLU484-P003
Clinical Investigation Type:	Postmarket Interventional / Confirmatory
Test Product:	DAILIES TOTAL1® spherical soft contact lenses (DT1; [redacted])
Sponsor Name and Address:	Alcon Research, LLC, and its affiliates ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099

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 Practices; applicable international and national regulations, laws, guidelines, and standards; the conditions of approval imposed by the reviewing IRB or regulatory authority; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki.
- 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:

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1 GLOSSARY OF TERMS

Names of Test Product(s)	Throughout this document, test product(s) will be referred to as DAILIES TOTAL1® spherical soft contact lenses (DT1; [redacted]).
Name of Comparator Product(s)	N/A
Adverse Device Effect (ADE)	Adverse event related to the use of an investigational medical device or comparator. *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.*
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 or comparator and whether anticipated or unanticipated. *Note: For subjects, this definition includes events related to the investigational medical device, comparator, or the procedures involved. For users or other persons, this definition is restricted to the use of the investigational medical device or comparator.* Requirements for reporting Adverse Events in the study can be found in Section 11.

Clinical Investigation Plan (CIP)	The document(s) stating the rationale, objectives, design, and prespecified analysis, methodology, organization, monitoring, conduct, and record-keeping of the clinical investigation. *Note: The protocol and other documents referenced in the protocol (for example, the Statistical Analysis Plan, the Manual of Procedures, the Deviations and Evaluability Plan, and the Protocol Monitoring Plan) comprise the CIP.*
Clinical Investigation Report (CIR) / Clinical Study Report	The document describing the design, execution, statistical analysis, and results of a clinical investigation. The CIR is synonymous with the Clinical Study Report.
Device Deficiency	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance. *Note: This definition includes malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling related to the investigational medical device or the comparator.* 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 pre- or postmarket clinical investigation where the assignment of a subject to a particular medical device is decided in advance by a CIP, or diagnostic or monitoring procedures requested in the CIP are in addition to those available as normal clinical practice and burden the subject.

Investigational Product (IP)	A preventative (vaccine), a therapeutic (drug or biologic), device, diagnostic, or palliative used as a test or comparator 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 an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or CIP, or investigator's brochure (IB).
Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Postapproval Study	A study required by the Food and Drug Administration or other health authority at the time of approval of a premarket approval, humanitarian device exemption, or product development protocol application. Postapproval studies are conducted to provide patients, health care professionals, the device industry, the Food and Drug Administration, and other stakeholder's information on the continued safety and effectiveness (or continued probable benefit, in the case of a humanitarian device exemption) of approved medical devices.
Postmarketing / Postauthorization study	Any study conducted within the conditions laid down in product labelling and other conditions laid down for the marketing of the product or under normal conditions of use. A postmarketing study falls either within the definitions of an interventional or a noninterventional study and may also fall within the definition of a postapproval study.

Product Complaint	Any oral, electronic, or written communication that alleges deficiencies related to the identity (labeling), quality, durability, reliability, safety, effectiveness, or performance of a marketed product, including failure of the product, labeling, or packaging to meet specifications, whether or not the product is related to or caused the alleged deficiency. A complaint may allege that an adverse event or medical device malfunction has occurred.
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, users or other persons as defined by one or more of the following: 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 including chronic diseases. c) inpatient hospitalization or prolonged hospitalization. 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, congenital abnormality or birth defect including physical or mental impairment. *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 11 for additional SAEs.*
Study Completion	The completion of the study is considered to coincide with the study-level last subject last visit or the decision to terminate the trial, whichever is later.

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.* e) *A malfunction of a medical device that causes an unexpected result is not considered 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
BCVA	Best corrected visual acuity
CI	Confidence interval
CIP	Clinical investigation plan
CIR	Clinical investigation report
CL	Confidence limit
CRF	Case report form
D	Diopter
DEP	Deviations and evaluability plan
DT1 or DT1 soft contact lenses	DAILIES TOTAL1® spherical soft contact lenses
eCRF	Electronic case report form
EDC	Electronic Data Capture
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
IB	Investigator's brochure
ICF	Informed consent form
IEC	Independent ethics committee
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
LID	Lens Identification
LogMAR	Logarithm of the minimum angle of resolution
m	Meter
mm	Millimeter
MOP	Manual of procedures
N/A	Not applicable
OD	Right Eye
OS	Left Eye
PP	Per Protocol
[redacted]	[redacted]
SADE	Serious adverse device effect
SAE	Serious adverse event
SD	Standard deviation
SLE	Slit lamp examination
SOP	Standard operating procedure
US	United States
VA	Visual acuity

3 PROTOCOL SUMMARY

Investigational product type	Device
Study type	Interventional
Investigational products	Test Product: DAILIES TOTAL1 spherical soft contact lenses (DT1; [redacted]) Comparator Product: N/A
Purpose and Scientific Rationale for the Study	The purpose of this study is to assess the clinical performance of DT1 soft contact lenses over approximately 1 week of daily wear. The primary [redacted] endpoints were selected to fulfill the primary [redacted] objectives of the study.
Brief Summary of the Protocol	This clinical study will evaluate the clinical performance of DT1 soft contact lenses in habitual spherical soft contact lens wearers, excluding habitual wearers of the test product. [redacted]
Objective(s)	• The primary objective is to evaluate distance VA of the DT1 soft contact lenses over approximately 1 week of wear. [redacted] • To describe the safety profile of the test lenses.
Endpoint(s)	Primary Effectiveness • Distance VA (Snellen) with study lenses at Week 1 [redacted]

	[redacted] Safety • AEs • Biomicroscopy findings • Device deficiencies
Assessment(s)	Effectiveness • Manifest Refraction • BCVA with Manifest Refraction (Snellen distance, OD, OS) • VA with Habitual Correction (Snellen distance, OD, OS) • Habitual Lens Brand • Power Optimization • VA with study lenses (Snellen distance, OD, OS) [redacted]

	Safety • AEs • Biomicroscopy • Device deficiencies
Study Design	This is a prospective, interventional, nonrandomized, single-arm, subject-masked, multicenter, daily wear clinical study in the US assessing clinical performance of DT1 soft contact lenses. Subjects will be expected to attend 2 visits (Visit 1 Screen/ Baseline/ Dispense and Visit 2 Week 1 Follow-up/ Exit). The total duration of a subject's participation in the study as well as exposure to the IP is approximately 1 week (6-8 days of lens wear). Subjects will be expected to wear their study contact lenses each day for the typical number of hours they do with their habitual contact lenses. At Visit 2 Follow-up/Exit, subjects will be expected to have worn study lenses between 6 to 10 hours that day at time of Exit Visit. All contact lenses will be prescribed according to subject's manifest refraction and prescription.
Subject population	Habitual spherical soft contact lens wearers aged 18 or older, with at least 3 months of spherical soft contact lens wearing experience, and who wear their habitual contact lenses for at least 5 days per week and at least 10 hours per day. [redacted] Planned number of subjects enrolled/consented: approximately 96 Planned number of completed subjects: 90
Sites and Locations	Planned number of clinical sites: approximately 6 Planned locations (initial list of locations, which may change during start up or conduct according to study needs): US

Key inclusion criteria (See Section 8.1 for a complete list of inclusion criteria)	• Current wearers of commercial spherical soft contact lenses in both eyes with at least 3 months wearing experience, with a minimum wearing time of 5 days per week and 10 hours per day. • Manifest cylinder ≤ 0.75 D in each eye • Best corrected distance VA (as determined by manifest refraction at screening) better than or equal to 20/25 (Snellen) in each eye
Key exclusion criteria (See Section 8.2 for a complete list of exclusion criteria)	• Current or prior habitual DT1 soft contact lens wearers in the past 3 months prior to consent • Monovision contact lens wearers • Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment

Data analysis and sample size justification	**Planned Data Analysis** All effectiveness endpoints will be summarized descriptively according to their respective measurement scales. [redacted] **Sample Size Justification** Formal sample size calculation was not carried out since inferential testing is not being planned.
Associated materials	Lubrication/rewetting drops will not be permitted during study lens wear. However, habitual lubrication/rewetting drop usage is allowed up to 10 minutes prior to study lens insertion and any time after study lens removal. No lubrication/rewetting drop use will be allowed during clinic visits.

Table 3–1 Schedule of Study Procedures and Assessments

	Visit 1 Screen/Baseline/ Dispense	**Visit 2 Week 1 Follow-up/Exit^**	**Unscheduled Visit(s)**	**Early Exit**
Procedure/ Assessment	**Day 1**	**Day 6 + 2 Days**	**N/A**	**N/A**
Informed Consent	X			
Demographics	X			
Medical History and Concomitant Medications	X	X	X	X
Inclusion/Exclusion	X			
[redacted]				
VA with Habitual Correction (Snellen distance, OD, OS)*	X	X	(X)	(X)
Habitual Lens Brand	X			
Manifest Refraction*	X	(X)	(X)	(X)
BCVA with Manifest Refraction (Snellen distance, OD, OS)*	X	(X)	(X)	(X)

	Visit 1 Screen/Baseline/ Dispense	Visit 2 Week 1 Follow-up/Exit^	Unscheduled Visit(s)	Early Exit
Procedure/ Assessment	**Day 1**	**Day 6 + 2 Days**	**N/A**	**N/A**
Biomicroscopy	X	X	X	X
Power Optimization and Dispense Study Lens*	X			
VA with Study Lenses (Snellen distance, OD, OS)	X	X	(X)	X
[redacted]				
Collect worn lenses and dispose		X		X
AEs	X	X	X	X
Device deficiencies	X	X	X	X
Exit form		X		X

*Source only
^Schedule Exit Visit to occur 6 – 10 hours after lens insertion on that day
(X) assessment performed as necessary, e.g., decrease of VA by 2 lines or more with IP

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.

Refer to Appendix A for detailed description of amendments.

5 INTRODUCTION

5.1 Rationale and Background

DT1 soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with nondiseased eyes with up to approximately 1.50 diopters (D) of astigmatism that does not interfere with VA. These lenses are made from a lens material that is 33% water and 67% (delefilcon A) polymer, a silicone containing hydrogel with added phosphatidylcholine. The core lens material containing 33% water transitions through a water gradient to a hydrogel surface layer that exceeds 80% water.

It is estimated that soft contact lenses account for 87% of lens fits in 2019. Moreover, almost 45% of soft contact lenses were prescribed in a daily disposable modality. DT1 soft contact lenses were introduced as a unique dual technology that combines a low water content silicone hydrogel core, to achieve optimal oxygen supply, with a high water content hydrogel surface, to provide a highly lubricious, wettable lens. Previous studies support the hypothesis that Water Gradient Technology in DT1 soft contact lenses produces desirable clinical performance and subjective acceptance.

5.2 Purpose of the Study

The purpose of this study is to assess the clinical performance of DT1 soft contact lenses over approximately 1 week of daily wear. [redacted] The endpoints for this study were selected to fulfil the primary [redacted] objectives of the study. Procedures for measurement of these endpoints were selected based on common practice for these assessments.

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

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

5.3 Risks and Benefits

The clinical investigation process risks are managed through appropriate training and monitoring according to the protocol-specific monitoring plan. Investigational device risks,

including risks associated with use of device and methods and procedures for application of device, are defined in the IB and/or product labeling and are managed through review of safety assessments outlined in this protocol.

Contact lenses may offer improved peripheral vision and the convenience of not wearing spectacles. Material properties and design characteristics of the contact lens in development are features consistent with successful contact lens wear.

The test products are for daily wear use under a daily disposable wear modality; further details on any known potential risks and benefits can be found in the package insert. The test products are not intended for use with a cleaning/disinfecting solution, and the biocompatibility with lens care solutions and any associated clinical effects are unknown.

A summary of the known potential risks and benefits associated with DT1 soft contact lenses can be found in the package insert. Risks are minimized by compliance with the eligibility criteria and study procedures, and through close supervision by a licensed clinician during exposure to the study lenses.

There may also be unknown risks to use of DT1 soft contact lenses. Any risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria, study procedures, and clinical oversight and monitoring.

Refer to the product label for additional information.

6 STUDY OBJECTIVES

6.1 Primary Objective(s)

Table 6–1 Primary Objective(s)

Objective(s)	Endpoint(s)
To evaluate distance VA of the DT1 soft contact lenses over approximately 1 week of wear	Distance VA (Snellen) with study lenses at Week 1

6.2 Secondary Objective(s)

N/A

6.4 Safety Objective(s)

Table 6–3 Safety Objective(s)

Objective(s)	Endpoint(s)
To describe the safety profile of the test lenses	• AEs • Biomicroscopy findings • Device deficiencies

7 INVESTIGATIONAL PLAN

7.1 Study Design

This is a prospective, interventional, nonrandomized, single-arm, subject-masked, multicenter, daily wear clinical study in the US assessing clinical performance of DT1 soft contact lenses. Interim analysis will not be performed.

The total expected duration of a subject's participation is approximately 1 week with approximately 6-8 days of lens wear. Subjects will be expected to attend 2 office visits, Visit 1 Screen/Baseline/Dispense and Visit 2 Week 1/Follow-up/Exit. [redacted] The study is expected to be completed in approximately 1 month.

7.2 Rationale for Study Design

[redacted] The study will include only those subjects who are current wearers of spherical soft contact lenses in both eyes with at least 3 months wearing experience, with a minimum wearing time of 5 days per week and 10 hours per day. [redacted] Furthermore, the subjects will not be permitted to use lubrication/rewetting drops during lens wear as this may confound the primary effectiveness endpoint. The study will exclude any current or prior habitual soft contact lens wearers who wore DT1 soft contact lenses in the past 3 months prior to consent in order to reduce potential bias of wearers to their habitual contact lenses. The study will also exclude subjects who are monovision contact lens or multifocal contact lens wearers.

7.3 Rationale for Duration of Treatment/Follow-Up

The duration of use of the product is in accordance with product labeling. Subjects will wear study lens bilaterally for approximately 1 week in a daily disposable modality. The lenses will be over-labelled and provided by a qualified study staff member in such a manner that the subject remains masked to the lens type. The primary endpoint [redacted] endpoints will be assessed at Visit 1 Screen/ Baseline/ Dispense and Visit 2 Week 1 Follow-up/ Exit or Early Exit. [redacted]

7.4 Data Monitoring Committee

N/A

8 STUDY POPULATION

The study population consists of male and female subjects (18 years or older) with a diagnosis of refractive ametropia (myopia and hyperopia). It is aimed to enroll (consent) approximately 96 subjects in approximately 6 sites throughout the United States, [redacted] Estimated time needed to recruit subjects for the study is approximately 3 weeks; however, unanticipated circumstances may shorten or lengthen this time and would not require amendment of this protocol. Because a 3% screening failure rate is expected, approximately 96 subjects are expected to be enrolled.

Sites will be encouraged to enroll subjects that wore habitual lenses made from a variety of lens material (e.g., verofilcon A, senofilcon A, nesofilcon A).

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 able to understand and sign an IRB/IEC approved ICF.
2. Subject must be willing and able to attend all scheduled study visits as required per protocol.
3. Subject must be at least 18 years of age.
4. Current wearers of commercial spherical soft contact lenses in both eyes with at least 3 months wearing experience, with a minimum wearing time of 5 days per week and 10 hours per day.
5. Manifest cylinder ≤ 0.75 D in each eye.
6. Best corrected distance VA (as determined by manifest refraction at screening) better than or equal to 20/25 (Snellen) in each eye.

7. Able to wear contact lenses within a range of sphere power -1.00 to -6.00 D in 0.25 D step and willing and able to wear the study lenses for the full duration of the study.

8. Subject must be willing to stop wearing their habitual contact lenses for the duration of study participation.

9. Subject must possess spectacles and be willing to wear habitual spectacles for vision correction when study lenses are not worn, as needed for the duration of study participation.

8.2 Exclusion Criteria

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

1. Any anterior segment infection, inflammation, or abnormality or disease (including systemic) that contraindicates contact lens wear, as determined by the investigator.

2. Any use of systemic or ocular medications for which contact lens wear could be contraindicated, as determined by the investigator.

3. History of refractive surgery or plan to have refractive surgery during the study or irregular cornea in either eye.

4. Ocular or intraocular surgery (excluding placement of punctal plugs) within the previous 12 months or planned during the study.

5. Biomicroscopy findings at screening that are moderate (Grade 3) or higher and/or corneal vascularization that is mild (Grade 2) or higher; presence of corneal infiltrates.

6. Current or history of pathologically dry eye in either eye that, in the opinion of the investigator, would preclude contact lens wear.

7. Current or history of herpetic keratitis in either eye.

8. Eye injury in either eye within 12 weeks immediately prior to enrollment for this trial.

9. Current or history of intolerance, hypersensitivity, or allergy to any component of the study product.

10. Any use of topical ocular medications, artificial tears, or rewetting drops that would require instillation during contact lens wear.

[redacted]

12. Participation of the subject in a clinical trial within the previous 30 days or currently enrolled in any clinical trial.

13. Monovision contact lens wearers.

14. Current or prior habitual DT1 soft contact lens wearers in the past 3 months prior to consent.

15. Wearing habitual contact lenses in an extended wear modality (routinely sleeping in lenses for at least 1 night per week) over the last 3 months prior to enrollment.

8.3 Rescreening of Subjects

Rescreening of subjects is not allowed in this study.

9 TREATMENTS ADMINISTERED

9.1 Investigational Product(s)

Test Product(s):	DAILIES TOTAL1 spherical soft contact lenses
Comparator Product(s) (If applicable):	N/A

Table 9–1 Test Product

Test Product	DAILIES TOTAL1 spherical soft contact lenses (DT1; [redacted])
Manufacturer	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099 USA
Indication for use and intended	The intended use of this product is for vision correction.

purpose in the current study	
Product description and parameters available for this study	• Material: delefilcon A • Water content: 33% core • Power range: -1.00 to -6.00 D in 0.25 D step • Base curve (mm): 8.5 • Diameter (mm):14.1
Formulation	• Refer to package insert

Usage	• Wear:
	  o Daily Wear
	  o Bilateral
	• Replacement period: Daily Disposable
	• Exposure: Typical contact lens wearing hours each day for a period of 6 to 8 days
	• Lens Care: N/A

Number/Amount of product to be provided to the subject	At dispense visit, sites will ensure that subjects are given adequate lenses to last the entire study. Spare lenses will be provided to the subject.
Packaging description	Blister foil pack
Labeling description	Lens foil label includes: • lens identifier • base curve • diameter • packing solution • power • lot number • expiration date • LID # • content statement • investigational device statement • sponsor information Lens inventory will be provided in packages and identified with the following: • a color-coded label stating the protocol number

	• LID Number • power • an investigational use only statement • handling unit/tracking number
Storage conditions	Lens to be stored at room temperature.
Supply	• Fitting sets will be provided by the sponsor before the start of the study to be used during Visit 1. Fitting sets will include sphere powers ranging from -1.00 to -6.00 D, in -0.25 D steps. • Small inventories of each power will be provided for dispense to subjects at Visit 1. If needed, additional IP can be ordered and provided upon request. Refer to the MOP for a detailed description.

9.2 Other Medical Device or Medication Specified for Use During the Study

No other medical devices or medications are required to be used in conjunction with the treatments during the clinical study.

9.3 Treatment Assignment / Randomization

Enrolled subjects that meet the inclusion/exclusion criteria will proceed with the study and be dispensed study lens.

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

Randomization is not applicable for this single product study.

9.4 Treatment masking

This study is subject-masked, with all qualified subjects receiving study product. All members associated with the study (at the site and the study sponsor) are unmasked to the assigned treatment.

9.5 Accountability Procedures

Upon receipt of the IPs, the investigator or delegate must conduct an inventory. During the study, investigator or designated study staff must provide the IPs to the subjects. 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.

The investigator should make every effort to collect unused lenses, foils, and supplies from subjects.

It is the investigator's responsibility to ensure that:

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

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

9.6 Changes to concomitant medications, treatments/ procedures

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

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

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

10 STUDY PROCEDURES AND ASSESSMENTS

10.1 Informed Consent and Screening

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

The investigator or delegate must provide a copy of the signed document to the subject and place the original signed document in the subject's chart, or provide documentation as required by local regulations.

10.2 Description of Study Procedures and Assessments

Study-specific procedures and assessments described here may include standard of care; other standard of care procedures performed in the clinical management of the subject are not excluded.

Detailed descriptions of assessments and procedures are provided in the MOP. The investigator is responsible for ensuring responsibilities for all procedures and assessments are delegated to appropriately qualified site personnel.

10.2.1 Demographics

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

10.2.2 Medical History and Concomitant Medications

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. To be completed at all visits.

Medical History and Concomitant Medications will be collected in the eCRF as outlined in the MOP.

10.2.3 Investigational Product compliance

Review subject compliance with the IP usage and adjunct product usage and collect all unused study IPs.

10.2.4 Adverse Event Collection: Safety Assessment

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

10.2.5 Slit Lamp Biomicroscopy: Safety Assessment

SLE of the cornea, adnexa, and anterior segment of the eye 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 since the previous visit. Requirements for reporting device deficiencies in the study can be found in Section 11.

10.3 Unscheduled Visits

If a subject visit occurs between any regularly scheduled visit and the visit is conducted by study personnel, this visit must be documented as an Unscheduled Visit. If the subject seeks medical attention outside the clinic (for example, at an Emergency Room) or at the clinic but is seen by nonstudy personnel, the investigator is to capture AE-related information on the AE form upon becoming aware.

During all unscheduled visits, the investigator must conduct the following procedures:

- Collect AE information
- Record changes in medical condition or concomitant medication
- Collect device deficiencies information

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 and Section 10.4.3, as possible.

10.4 Discontinued Subjects

10.4.1 Screen Failures

Subjects who were excluded from the study after signing the informed consent and prior to 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 dispensing of study product.

Subject numbers of discontinued subjects must not be re-used (i.e., subject replacement is not allowed).

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 and Section 10.4.3, 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

N/A; Subjects will not be followed after discontinuation of study treatment. Subjects discontinued from study product will be discontinued from the study. Subject should undergo an Early Exit Visit.

10.5 Clinical Study Termination

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

If the clinical study is prematurely terminated or suspended by the study sponsor:

- The study sponsor must:
    - Immediately notify the investigator(s) and subsequently provide instructions for study termination.
    - Inform the investigator and the regulatory authorities of the termination/suspension and the reason(s) for the termination/suspension.
- The investigator must:
    - Promptly notify the IRB/IEC of the termination or suspension and of the reasons.
    - Provide subjects with recommendations for poststudy 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. Refer to the Glossary of Terms and figures below for categories of AEs and SAEs.

Figure 11-1 Categorization of All Adverse Events

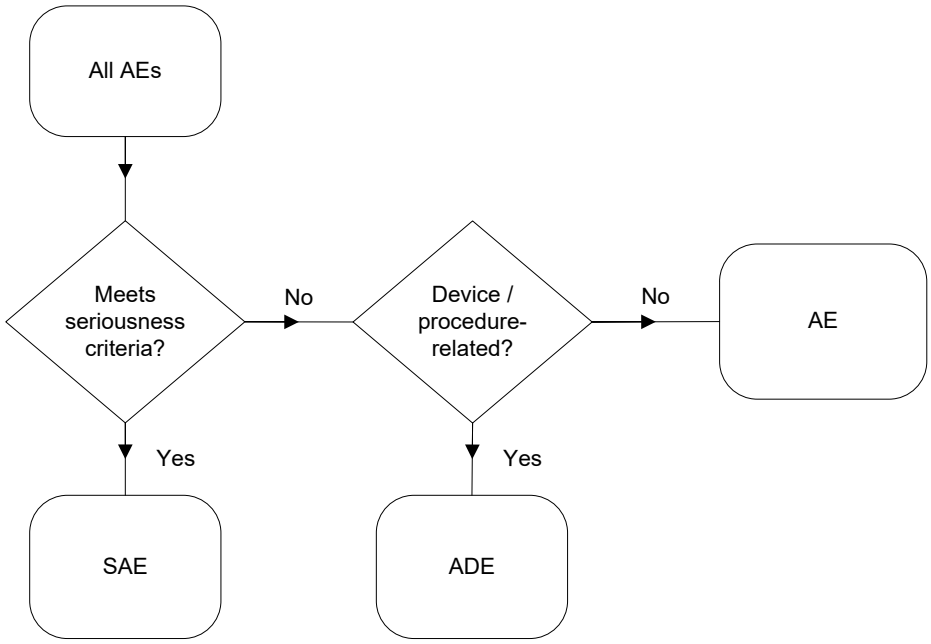
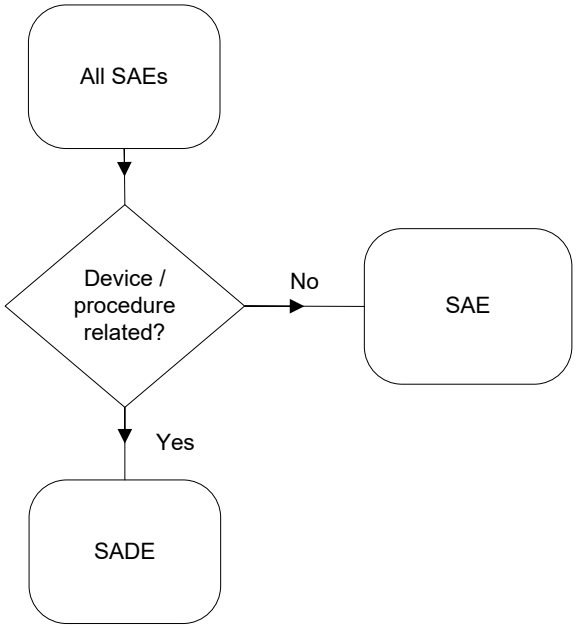


Figure 11-2 Categorization of All Serious Adverse Events



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 shown below and report as applicable:

- "Have you had any health problems since your last study visit?"
- "Have there been any changes in the medicines you take because of a new health issue or worsening of an existing health issue since your last study visit?"

In addition, changes in biomicroscopy findings [redacted] evaluated during the study are to be reviewed by the investigator. Any untoward (unfavorable and unintended) change in a biomicroscopy finding [redacted] 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.

Responses that are less than favorable on the grading scale should be evaluated by the investigator to indicate whether an AE occurred.

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 (i.e., before informed consent is signed) are not considered AEs in the study and should be recorded in the medical history section of the eCRF.

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

For each recorded event, the ADE and SAE documentation must include: the date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness and causality. In addition, the investigator must document all device deficiencies reported or observed with test and comparator products on the device deficiency eCRF. The site must submit all available information on ADEs, SAEs, and device deficiencies to the study sponsor immediately as follows:

- All SAEs must be reported immediately (within 24 hours) of the investigator's or site's awareness.
- ADEs that do not meet seriousness criteria and device deficiencies must be reported

within 10 calendar days of the investigator's or site's awareness.

- 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 *SAE and ADE* eCRF.

Note: Should the EDC system become nonoperational, the site must complete the appropriate paper *SAE and ADE* and/or device deficiency form. [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 on medical judgment with consideration of any subjective symptom(s), as defined below:

Intensity (Severity)

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

For every AE in the study, the investigator must assess the causality (related or not related to the medical device or study procedure). An assessment of causality will also be performed by study sponsor utilizing the same definitions, as shown below:

Causality

Related	An AE classified as related may be either definitely related or possibly related where a direct cause and effect relationship with the medical device or study procedure has not been demonstrated, but there is a reasonable possibility that the AE was caused by the medical device or study procedure.
Not Related	An AE classified as not related may either be definitely unrelated or simply unlikely to be related (i.e., 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 nonserious to serious or from unrelated to related.

11.4 Return Product Analysis

Study sponsor representatives and their contact information are provided in the MOP that accompanies this protocol.

[redacted]

11.5 Unmasking of the Study Treatment

Masked information on the identity of the assigned medical device should not be disclosed to subjects during the study (refer to Section 9.4). All members associated with the study (at the site and the study sponsor) are unmasked to the assigned treatment.

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 (i.e., database lock). Any additional data received up to 3 months, after subject has completed the study should be documented and available upon the study sponsor's request.

All complaints received after this time period will be considered and processed as spontaneous (following the postmarket vigilance procedures) and should be communicated to the medical device's manufacturer as per local requirements.

11.7 Pregnancy in the Clinical Study

Women of childbearing potential or women who are pregnant at the time of study entry are not excluded from participation. However, pregnancy should be included in the corresponding eCRF if a woman becomes pregnant (as stated by the subject) during the study. Pregnancy is not reportable as an AE; however, complications may be reportable and will be decided on a case-by-case basis.

12 ANALYSIS PLAN

Continuous variables will be summarized using the number of observations, mean, SD, median, minimum, and maximum, as well as CIs or CLs where applicable. 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.

12.1 Subject Evaluability

Final subject evaluability must be determined prior to locking the database, based upon the DEP.

12.2 Analysis Sets

12.2.1 Safety Analysis Set

Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. As such, the safety analysis set will include all subjects/eyes exposed to the study lenses evaluated in this study. Lenses used for power optimization at Visit 1 are not considered study lenses in this context, as they are not used for intended study treatment. Therefore, any AE or

device deficiency occurring after Informed Consent and prior to the initial exposure to the study lenses under evaluation in this clinical protocol will be listed as pretreatment.

12.2.2 Per Protocol Analysis Set

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

12.3 Demographic and Baseline Characteristics

Demographics and baseline information will be summarized. Frequencies and percentages will be presented for categorical variables such as age group (< 40 years of age, ≥ 40 years of age). Number of observations, mean, SD, median, minimum, and maximum will be presented for continuous variables such as age.

12.4 Effectiveness Analyses

This study defines 1 primary effectiveness endpoint, [redacted]. All effectiveness evaluations will use the safety analysis set as the primary analysis set.

[redacted]

12.4.1 Analysis of Primary Effectiveness Endpoint(s)

The primary objective of this study is to evaluate distance VA of the DT1 soft contact lenses over approximately 1 week of wear.

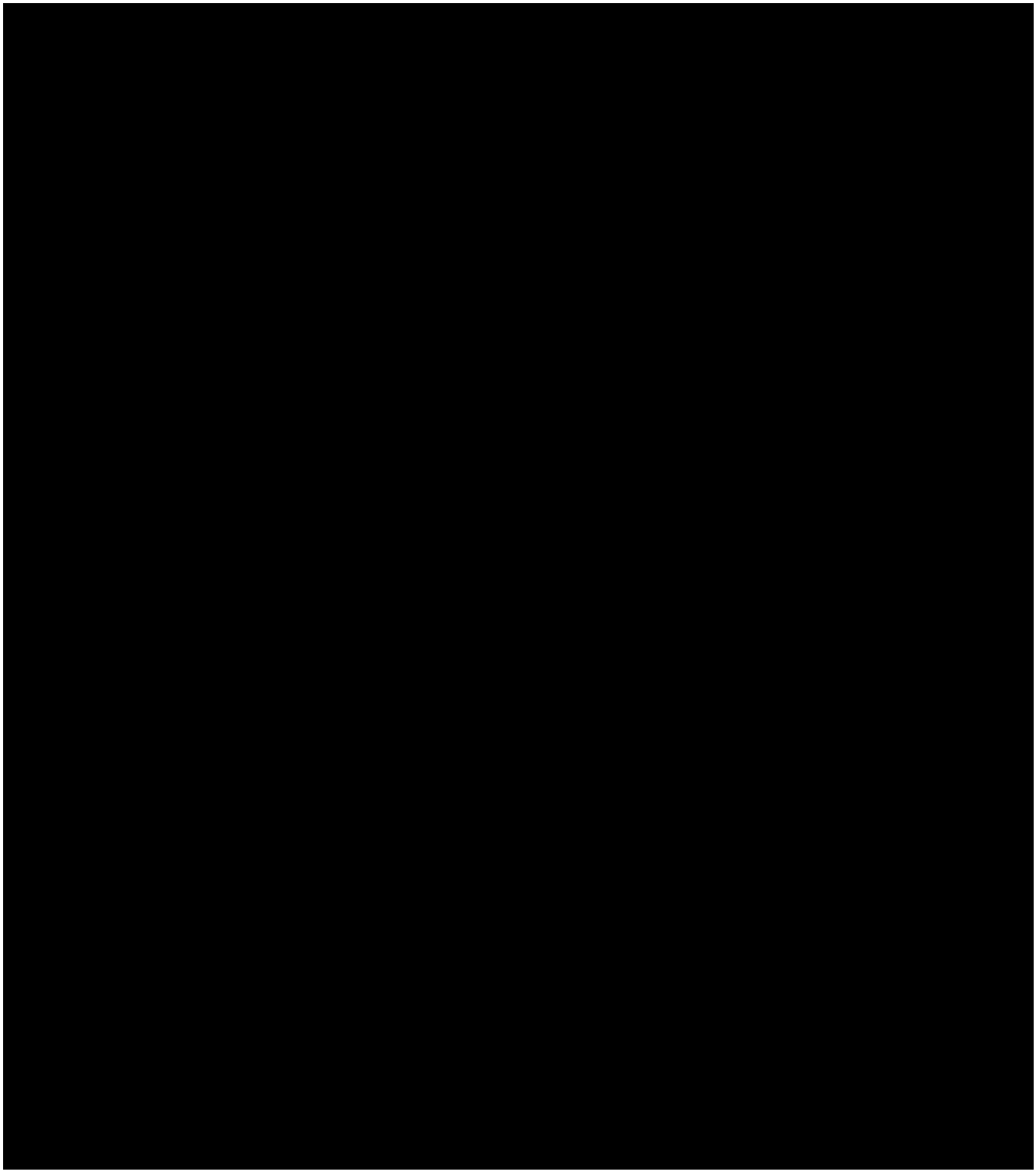
The primary endpoint is distance VA with study lenses at Week 1, collected for each eye, in Snellen.

12.4.1.1 Statistical Hypotheses

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

12.4.1.2 Analysis Methods

Descriptive statistics will be provided as frequency and percentage for each Snellen category. For the converted logMAR values, descriptive statistics will be provided as number of observations, mean, SD, median, minimum, and maximum.



12.5 Handling of Missing Data

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

12.6 Safety Analyses

The safety endpoints are:

- AEs
- Biomicroscopy findings
- Device deficiencies

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

All AEs occurring from the time a subject signs the Informed Consent to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. Descriptive summaries (frequencies and percentages) for ocular and nonocular AEs will be presented by Medical Dictionary for Regulatory Activities Preferred Terms. AEs leading to study discontinuation and SAEs will be identified. Individual subject listings will be provided, as necessary. Individual subject listings will be provided for AEs that occur after signing informed consent but prior to exposure to IP.

Each biomicroscopy parameter will be tabulated by its grade. For each biomicroscopy parameter, counts and percentages of eyes that experience an increase of ≥ 2 grades from baseline (last assessment prior to study lens exposure) to any subsequent visit will be presented. A supportive listing will be generated which will include all biomicroscopy data from all visits for those eyes experiencing the increase.

Two listings for device deficiencies, prior to exposure to study lenses and treatment-emergent, will be provided. Additionally, each device deficiency category will be tabulated.

No inferential testing will be conducted for the safety analyses.

12.7 Interim Analyses and Reporting

There are no plans to conduct an interim analysis and no criteria by which the study would be terminated early based upon statistical determination.

12.8 Sample Size Justification

Although inferential testing is not planned for the primary [redacted], expected precision of the observed results is provided. With a sample size of 90 subjects, degrees of precision achieved with the primary effectiveness endpoint [redacted] are as follows:

Visual acuity

With the assumed standard deviation of 0.08 [redacted] a one-sided 95% CI for the mean of distance VA based on t-statistics will extend 0.015 from the observed mean.

[redacted]

13 DATA HANDLING AND ADMINISTRATIVE REQUIREMENTS

13.1 Subject Confidentiality

The investigator must ensure that the subject's identity is kept confidential 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. The study sponsor may collect a copy of the enrollment log ***without any directly identifying subject information***.

The study sponsor may share patient-level data collected in this trial with qualified researchers to help facilitate product development or enhancements in research that is not

directly related to the study objectives. The Informed Consent explains this to the study subject.

13.2 Completion of Source Documents and Case Report Forms

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

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

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

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

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

Only designated individuals at the site will complete the CRFs. The CRFs must be completed at regular intervals following the clinical study visit schedule. It is expected that all data reported have corresponding entries in the source documents. The principal investigator is responsible for reviewing and certifying that the CRFs are accurate and complete. The only subject identifiers recorded on the CRFs will be subject number, and subject demographic information.

13.3 Data Review and Clarifications

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

13.4 Sponsor and Monitoring Responsibilities

The study sponsor will select principal investigators that are qualified by education, training, and experience to assume responsibility for the proper conduct of this clinical trial.

The study sponsor is financially funding this clinical trial and will compensate the investigator and/or the institution(s) at which the study is conducted in accordance with a signed clinical trial agreement.

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

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

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

13.5 Regulatory Documentation and Records Retention

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

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

13.6 Quality Assurance and Quality Control

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

14 ETHICS

Investigations are conducted in compliance with GCPs; international and national regulations, laws, and guidelines; the conditions of approval imposed by reviewing IRBs/IECs or regulatory authorities; and in accordance with the ethical medical research principles outlined in the Declaration of Helsinki and GCPs outlined within ISO 14155.

- The SOPs of the study sponsor and contract research organizations participating in the conduct of the clinical study and all other applicable regulations shall apply.
- 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. The investigator is not allowed to deviate from the protocol except to protect the rights, safety, and well-being of human subjects under emergency circumstances. Emergency deviations may proceed without prior approval of the sponsor and the IRB/IEC, but shall be documented and reported to the sponsor and the IRB/IEC as soon as possible. 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. Failure to implement identified corrective and preventative actions may result in site closure by the sponsor. Use of waivers to deviate from the clinical protocol is prohibited.

Before clinical study initiation, this protocol, the ICF 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), ICF, assent form (if any), all applicable recruiting materials, written information for subject, and subject compensation programs. The IRB/IEC must be provided with a copy of the Package Insert, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. Any additional requirements imposed by the ethics committee or regulatory authority shall be followed. 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. The obtaining of consent 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 the required 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 ICF. The subject must be provided an opportunity to ask questions of the investigator, and if required by local regulation, other qualified personnel. The investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and sponsor-designated personnel. The investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

The study sponsor assures that the key designs of this protocol will be registered on public databases where required by current regulations, and, as applicable, results will be posted.

15 REFERENCES

15.1 Regulations and Standards

The following references may be applicable in whole or in part for this clinical trial.

- ISO 11980:2012 Ophthalmic optics - Contact lenses and contact lens care products - Guidance for clinical investigations
- EN ISO 14155:2020 - Clinical Investigation of Medical Devices for Human Subjects - Good Clinical Practice
- 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, if applicable

15.2 Scientific and Other References

Not applicable. There are no references.

16 APPENDIX A – Protocol Amendments

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