

Clinical Performance Evaluation of Two Frequent  
Replacement  
Silicone Hydrogel Toric Contact Lenses

STUDY ID

CLN109-C001



PROTOCOL

NCT05959200



**Device Protocol for CLN109-C001**

**Title: Clinical Performance Evaluation of Two Frequent Replacement  
Silicone Hydrogel Toric Contact Lenses**

Protocol Number:	CLN109-C001
Clinical Investigation Type:	Pivotal
Test Product:	Alcon Serafilcon A Toric Contact Lenses (LID226397)
Sponsor Name and Address:	Alcon Research, LLC, and its affiliates (“Alcon”) 6201 South Freeway Fort Worth, Texas 76134-2099
	

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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? <input type="checkbox"/> No <input type="checkbox"/> Yes
Have you ever been involved in a study or other research that was terminated? <input type="checkbox"/> No <input type="checkbox"/> Yes If yes, please explain here:

Principal investigator (PI):

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

Name and professional position:

Address:

Phone Number:

Off-hours Emergency Phone Number:

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## 1 GLOSSARY OF TERMS

Names of Test Product(s)	Throughout this document, test product(s) Alcon Serafilcon A Toric Contact Lenses [REDACTED] will be referred to as LID226397.
Name of Comparator Product(s)	ACUVUE® OASYS for ASTIGMATISM with HYDRACLEAR® PLUS (AOFAHP) contact lenses (senofilcon A)
Adverse Device Effect (ADE)	<p>Adverse event related to the use of an investigational medical device or comparator.</p> <p><i>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.</i></p>
Adverse Event (AE)	<p>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.</p> <p><i>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.</i></p> <p>Requirements for reporting Adverse Events in the study can be found in Section 11.</p>
Anticipated Serious Adverse Device Effect (ASADE)	An effect which by its nature, incidence, severity, or outcome has been identified in the risk assessment.
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



	<p>investigation.</p> <p><i>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.</i></p>
Clinical Investigation Report (CIR) / Clinical Study Report	The document describing the design, execution, statistical analysis, and results of a clinical investigation. The Clinical Investigation Report is synonymous with the Clinical Study Report.
Device Deficiency	<p>Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.</p> <p><i>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.</i></p> <p>Requirements for reporting Device Deficiencies in the study can be found in Section 11.</p>
Enrolled Subject	Any subject who signs an informed consent form for participation in the study.
Point of Enrollment	The time at which, following recruitment and before any clinical investigation-related procedures are undertaken, a subject signs and dates the informed consent form.
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 clinical investigation plan, 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	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 clinical investigation plan (CIP), or investigator’s brochure (IB).
Noninterventional Study	Clinical investigation that draws inferences about the possible effect of an intervention on subjects, but the investigator has not assigned subjects into intervention groups based on a protocol and has not made any attempts to collect data on variables beyond those available throughout the course of normal clinical practice and burden to the subject.  <i>NOTE: The term “noninterventional” is synonymous with “observational.”</i>
Nonserious Adverse Event	Adverse event that does not meet the criteria for a serious adverse event.
Postapproval Study (PAS)	A study required by the FDA or other health authority at the time of approval of a premarket approval (PMA), humanitarian device exemption (HDE), or product development protocol (PDP) application. Postapproval studies are conducted to provide patients, health care professionals, the device industry, the FDA and other stakeholder’s information on the continued safety and effectiveness (or continued probable benefit, in the case of an HDE) 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.

	<p>A post-marketing study falls either within the definitions of an interventional or a noninterventional study and may also fall within the definition of a post-approval study.</p>
Product Complaint	<p>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.</p>
Randomized Subject	<p>Any subject who is assigned a randomized treatment.</p>
Serious Adverse Device Effect (SADE)	<p>Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.</p>
Serious Adverse Event (SAE)	<p>Adverse event that led to any of the following:</p> <ul style="list-style-type: none"><li>• Death.</li><li>• A serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:<ol style="list-style-type: none"><li>a) a life-threatening illness or injury <i>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.</i></li><li>b) any potentially sight-threatening event or permanent impairment to a body structure or a body function including chronic diseases.</li><li>c) inpatient hospitalization or prolonged hospitalization.</li><li>d) a medical or surgical intervention to prevent a) or b).</li><li>e) any indirect harm as a consequence of incorrect diagnostic test results when used within</li></ol></li></ul>

	<p>manufacturer's instructions for use.</p> <ul style="list-style-type: none"><li>• Fetal distress, fetal death, congenital abnormality or birth defect including physical or mental impairment.</li></ul> <p><i>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.</i></p> <p><i>Refer to Section 11 for additional SAEs.</i></p>
Serious Public Health Threat	<p>Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users, or other persons, and that requires prompt remedial action for other subjects, users, or other persons.</p> <p><i>Note: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.</i></p>
Significant Nonserious Adverse Event	<p>A symptomatic, device-related, nonsight-threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks.</p> <p><i>Refer to Section 11 for additional Significant Nonserious AEs.</i></p>
Study Start	<p>The start of the study is considered to coincide with the enrollment of the first patient.</p>
Study Completion	<p>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.</p>
Unanticipated Serious Adverse Device Effect (USADE)	<p>Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the risk assessment.</p>

Use Error	<p>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.</p> <p><i>Note:</i></p> <ul style="list-style-type: none"><li><i>a) Use error includes the inability of the user to complete a task.</i></li><li><i>b) Use errors can result from a mismatch between the characteristics of the user, user interface, task, or use environment.</i></li><li><i>c) Users might be aware or unaware that a use error has occurred.</i></li><li><i>d) An unexpected physiological response of the patient is not by itself considered a use error.</i></li><li><i>e) A malfunction of a medical device that causes an unexpected result is not considered a use error.”</i></li></ul>
Vulnerable Subject	<p>An individual who is unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of retaliatory response.</p>

## 2 LIST OF ACRONYMS AND ABBREVIATIONS

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

<b>Abbreviation</b>	<b>Definition</b>
ADE	Adverse device effect
AE	Adverse event
AOfAHP	ACUVUE OASYS for ASTIGMATISM with HYDRACLEAR PLUS contact lenses
ASADE	Anticipated serious adverse device effect
BCVA	Best corrected visual acuity
CFR	Code of Federal Regulations
CI	Confidence interval
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
COL	Clinical Operation Lead
CRF	Case report form
CSM	Clinical Site Manager
CTT	Clinical Trial Team
D	Diopter
D/C	Discontinue
DEP	Deviations and evaluability plan
ECP	Eye Care Practitioner
EDC	Electronic Data Capture
eCRF	Electronic case report form
FAS	Full analysis set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GPCMS	Global Product Complaint Management System
HDE	Humanitarian Device Exemption
█	█
hrs	Hours
IB	Investigator’s brochure
ICF	Informed consent form
IEC	Independent ethics committee
IP	Investigational product
IRB	Institutional review board
ISO	International Organization for Standardization
█	█
LogMAR	Logarithm of the minimum angle of resolution
min	Minutes
MOP	Manual of procedures
█	█
N/A	Not applicable
OD	Right Eye

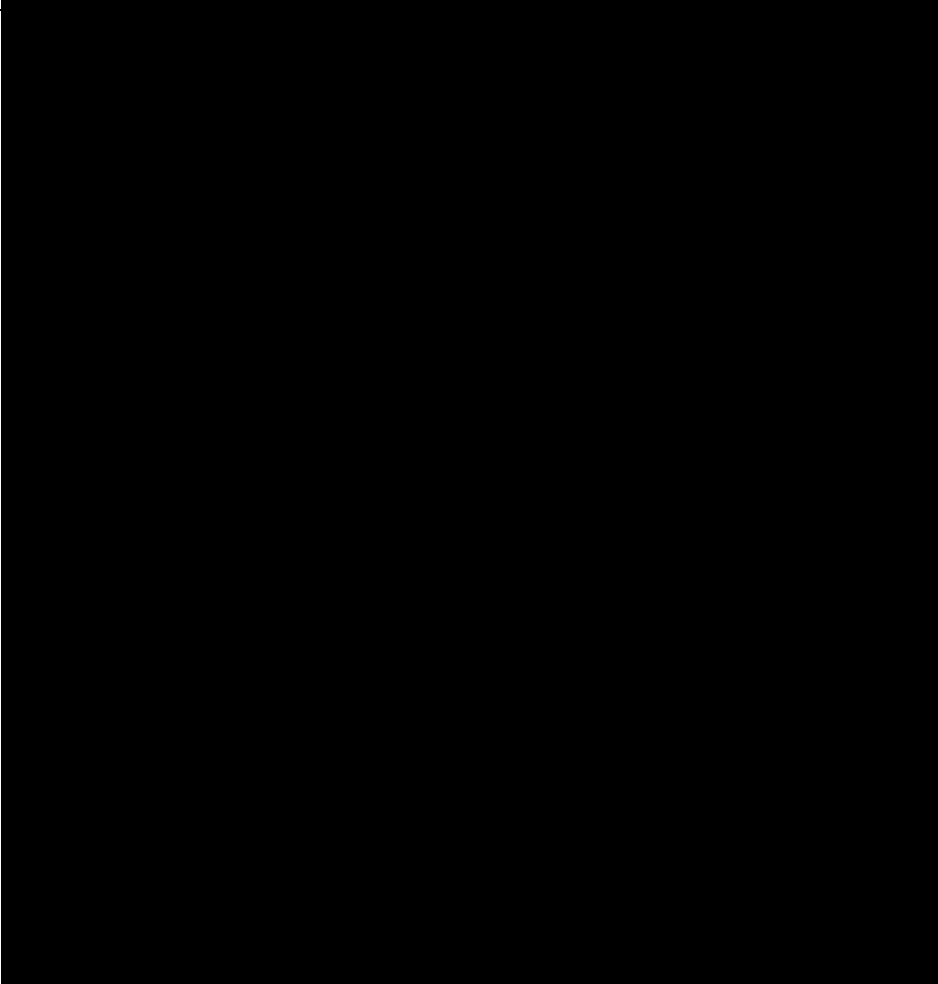


<b>Abbreviation</b>	<b>Definition</b>
OS	Left Eye
OU	Both Eye
PAS	Postapproval Study
PDP	Product development protocol
PI	Principal investigator
PMA	Premarket approval
PP	Per protocol
SAE	Serious adverse effect
SADE	Serious adverse device event
SD	Standard Deviation
SiHy	Silicone Hydrogel
SLE	Slit lamp examination
SOP	Standard operating procedure
US	United States
USADE	Unanticipated serious adverse device effect
UV	Ultraviolet
VA	Visual acuity
████	████████████████████

### 3 PROTOCOL SUMMARY

<b>Investigational product type</b>	Device
<b>Study type</b>	Interventional
<b>Investigational products</b>	Test Product: LID226397 Comparator Product: ACUVUE OASYS for ASTIGMATISM with HYDRACLEAR PLUS (AOFAHP) contact lenses
<b>Purpose and Scientific Rationale for the Study</b>	<ul style="list-style-type: none"><li>For performance confirmation purposes, the study will evaluate the on-eye clinical performance of investigational LID226397 contact lenses to support contact lens product development/launch and to evaluate product performance in the intended population. [REDACTED]</li></ul>
<b>Brief Summary of the Protocol</b>	The overall objective of this study aims to evaluate the on-eye toric clinical performance of investigational LID226397 contact lenses and AOFAHP contact lenses in a daily wear dispensing trial. Volunteer subjects aged 18 or over who are habitual soft toric contact lens wearers, have at least 3 months of contact lens wearing experience (excluding AOFAHP habitual lens wearers and habitual daily disposable lens wearers), and who wear their habitual lenses at least 5 days per week and at least 10 hours per day, will be included. This is a prospective, randomized [REDACTED] bilateral, crossover, controlled, double-masked, multicenter clinical study.
<b>Objective(s)</b>	The <b>primary objective</b> is to evaluate the percentage of LID226397 contact lenses with axis orientation within $\pm 30$ degrees from the 90° axis (ideal location), 10 min after lens insertion at dispense visit. [REDACTED]



	<p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>The <b>safety objective</b> is to describe the safety profile of the study products.</p>
<b>Endpoint(s)</b>	<p>Primary Effectiveness</p> <ul style="list-style-type: none"><li>• Percent of lenses with axis orientation within <math>\pm 30</math> degrees from the intended axis, 10 min after insertion</li></ul> <p>[REDACTED]</p>

	
<b>Assessment(s)</b>	<p data-bbox="565 1186 649 1222">Safety</p> <ul data-bbox="613 1249 971 1354" style="list-style-type: none"><li>• Adverse events</li><li>• Biomicroscopy findings</li><li>• Device deficiencies</li></ul> <p data-bbox="565 1369 743 1402"><b>Effectiveness</b></p> <ul data-bbox="613 1444 1388 1522" style="list-style-type: none"><li>• Axis orientation (degrees, as deviation from 90° axis), at  10 min after lens insertion</li></ul> 



	<div data-bbox="553 182 1357 514" style="background-color: black; width: 100%; height: 100%;"></div> <p><b>Safety</b></p> <ul style="list-style-type: none"><li>• Adverse events</li><li>• Biomicroscopy</li><li>• Device deficiencies</li></ul> <div data-bbox="527 884 938 1003" style="background-color: black; width: 100%; height: 100%;"></div>
<p><b>Study Design</b></p>	<p>This will be a prospective, randomized [REDACTED], bilateral, crossover, controlled, double-masked, multicenter clinical study.</p> <p>Subjects will be expected to attend 7 visits including screening visit. The total duration of a subject’s participation in the study will be approximately 40 days. Subjects will be exposed to each lens for bilateral wear for approximately 14 days and will be followed up weekly. [REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>Subjects will be [REDACTED] and randomized 1:1 to one of two sequences:</p> <p>Sequence 1 = LID226397/AOfAHP Sequence 2 = AOfAHP/LID226397</p>
<p><b>Subject population</b></p>	<p>Volunteer subjects aged 18 or over who are habitual soft toric contact lens wearers (excluding AOfAHP habitual lens wearers and habitual daily disposable lens wearers) with normal eyes (other than correction for refractive error). Subjects should have</p>



	<p>██████████ only descriptive statistics will be provided. ██████████ ██ ██ No inferential testing will be performed.</p> 
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	<p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p> <p>[REDACTED]</p>
<b>Associated materials</b>	<p>The use of marketed rewetting drops will not be permitted during clinical study.</p> <p>Subjects will be provided with CLEAR CARE® Cleaning &amp; Disinfecting Solution to use with the study lenses.</p> <p>LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.</p>

**Table 3–1 Schedule of Study Procedures and Assessments**

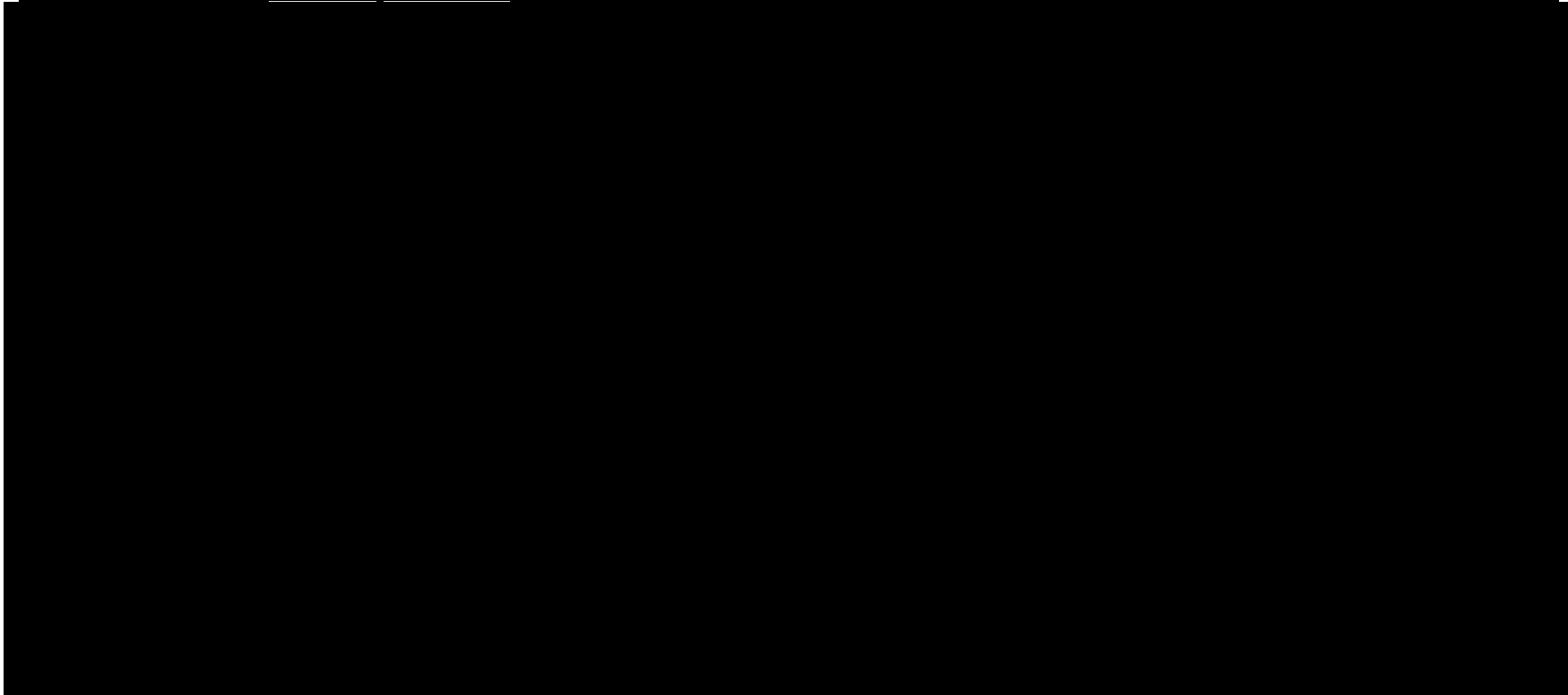
Procedure/ Assessment	Pre- screening	Visit 1 Screening/ Baseline/ Trial fit	Lens 1 (Period 1)				Lens 2 (Period 2)			Early Exit	Unscheduled Visit
			Visit 2 Dispense Lens 1 (3 - 4 days after Visit 1 [Washout period with habitual spectacles only after Visit 1])	Visit 3 Week 1 Follow- up Lens 1 (7 -0/+1 days after Visit 2)	Visit 4 Week 2 Follow- up Lens 1 (7 -0/+1 days after Visit 3)	Visit 5 Dispense Lens 2 (2 [at least 48 hours] - 4 days after Visit 4 [Washout period with habitual spectacles only after Visit 4])	Visit 6 Week 1 Follow- up Lens 2 (7 -0/+1 days after Visit 5)	Visit 7 Week 2 Follow- up Lens 2/Exit (7 -0/+1 days after Visit 6)			
Informed Consent		X									
Demographics		X									
Medical History		X	X	X	X	X	X	X	X	X	X
Concomitant Medications		X	X	X	X	X	X	X	X	X	X
Inclusion/ Exclusion		X									
Habitual lens (brand, lens power*, lens care*)		X									
Habitual Lens wear & Drop Usage*		X									
Keratometry (OD, OS)		X									
VA w/ habitual correction <sup>+</sup> (OD, OS, logMAR distance)*		X						X	X	(X)	
Manifest refraction*		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
BCVA* (OD, OS, logMAR distance		X	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)



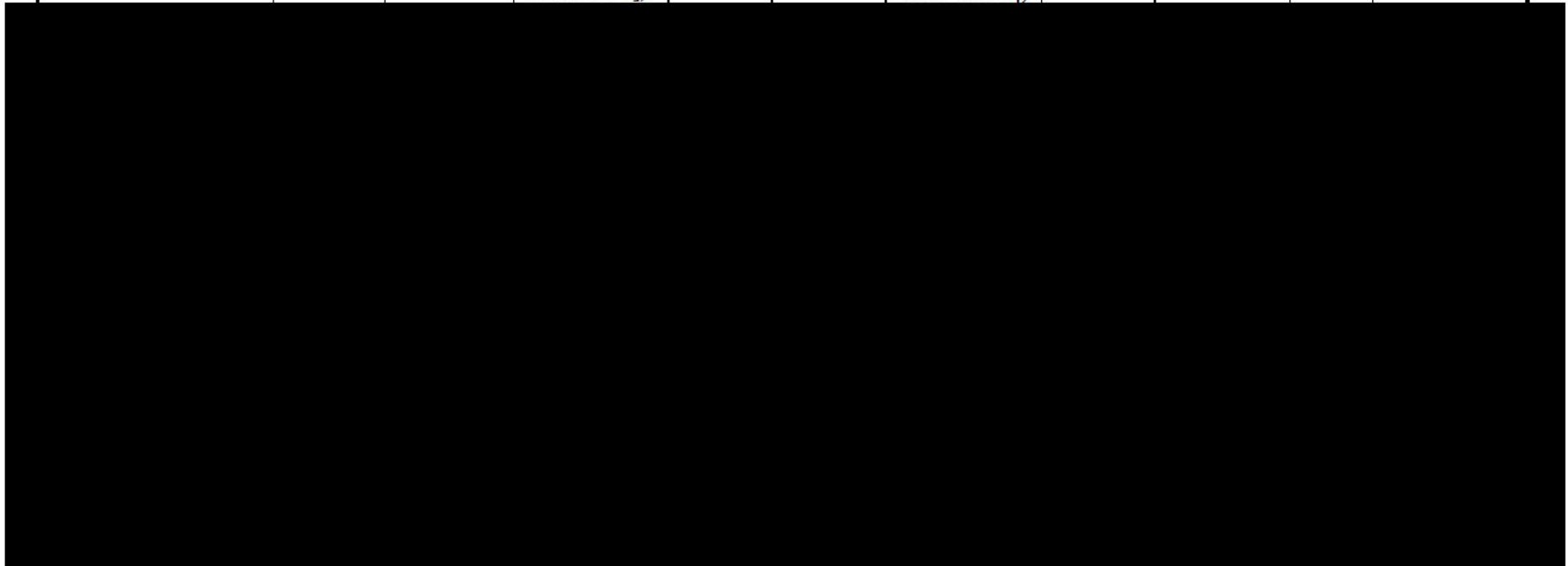
Procedure/ Assessment	Pre- screening	Visit 1 Screening/ Baseline/ Trial fit	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
			Visit 2 Dispense Lens 1 (3 - 4 days after Visit 1 [Washout period with habitual spectacles only after Visit 1])	Visit 3 Week 1 Follow- up Lens 1 (7 -0/+1 days after Visit 2)	Visit 4 Week 2 Follow- up Lens 1 (7 -0/+1 days after Visit 3)	Visit 5 Dispense Lens 2 (2 [at least 48 hours] - 4 days after Visit 4 [Washout period with habitual spectacles only after Visit 4])	Visit 6 Week 1 Follow- up Lens 2 (7 -0/+1 days after Visit 5)	Visit 7 Week 2 Follow- up Lens 2/Exit (7 -0/+1 days after Visit 6)		
with manifest refraction)										
Biomicroscopy		X	X	X	X	X	X	X	X	X
Randomization		X								
Fitting of investigational products (trial assessments): (Test and Comparator)* • VA (OD, OS, logMAR, distance) • Lens movement (overall fit- primary and peripheral gazes) • Lens position (centration; decentration – direction and amount)		X								
Study lens power to be dispensed		X								

Procedure/ Assessment	Pre- screening	Visit 1 Screening/ Baseline/ Trial fit	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
			Visit 2 Dispense Lens 1 (3 - 4 days after Visit 1 [Washout period with habitual spectacles only after Visit 1])	Visit 3 Week 1 Follow- up Lens 1 (7 -0/+1 days after Visit 2)	Visit 4 Week 2 Follow- up Lens 1 (7 -0/+1 days after Visit 3)	Visit 5 Dispense Lens 2 (2 [at least 48 hours] - 4 days after Visit 4 [Washout period with habitual spectacles only after Visit 4])	Visit 6 Week 1 Follow- up Lens 2 (7 -0/+1 days after Visit 5)	Visit 7 Week 2 Follow- up Lens 2/Exit (7 -0/+1 days after Visit 6)		
Dispense study lenses**			X	X		X	X			(X)
Axis orientation at ██████████ ██████ 10 min after lens insertion			X			X				

			Lens 1 (Period 1)			Lens 2 (Period 2)				
Procedure/ Assessment	Pre- screening	Visit 1 Screening/ Baseline/ Trial fit	Visit 2 Dispense Lens 1 (3 - 4 days after Visit 1 [Washout period with habitual spectacles only after Visit 1])	Visit 3 Week 1 Follow- up Lens 1 (7 -0/+1 days after Visit 2)	Visit 4 Week 2 Follow- up Lens 1 (7 -0/+1 days after Visit 3)	Visit 5 Dispense Lens 2 (2 [at least 48 hours] - 4 days after Visit 4 [Washout period with habitual spectacles only after Visit 4])	Visit 6 Week 1 Follow- up Lens 2 (7 -0/+1 days after Visit 5)	Visit 7 Week 2 Follow- up Lens 2/Exit (7 -0/+1 days after Visit 6)	Early Exit	Unscheduled Visit



Procedure/ Assessment	Pre- screening	Visit 1 Screening/ Baseline/ Trial fit	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
			Visit 2 Dispense Lens 1 (3 - 4 days after Visit 1 [Washout period with habitual spectacles only after Visit 1])	Visit 3 Week 1 Follow- up Lens 1 (7 -0/+1 days after Visit 2)	Visit 4 Week 2 Follow- up Lens 1 (7 -0/+1 days after Visit 3)	Visit 5 Dispense Lens 2 (2 [at least 48 hours] - 4 days after Visit 4 [Washout period with habitual spectacles only after Visit 4])	Visit 6 Week 1 Follow- up Lens 2 (7 -0/+1 days after Visit 5)	Visit 7 Week 2 Follow- up Lens 2/Exit (7 -0/+1 days after Visit 6)		



Lens wear calendar*			X (Dispense Calendar)	X (Review Calendar)	X (Collect & Review)	X (Dispense Calendar)	X (Review Calendar)	X (Collect & Review Calendar)	X (Collect & Review)	X (Review Calendar)
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Procedure/ Assessment	Pre- screening	Visit 1 Screening/ Baseline/ Trial fit	Lens 1 (Period 1)			Lens 2 (Period 2)			Early Exit	Unscheduled Visit
			Visit 2 Dispense Lens 1 (3 - 4 days after Visit 1 [Washout period with habitual spectacles only after Visit 1])	Visit 3 Week 1 Follow- up Lens 1 (7 -0/+1 days after Visit 2)	Visit 4 Week 2 Follow- up Lens 1 (7 -0/+1 days after Visit 3)	Visit 5 Dispense Lens 2 (2 [at least 48 hours] - 4 days after Visit 4 [Washout period with habitual spectacles only after Visit 4])	Visit 6 Week 1 Follow- up Lens 2 (7 -0/+1 days after Visit 5)	Visit 7 Week 2 Follow- up Lens 2/Exit (7 -0/+1 days after Visit 6)		
					Calendar )				Calen dar)	
Collect worn study lenses*				X	X		X	X	X	(X)
AEs		X	X	X	X	X	X	X	X	X
Device deficiencies		X	X	X	X	X	X	X	X	X
Exit Form		(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)

(X) Assessment performed as necessary, e.g., decrease of VA by 2 lines or more with investigational product (IP)

\* Source only

+ Subject must have visual acuity with habitual correction of 0.30 logMAR (20/40) or better OU in order to leave the office





## **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.



## **5 INTRODUCTION**

### **5.1 Rationale and Background**

LID226397 contact lenses are indicated for the optical correction of refractive ametropia (myopia or hyperopia, with astigmatism) in persons with nondiseased eyes. The LID226397 contact lenses are a frequent replacement silicone hydrogel (SiHy) contact lenses being developed in an effort to maintain prolonged on-eye performance by utilizing an inherently wettable core lens material. These SiHy lenses have a water content of 55%, contain a UV blocker, High Energy Visible Light (HEVL) filter, and light blue handling tint. LID226397 contact lenses use the Precision Balance 8|4™ ballasted toric design concept, successfully

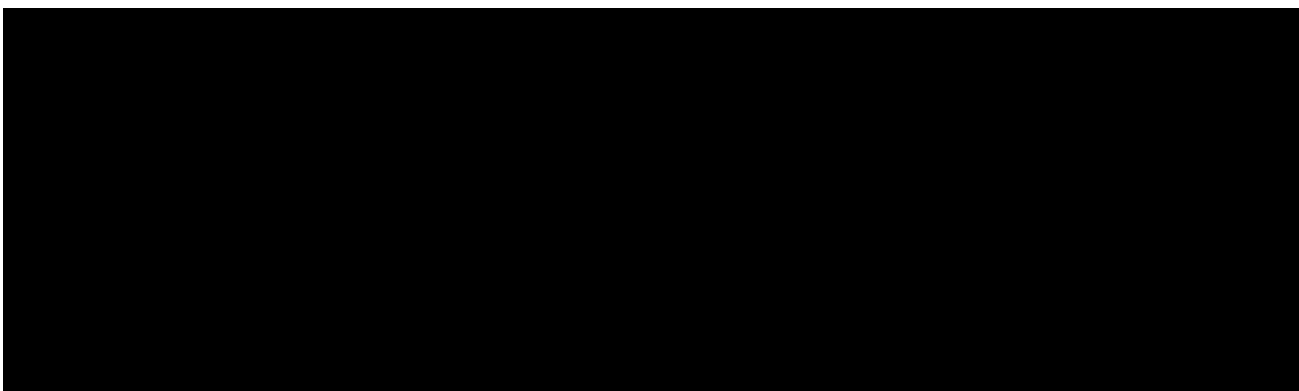
adopted for AIR OPTIX™ for Astigmatism. A front-curve orientation feature will consist of a fiducial mark at 6 o'clock for on-eye assessment of lens rotation.

In order for the toric contact lenses to perform effectively, they must maintain the correcting cylindrical axis in appropriate and stable orientation. Therefore, it is critical to have timely lens orientation to ideal axis, minimal lens rotation, and lens oscillation to achieve optimal performance and stable correction of astigmatism with minimal visual blur. For performance confirmation purpose, the study aims to evaluate the on-eye clinical performance of investigational LID226397 contact lenses to support contact lens product development and to evaluate product performance in the intended population. [REDACTED]

[REDACTED]

[REDACTED]

The AOfAHP contact lenses have been chosen as the comparator product because these lenses have the comparable wear modality and same indication for correction of astigmatism.



## 5.2 Purpose of the Study

The overall objective of this study aims to evaluate the on-eye toric clinical performance of investigational LID226397 contact lenses and AOfAHP contact lenses in a daily wear dispensing trial. Volunteer subjects aged 18 or over who are habitual toric soft contact lens wearers, have at least 3 months of contact lens wearing experience (excluding AOfAHP habitual lens wearers and habitual daily disposable lens wearers), and who wear their habitual lenses at least 5 days per week and at least 10 hours per day, will be included. This is a prospective, randomized [REDACTED], bilateral, crossover, controlled, double-masked, multicenter clinical study. The outcomes of this study will be used to support contact lens product development [REDACTED]

[REDACTED]

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.

Alcon reserves the right of prior review of any publication or presentation of information related to the study. The author(s) of the publication will be the individual with substantial contribution to the conception or design of the work, OR the acquisition, analysis, or interpretation of data. Additionally, the author will draft the work or revise it critically for important intellectual content; provide final approval of the version to be published; and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

### **5.3 Risks and Benefits**

Risk management principles have been applied to both the planning and the intended conduct of the clinical investigation, in order to ensure the reliability of the clinical data generated and the safety of the subjects. 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 investigator's brochure 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 serafilcon A contact lenses are features consistent for successful contact lens wear. Based upon nonclinical testing and documented rationale for applicability of test results, LID226397 contact lenses, which is made of the same material as Alcon serafilcon A sphere contact lens, are assessed to be nontoxic and biocompatible for on-eye use.

In the US, Acuvue Oasys contact lenses have approved indications for use for both daily wear and extended wear for up to 6 continuous nights. Further details on any known potential risks and benefits can be found in the product package insert.



A summary of the known potential benefits and risks associated with LID226397 contact lenses can be found in the IB. The potential harms associated with on-eye exposure to the new lens materials include toxicity response, blurred vision, and ocular discomfort. In general, when worn for daily wear, the risks with LID226397 contact lenses are anticipated to be similar to other marketed soft contact lenses worn for daily wear.

There may also be unknown risks to use of LID226397 contact lenses. Any risk to subjects in this clinical study will be minimized by compliance with the eligibility criteria and study procedures, clinical oversight, and monitoring. Site personnel will educate subjects on proper hygiene and lens handling, and compliance with the use of contact lenses for daily wear according to the protocol. Subjects should be instructed not to wear contact lenses while

swimming due to increased risk of infection, or while sleeping. Site personnel should advise the subjects to remove contact lenses and return for prompt follow-up of symptoms such as ocular discomfort, foreign body sensation, excessive tearing, vision changes, or hyperemia.

Refer to the IB for additional information.

## 6 STUDY OBJECTIVES

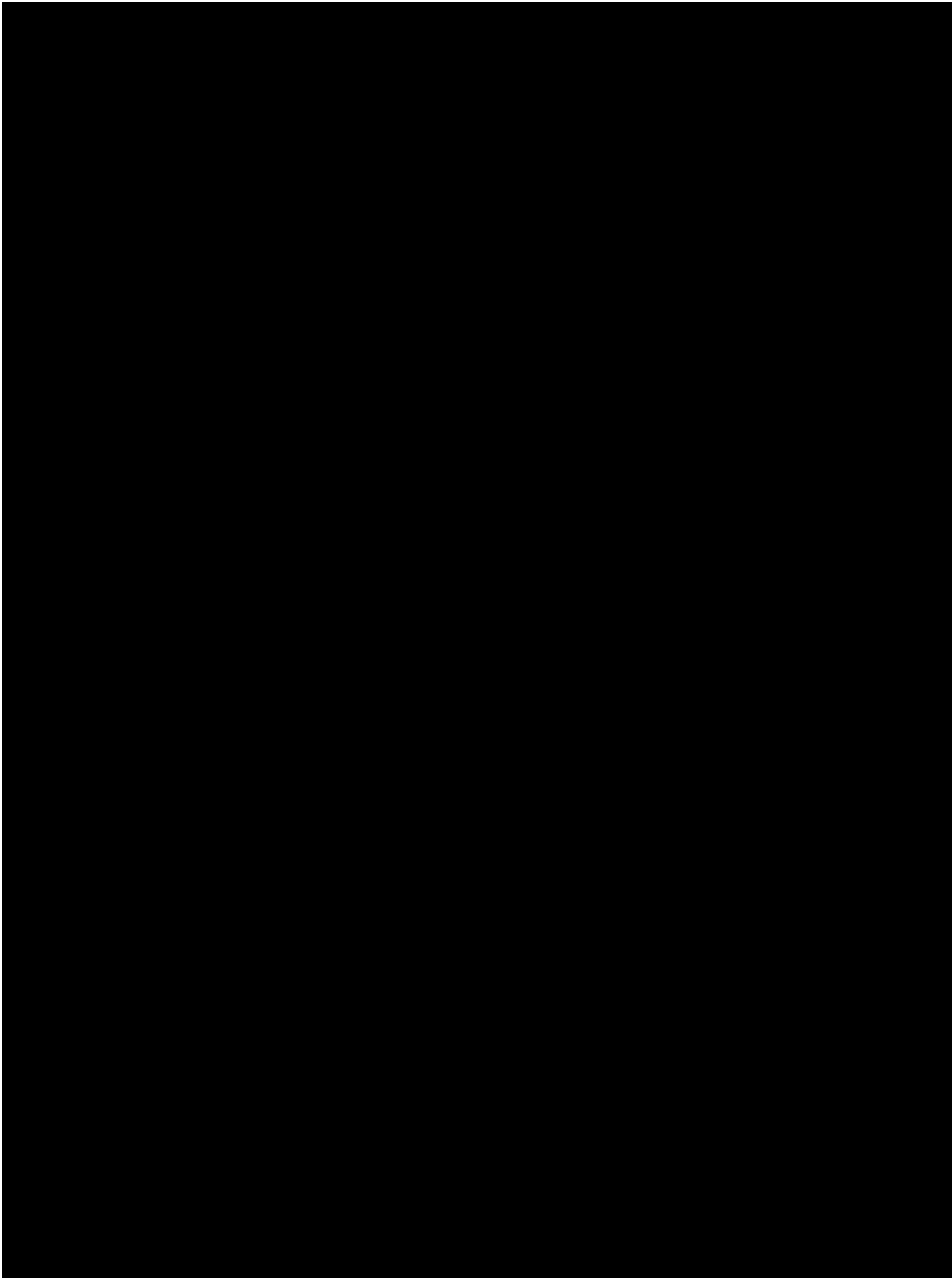
### 6.1 Primary Objective(s)

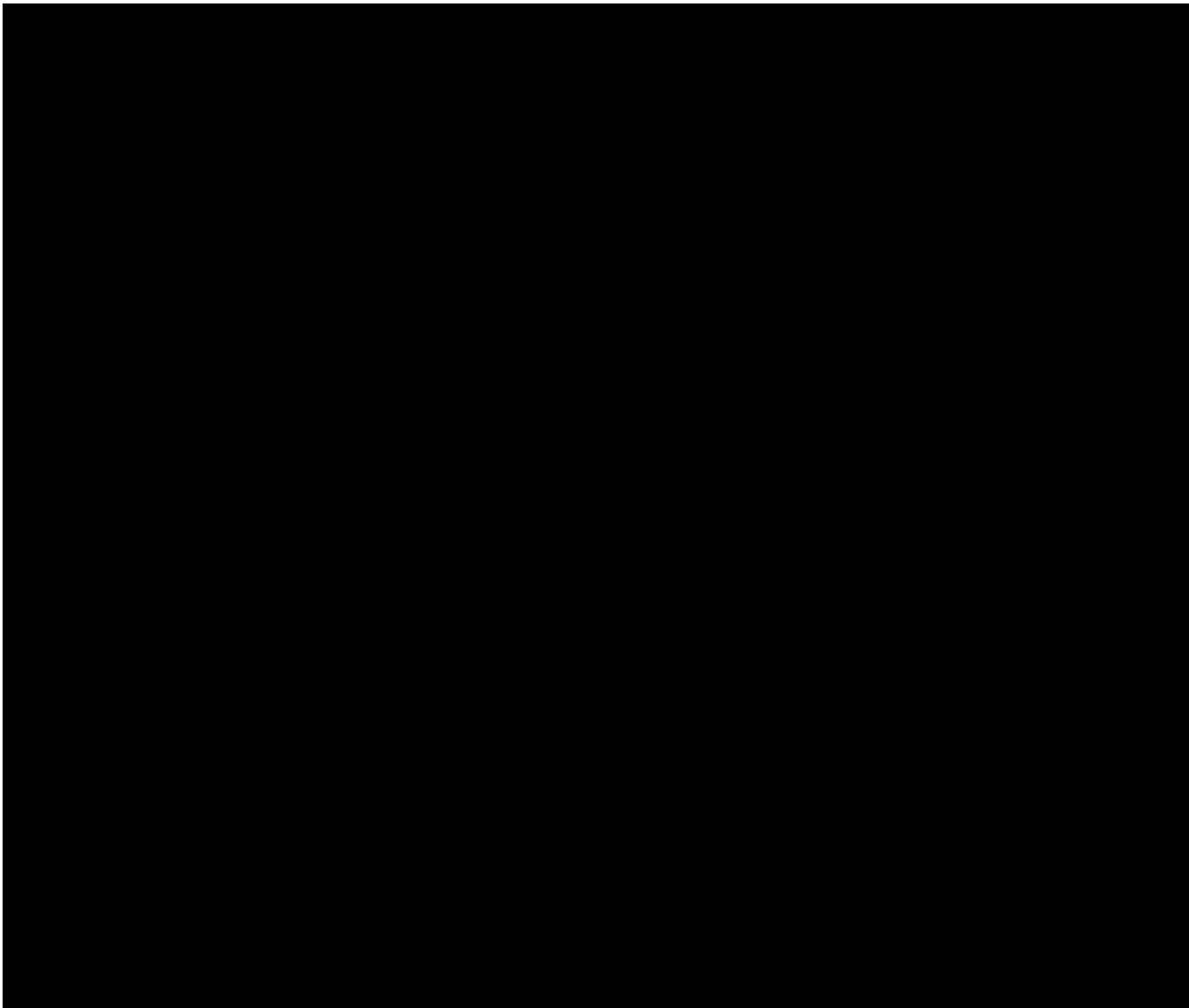
**Table 6–1 Primary Objective(s)**

<u>Objective(s)</u>	<u>Endpoint(s)</u>
To evaluate the percentage of LID226397 contact lenses with axis orientation within $\pm 30$ degrees from the 90° axis (ideal location), 10 min after lens insertion at dispense visit.	Percent of lenses with axis orientation within $\pm 30$ degrees from the intended axis, 10 min after insertion

### 6.2 Secondary Objective(s)

Not applicable.





## 6.4 Safety Objective(s)

**Table 6-3 Safety Objective(s)**

<u>Objective(s)</u>	<u>Endpoint(s)</u>
To describe the safety profile of the study products	<ul style="list-style-type: none"><li>• Adverse events</li><li>• Biomicroscopy findings</li><li>• Device deficiencies</li></ul>

## 7 INVESTIGATIONAL PLAN

### 7.1 Study Design

This is a prospective, randomized [REDACTED] bilateral, crossover, controlled, double-masked, multicenter clinical study, evaluating the LID226397 and AOfAHP contact lenses, to be conducted at approximately 6 sites.

Subjects will be randomized to 1 of 2 crossover sequences, [REDACTED] [REDACTED] and exposed to test and comparator lenses for bilateral wear. Subjects will be expected to complete all 7 scheduled visits. Subjects will be asked to wear their habitual spectacles only (no contact lens wear) during the washout periods for 3 to 4 days after Visit 1, and for 2 (at least 48 hours) to 4 days after Visit 4. All study contact lenses will be prescribed according to subject's prescription and fitted using the manufacturers fitting instructions. Investigator will insert the contact lenses with scribe mark in the direction of the intended 6 o'clock position (90° axis), [REDACTED] [REDACTED].

This is a double masked study design where both the investigator and the subjects will be masked to the details of the study products and assigned treatment (lens) sequences. Differences in scribe marks and lens thickness profile between the study lenses could result in potential inadvertent unmasking of investigator. [REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]

Subjects will be provided with CLEAR CARE Cleaning & Disinfecting Solution to use with the study lenses for the duration of study. LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.

## 7.2 Rationale for Study Design

This study design is justified based upon an evaluation of the results of relevant preclinical and clinical testing, as described within the IB.

The investigational contact lens is intended for the optical correction of refractive ametropia (myopia or hyperopia, with astigmatism) in persons with non-diseased eyes.

The purpose of this study is to evaluate the on-eye clinical performance of investigational LID226397 contact lenses to support contact lens product development and to evaluate product performance in the intended population. [REDACTED]

The primary and [REDACTED] endpoints were selected to fulfill the primary [REDACTED] objectives of the study. Procedures for measurement of these endpoints were selected based on common practice for these assessments. The design of this study is justified based upon preclinical and clinical testing, as described within the investigator's brochure. [REDACTED]

[REDACTED] AOfAHP contact lenses were chosen as the comparator product

because these lenses also are reusable contact lenses and have the comparable wear modality and same indication for correction of astigmatism (see Package Insert for AOHP contact lenses).

The intended use of this contact lens is vision correction in astigmatism; therefore, the measurement of lens axis orientation, 10 min after insertion is planned as the primary effectiveness endpoint. [REDACTED]

The crossover design will ensure that the same subject is exposed to both the test and comparator lens materials; therefore, [REDACTED] objective assessments [REDACTED] will be obtained for both lenses from the same subject.

[REDACTED]

[REDACTED] The study will exclude any current/habitual AOfAHP lens and daily disposable contact lens wearers, and any previous wearers of AOfAHP or daily disposable contact lenses in the past 3 months prior to consent in order to reduce potential bias of wearers to their habitual contact lenses. There are no immediate plans to submit the results of this pivotal 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.


### **7.2.1 Purpose and Timing of Interim Analyses and Resulting Design Adaptations**

Interim analyses will not be performed.

### **7.3 Rationale for Duration of Treatment/Follow-Up**

Subjects will wear each study product bilaterally for their respective wear cycles on a daily wear modality. [REDACTED]

[REDACTED] The lenses will be provided by a qualified unmasked study staff member in such a manner that the subject and the investigator remain masked to the lens type. The primary [REDACTED] endpoints will be assessed on dispense visits [REDACTED] respectively. [REDACTED]

 The duration of use of each study product is in accordance with the respective product labeling (see package inserts for AOHP contact lenses and IB for LID226397 contact lenses).

#### **7.4 Rationale for Choice of Comparator Product**

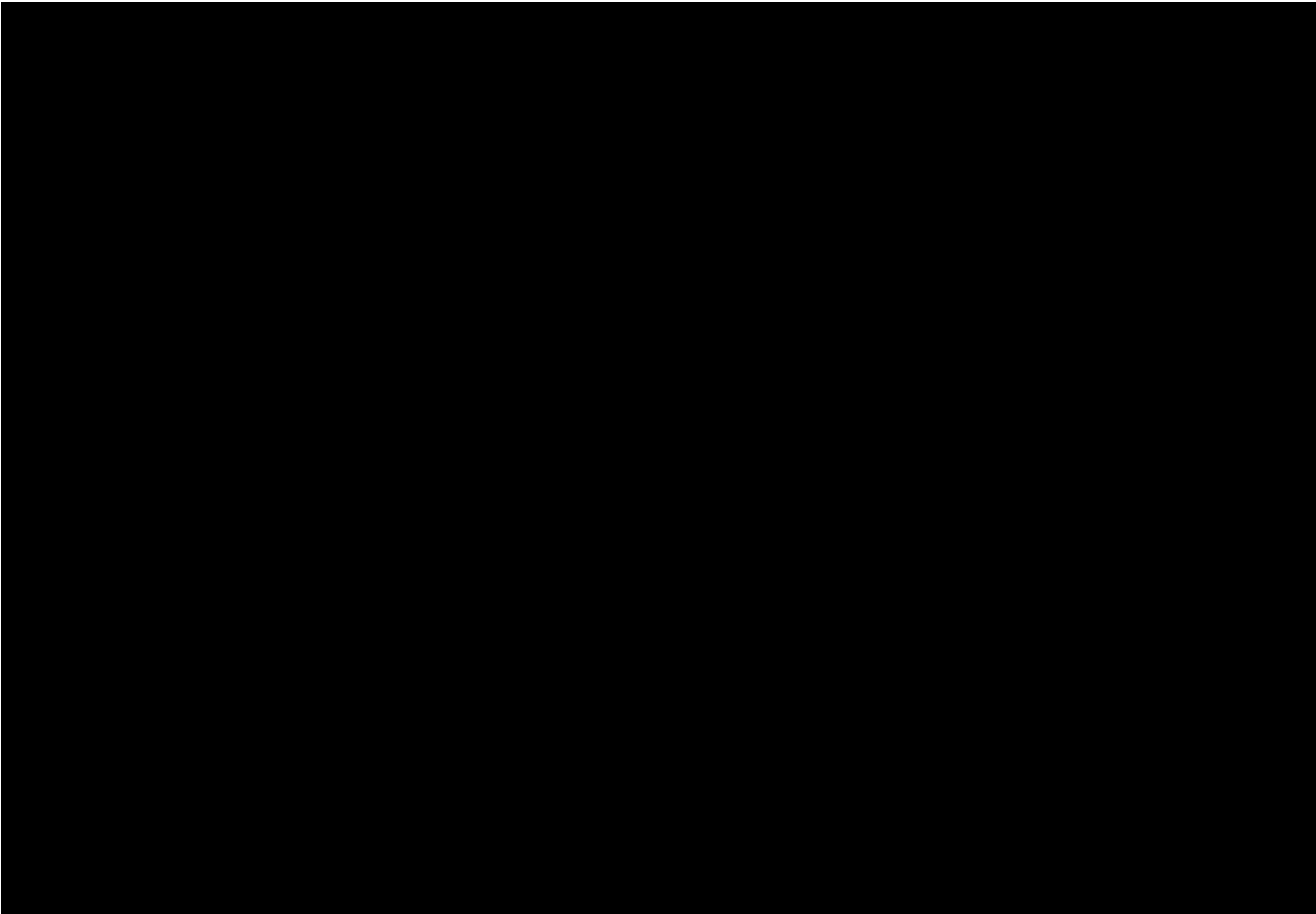
AOfAHP contact lenses were chosen as the comparator product because these lenses also are reusable contact lenses (see Package Insert for AOHP contact lenses) and have similar indications for correction of astigmatism.

#### **7.5 Data Monitoring Committee**

Not applicable.

### **8 STUDY POPULATION**

The study population consists of male and female subjects aged 18 or over and who wear any commercial soft toric contact lenses (excluding AOfAHP habitual lens wearers and habitual daily disposable lens wearer) 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.



The study population will include approximately 92 volunteer subjects to be enrolled (consented) at approximately 6 sites within the US, with a target of 80 total completed subjects. Site-specific targets may vary based upon individual site capabilities. Estimated time needed to recruit subjects for the study is approximately 4 weeks; however, unanticipated circumstances may shorten or lengthen this time and would not require amendment of this protocol. A 15% screening failure rate is expected requiring approximately 92 subjects are expected to be enrolled.

## 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.
2. Subject must be able to understand and must sign an informed consent form (ICF) that has been approved by an Institutional Review Board (IRB/IEC).
3. Successful wearers of any commercial toric soft contact lenses (except AOfAHP and daily disposable 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.
4. BCVA distance (as determined by manifest refraction at screening) 20/25 or better in each eye with a sphero-cylindrical refractive error within the available study lens parameter range in the study.

Note: Study lens parameters available in this study are:

-0.75 D and -1.25 D cylinder power with:

- (a) -0.25 to -4.00 D (in 0.25 D steps) spherical power in 10°, 90°, 170° and 180° axis as available
- (b) -5.00 to -10.00 D (in 1 D steps), -5.50 D & -6.50 D spherical power in 90° and 180° axis as available
- (c) +1.00 to +8.00 D (in 1 D steps) spherical power 90° and 180° axis as available

5. Distortion-free keratometric readings at screening



6. Subject must possess spectacles (with 0.3 logMAR or better vision OU) and be willing to wear habitual spectacles for vision correction when study lenses are not worn, as needed.
7. Subject must be willing to stop wearing their habitual contact lenses for the duration of study participation.



9. Willing to NOT use rewetting/lubricating drops at any time during the study.
10. Subjects must be willing and able to attend all scheduled visits.

## 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 irregular cornea in either eye.
4. Ocular or intraocular surgery (excluding placement of punctal plugs) within the previous 12 months.
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 twelve weeks immediately prior to enrollment for this trial.







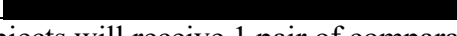
	<p>Fort Worth, Texas 76134-2099 USA</p>
<p>Indication for use and intended purpose in the current study</p>	<p>The investigational LID226397 contact lenses are indicated for the optical correction of ametropia (myopia or hyperopia, with astigmatism) in persons with non-diseased eyes.</p> <p>The lenses are intended for daily wear (less than 24 hours while awake), with removal for cleaning and disinfection (chemical, not heat) prior to reinsertion, or for disposal, as recommended by the eye care professional. [REDACTED] [REDACTED] [REDACTED]</p>
<p>Product description and parameters available for this study</p>	<ul style="list-style-type: none"> <li>• Material: Serafilcon A</li> <li>• Water content: 55%</li> </ul> <p>Power range: Limited lens parameters will be available for use in this study:</p> <ul style="list-style-type: none"> <li>• -0.75 D cylinder power with             <ul style="list-style-type: none"> <li>(a) -0.25 to -4.00 D (in 0.25 D steps) spherical power in 10°, 90°, 170° and 180° axis as available</li> <li>(b) -5.00 to -10.00 D (in 1 D steps), -5.50 D &amp; -6.50 D spherical power 90° and 180° axis as available</li> <li>(c) +1.00 to +8.00 D (in 1 D steps) spherical power 90° and 180° axis as available</li> </ul> </li> <li>• -1.25 D cylinder power with             <ul style="list-style-type: none"> <li>a) -0.25 to -4.00 D (in 0.25 D steps) spherical power in 10°, 90°, 170° and 180° axis as available</li> <li>b) -5.00 to -10.00 D (in 1 D steps), -5.50 &amp; -6.50 D spherical power 90° and 180° axis as available</li> <li>c) +1.00 to +8.00 D (in 1 D steps) spherical power 90° and 180° axis as available</li> </ul> </li> <li>• Base curve (mm): 8.6 mm (Target)</li> <li>• Diameter (mm): 14.5 mm (Target)</li> </ul>
<p>Formulation</p>	<p>Details are present in the IB for CLN109-C001 V3.0</p>
<p>Usage</p>	<ul style="list-style-type: none"> <li>• Wear:             <ul style="list-style-type: none"> <li>○ Daily Wear</li> </ul> </li> </ul>

	<ul style="list-style-type: none"><li>○ Bilateral</li></ul> <div style="background-color: black; width: 100%; height: 80px; margin: 10px 0;"></div> <ul style="list-style-type: none"><li>• 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. Until the replacement lens is obtained, the subject must store both study lenses in the provided lens care solution and wear their habitual spectacles.</li><li>• Exposure: Study lenses are to be worn during typical contact lens wearing hours, on all days during the study lens wearing period, at least 10 hours per day, over each treatment period (7 days [-0/+1] according to randomization assignment). <div style="background-color: black; width: 100%; height: 15px; margin: 5px 0;"></div><div style="background-color: black; width: 100%; height: 15px; margin: 5px 0;"></div><div style="background-color: black; width: 100%; height: 15px; margin: 5px 0;"></div></li></ul>
Number/Amount of product to be provided to the subject	Subjects will be provided a pair of test lenses at the applicable visit as per randomization, in parameters as determined during trial fitting as per the investigator's assessment. Fitting and Test Lenses will be provided in bulk by the sponsor before the start of the trial. (Any additional lenses needed can be requested by the site to the sponsor).
Packaging description	Blister foil pack
Labeling description	<ul style="list-style-type: none"><li>• Lens Foil label includes:<ul style="list-style-type: none"><li>- material name and identifier</li><li>- base curve</li><li>- diameter</li><li>- packing solution</li><li>- power</li><li>- lot number</li><li>- expiration date</li><li>- content statement</li><li>- investigational device statement</li><li>- sponsor information</li><li>- country of origin</li></ul></li></ul>

	<p>Provided in packages of ~ 18 lenses per power, identified with the following:</p> <ul style="list-style-type: none"> <li>- a color-coded label stating a protocol number</li> <li>- material identifier</li> <li>- power</li> <li>- an investigational use only statement</li> <li>- tracking number</li> </ul>
Training and/or experience requirements for device	No additional training or experience is required to administer the test product.
Storage conditions	Lenses stored at room temperature.
Lens Care	<ul style="list-style-type: none"> <li>• Cleaned and disinfected with CLEAR CARE Cleaning &amp; Disinfecting Solution after each use.</li> <li>• LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.</li> </ul>

**Table 9–2                      Comparator Product**

Comparator Product(s)	ACUVUE OASYS for ASTIGMATISM with HYDRACLEAR PLUS (AOfAHP) contact lenses (senofilcon A)
Manufacturer	Johnson & Johnson Vision Care, Inc.
Indication for Use	The ACUVUE OASYS Brand Contact Lenses for ASTIGMATISM are indicated for the optical correction of refractive ametropia (myopia or hyperopia, with astigmatism) in persons with non-diseased eyes.
Product description and parameters available for this study	<ul style="list-style-type: none"> <li>• Material: Senofilcon A</li> <li>• Water content: 38%</li> <li>• Power range:</li> </ul> <p>Available power range for the comparator lenses:</p> <ul style="list-style-type: none"> <li>• -0.75 D cylinder power with <ul style="list-style-type: none"> <li>(a) -0.25 to -4.00 D (in 0.25 D steps) spherical power in 10°, 90°, 170° and 180° axis as available</li> <li>(b) -5.00 to -9.00 D (in 1 D steps), -5.50 D &amp; -6.50 D spherical power 90° and 180° axis as available</li> </ul> </li> </ul>

	<p>(c) +1.00 to +6.00 D (in 1 D steps) spherical power 90° and 180° axis as available</p> <ul style="list-style-type: none"><li>-1.25 D cylinder power with</li></ul> <p>(a) -0.25 to -4.00 D (in 0.25 D steps) spherical power in 10°, 90°, 170° and 180° axis as available</p> <p>(b) -5.00 to -9.00 D (in 1 D steps), -5.50 D &amp; -6.50 D spherical power 90° and 180° axis as available</p> <p>(c) +1.00 to +6.00 D (in 1 D steps) spherical power 90° and 180° axis as available</p> <ul style="list-style-type: none"><li>Base curve (mm): 8.6 mm</li><li>Diameter (mm): 14.5 mm</li></ul>
Formulation	See package Insert for AOHP contact lenses
Usage	<ul style="list-style-type: none"><li>Wear:<ul style="list-style-type: none"><li>Daily Wear</li><li>Bilateral</li></ul></li></ul>  <ul style="list-style-type: none"><li>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. Until the replacement lens is obtained, the subject must store both study lenses in the provided lens care solution and wear their habitual spectacles.</li><li>Exposure: Study lenses are to be worn during typical contact lens wearing hours, on all days during the study lens wearing period, at least 10 hours per day, over each treatment period (7 days [-0/+1] according to randomization assignment).    </li></ul>
Number/Amount of Product to be Provided to the subject	Subjects will receive 1 pair of comparator lenses as per randomization, in parameters as determined during trial.
Packaging description	Provided in commercial packaging

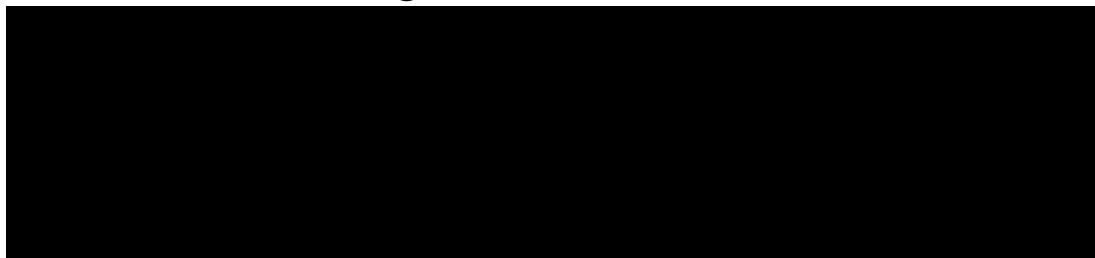
Labeling description	Commercial foil
Training and/or experience requirements for device	No additional training or experience is required to administer the test product.
Storage conditions	Store at room temperature
Lens Care	Cleaned and disinfected with CLEAR CARE Cleaning & Disinfecting Solution after each use.  LacriPure saline will be permitted for rinsing the lens(es) after removal and prior to insertion, if required.
Additional identifying information	N/A
Supply	<ul style="list-style-type: none"><li>• Each site will procure their own comparator lenses</li><li>• CLEAR CARE Cleaning &amp; Disinfecting Solution will be supplied by sponsor to be provided to subject.</li><li>• LacriPure saline will be procured by the sites.</li></ul> Refer to the MOP for a detailed description.

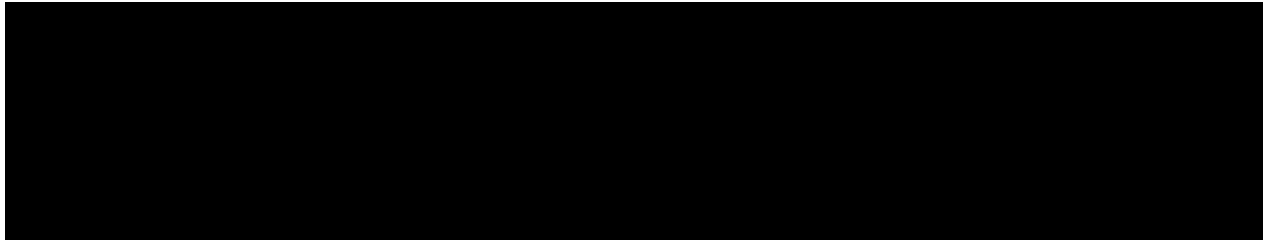
## 9.2 Other Medical Device or Medication Specified for Use During the Study

During the clinical study, additional medical devices and/or medications that are required in conjunction with the treatment include the following:

- Subjects will be provided with CLEAR CARE Cleaning & Disinfecting Solution to use with the study lenses.
- Lubrication/rewetting drops will not be permitted.

## 9.3 Treatment Assignment/Randomization





Eligible subjects will be randomized in a 1:1 ratio to receive treatment (lens) in one of the following crossover sequences:

- Sequence 1: LID226397/AOfAHP
- Sequence 2: AOfAHP/LID226397

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

A randomization list will be generated using a validated system that automates the random assignment of treatment arms to randomization numbers in the specified ratio. Subjects will be assigned treatment according to the randomization list uploaded in the randomization system. The randomization list will be generated and maintained by the study sponsor

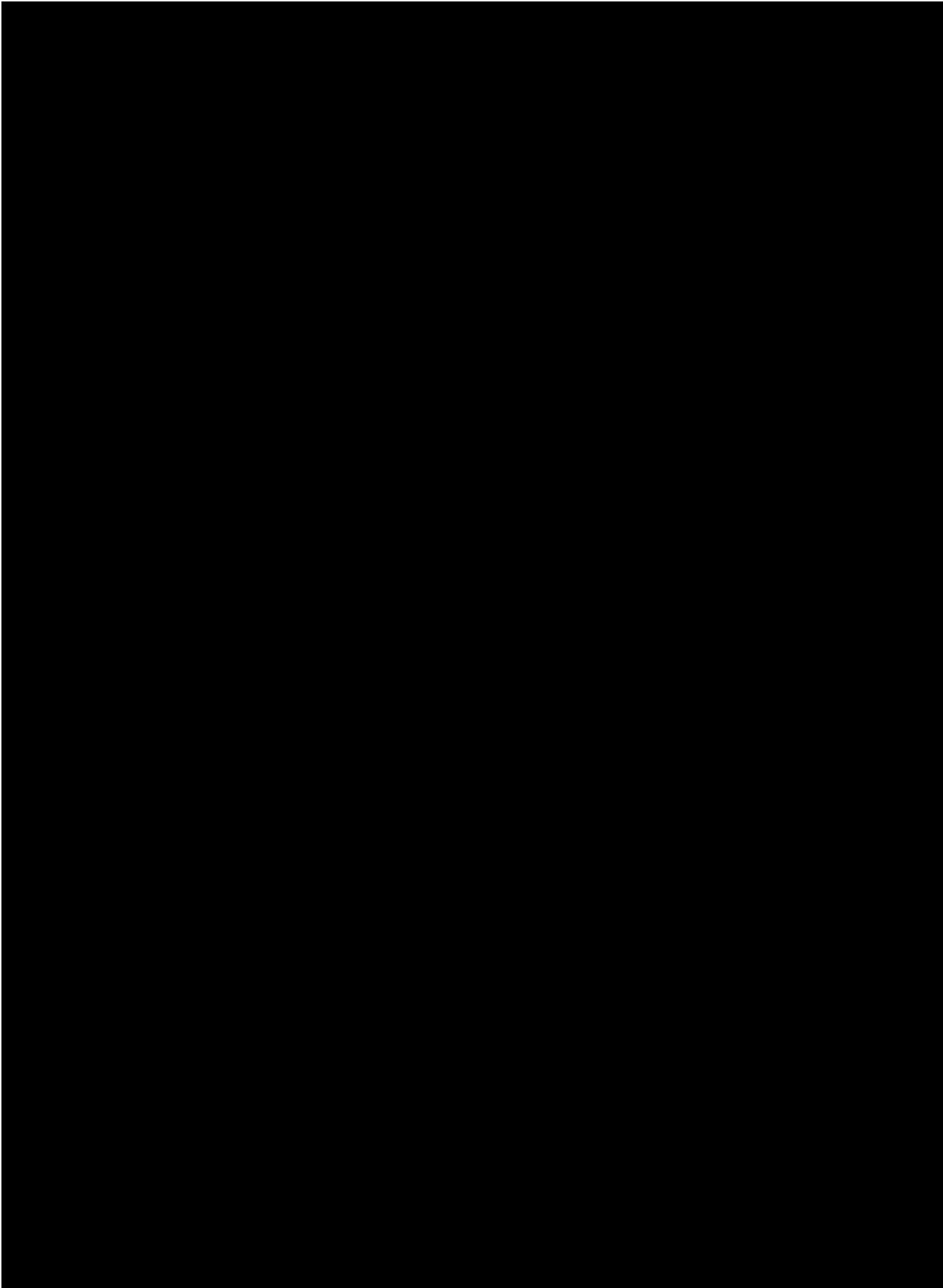
At Visit 1 all eligible subjects will be randomized via the EDC/randomization integration system to 1 of the treatments (lens sequences). The investigator's delegate will access the respective system after confirming that the subject meets all the eligibility criteria. A randomization number will be automatically assigned to the subject according to the subject randomization list but will not be communicated to the site user. The EDC/randomization integration system will inform the site user of the treatment (lens sequence) assignment be dispensed to the subject. The same randomization assignment will be followed for lens fitting.

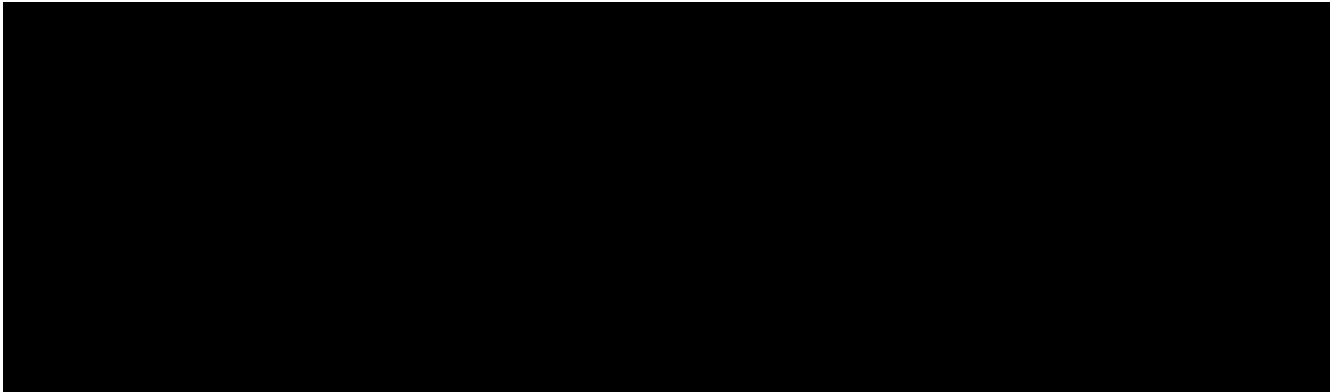
#### **9.4 Treatment Masking**

This study is double-masked (subject and the investigator), with subjects randomized to wear LID226397 and AOfAHP for the duration of the 2-week per treatment period. [REDACTED]

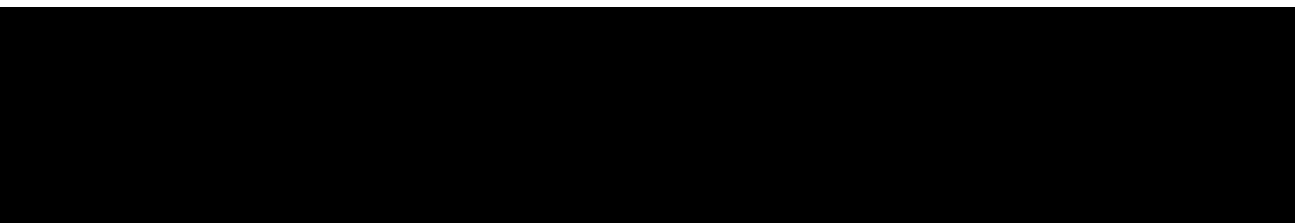
[REDACTED]







This level of masking will be maintained throughout the conduct of the study. Unmasking will occur only after all planned study data have been validated, and the database locked.



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.

## **9.5 Accountability Procedures**

Upon receipt of the IPs, the investigator or delegate must conduct an inventory. During the study, designated study staff must provide the IPs to the subjects in accordance with their randomization assignment. Throughout the study, the investigator or delegate must maintain records of IP dispensation and collection for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of IP supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation. All IPs sent to the investigator must be accounted for by study sponsor personnel, and in no case be used in an unauthorized situation.

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, solutions associated with a device deficiency or with any product-related adverse event (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

Subjects will be expected to attend 7 office visits, as shown below.

Visit #	Visit Type	Lens (Period)	Visit Window
Visit 1	Screening/ Baseline	N/A	N/A
Visit 2	Dispense Lens 1	Lens 1 (Period 1)	3 - 4 days after Visit 1 (Washout period with habitual spectacles only after Visit 1)
Visit 3	Week 1 Follow-up Lens 1	Lens 1 (Period 1)	7 -0/+ 1 days after Visit 2
Visit 4	Week 2 Follow- up Lens 1	Lens 1 (Period 1)	7 -0/+ 1 days after Visit 3

Visit #	Visit Type	Lens (Period)	Visit Window
Visit 5	Dispense Lens 2	Lens 2 (Period 2)	2 (at least 48 hours) - 4 days after Visit 4 (Washout period with habitual spectacles only after Visit 4)
Visit 6	Week 1 Follow-up Lens 2	Lens 2 (Period 2)	7 -0/+ 1 days after Visit 5
Visit 7	Week 2 Follow-up Lens 2 /Exit	Lens 2 (Period 2)	7 -0/+ 1 days after Visit 6

## 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

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

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.

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 used and unused study IPs and other products that were dispensed.

### **10.2.4 Adverse Event Collection: Safety Assessment**

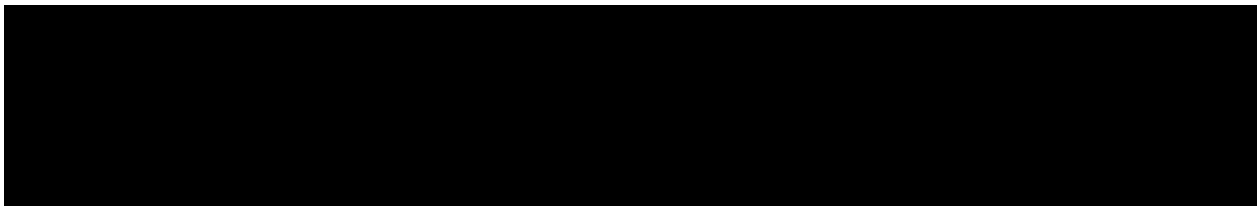
Assess and record any adverse events that are observed or reported since the previous visit, including those associated with changes in concomitant medication dosing. See Section 11 for further details regarding AE collection and reporting.

### **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 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 adverse event-related information on the Adverse Event form upon becoming aware.

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

- Collect Adverse Event information
- Collect Device Deficiency information
- Record changes in medical condition or concomitant medication

- Biomicroscopy
- Review lens wear calendar

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 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 reused.

### **10.4.2 Discontinuations**

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

Subject numbers of discontinued subjects must not be reused (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**

Other than screen failures, if a subject discontinues from the study, the subject should undergo an early exit visit. Refer to [Table 3–1](#) and the MOP for details.

## **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.

Breaking of the masked treatment codes will be done after locking the database.

### **10.5.1 Follow-up of Subjects after Study Participation has Ended**

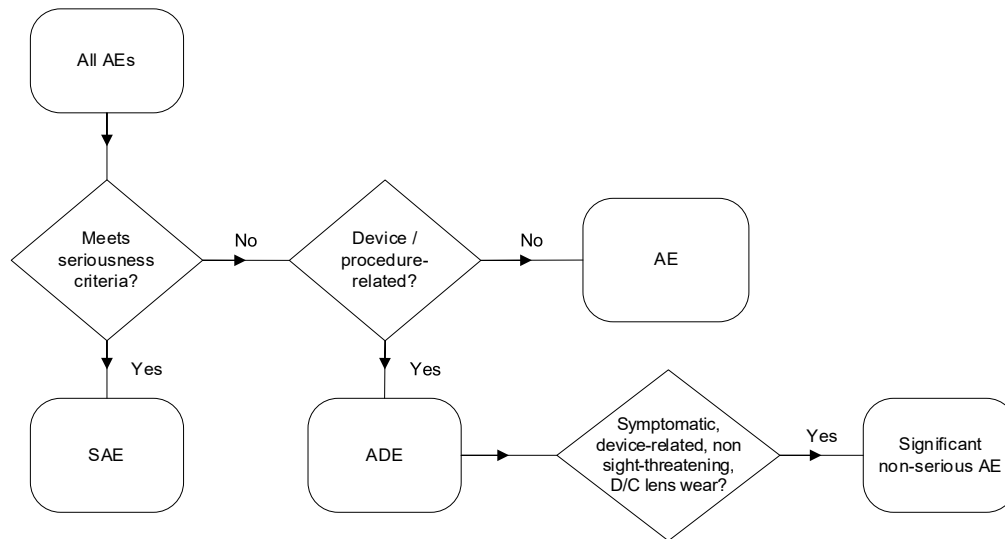
Following this study, the subject will return to their eye care professional for their routine eye care.

## 11 ADVERSE EVENTS AND DEVICE DEFICIENCIES

### 11.1 General Information

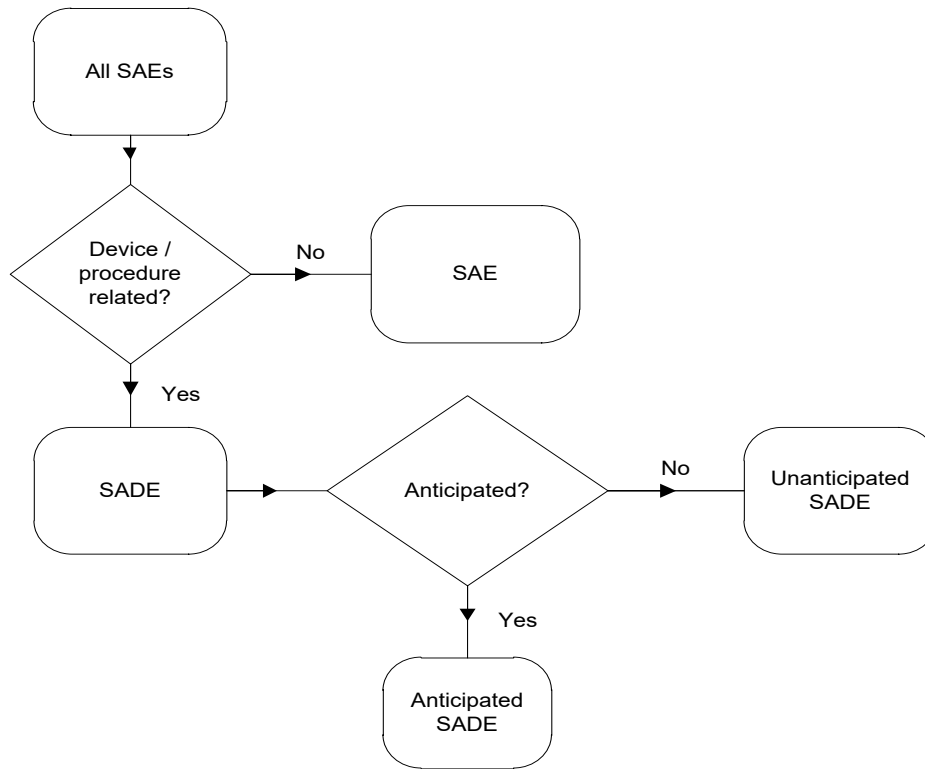
An AE is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device (test product). Refer to the Glossary of Terms and figures below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

**Figure 11-1**                      **Categorization of All Adverse Events**





**Figure 11-2                      Categorization of All Serious Adverse Events**



**Specific Events Relevant to this Protocol**

***Serious Adverse Events***

In addition to reporting all AEs (serious and nonserious) 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 (e.g., with manifest refraction or habitual correction) from enrollment visit that fails to resolve
- Uveitis (anterior, intermediate, or posterior)
- Corneal abrasion affecting  $\geq 50\%$  of corneal surface area

### ***Significant Nonserious Adverse Events***

A significant nonserious AE is a device-related, nonsight threatening adverse event that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks. In addition, the investigator must report any occurrence of the following as a Significant Nonserious Adverse Event:

- Peripheral nonprogressive noninfectious 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 (e.g., with manifest refraction or habitual correction) 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 on 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 (i.e., ADE or SADE); however, not all ADEs or SADEs are due to a device deficiency. The investigator should determine the applicable category listed in the Device

Deficiency eCRF for the identified or suspect device deficiency and report any patient harm separately. Examples of device deficiencies include the following:

- Failure to meet product specifications (e.g., incorrect lens power/diameter/base curve/color)
- Lens/solution cloudy
- Lens surface/edge defect
- Torn lens during handling/in pack
- Packaging deficit (e.g., mislabeled product, tampered seal, leaking bottle/container)
- Suspect product contamination

## 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 since your last study visit?”

In addition, 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 preexisting 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 ADEs and SAEs documentation must include date of occurrence, severity, treatment (if applicable), outcome, and assessments of the seriousness

and causality. In addition, the investigator must document all device deficiencies reported or observed with test and 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:

- 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. 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 *Adverse Device Effect* (for related AEs) and *Serious Adverse Event* eCRF.

Note: Should the EDC system become nonoperational, the site must complete the appropriate paper Serious Adverse Event and Adverse Device Effect and/or Device Deficiency Form. The completed form is emailed to the study sponsor at [msus.safety@alcon.com](mailto:msus.safety@alcon.com), for US, according to the timelines outlined above; however, the reported information must be entered into the EDC system once it becomes operational.

Study sponsor representatives may be contacted for any protocol-related question and their contact information is provided in the Manual of Procedures that accompanies this protocol.

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

### **Intensity and Causality Assessments**

Where appropriate, the investigator must assess the intensity (severity) of the AE based 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 AE that is 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.

Alcon products associated with device deficiencies and/or product related AEs should be returned and must include the Complaint #, which will be provided by study sponsor after the case is entered in the study sponsor's Global Product Complaint Management System (GPCMS), if applicable.

## **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 (i.e., medical emergency), the code may be broken prior to contact with the

study sponsor. The study sponsor must be informed of all cases in which the code was broken and of the circumstances involved. Additionally, the study sponsor may be required to unmask the information in order to fulfill expedited regulatory reporting requirements.

## **11.6 Follow-Up of Subjects with Adverse Events**

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

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

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

The investigator should also report complaints on non-Alcon products (i.e., ACUVUE OASYS for ASTIGMATISM with HYDRACLEAR PLUS) directly to the manufacturer as per the manufacturer's instructions or local regulatory requirements.

## **11.7 Pregnancy in the Clinical Study**

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

## **12 ANALYSIS PLAN**

Continuous variables will be summarized using the number of observations, mean, standard deviation (SD), median, minimum, and maximum, as well as CIs or confidence limits where applicable. Categorical variables will be summarized with frequencies 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 (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 any study lenses evaluated in this study. [REDACTED]

For treatment-emergent safety analyses, subjects/eyes will be categorized under the actual study lenses exposed in the corresponding lens sequence.

### 12.2.2 The Full Analysis Set

The full analysis set (FAS) is the set of all randomized subjects who are exposed to any study lenses evaluated in this study, except for lenses used for lens fitting at Visit 1.

### 12.2.3 Per Protocol Analysis set

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

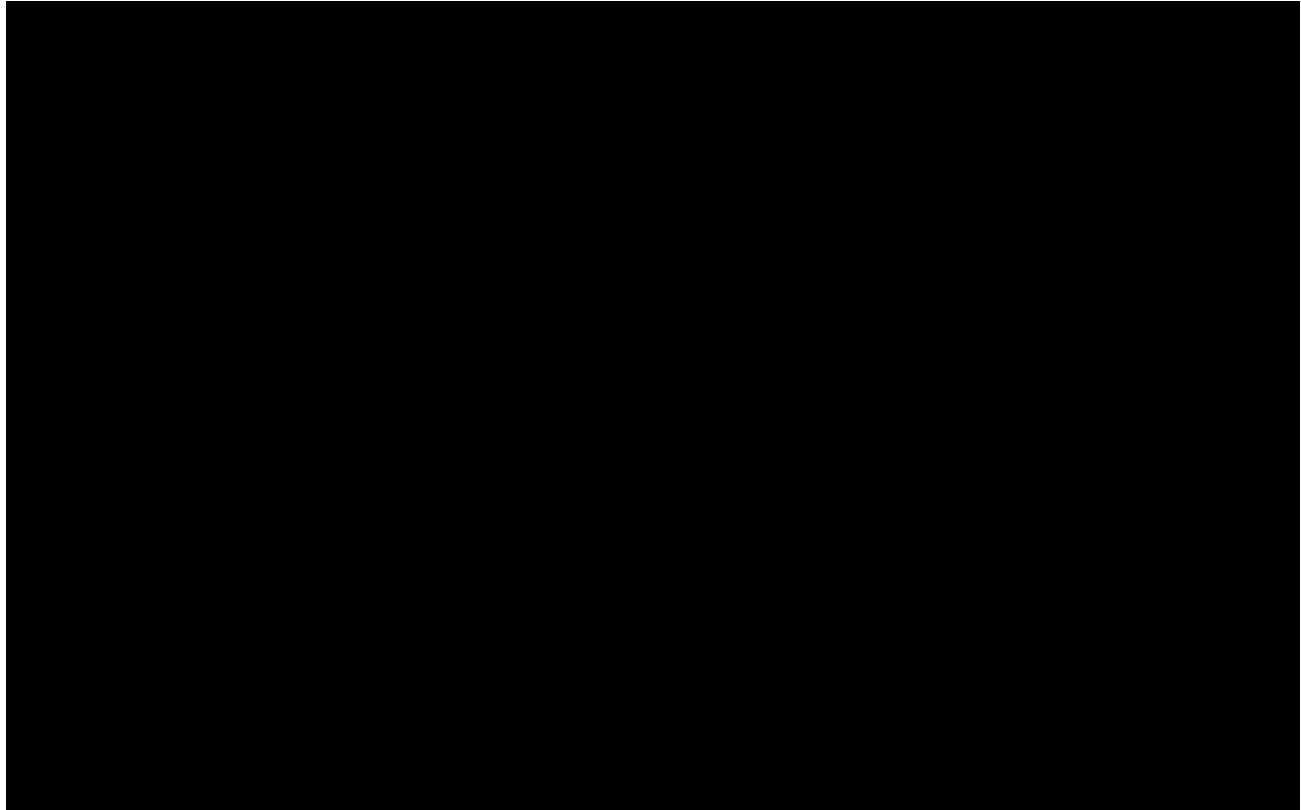
## 12.3 Demographic and Baseline Characteristics

Demographic information will be summarized by lens sequence and overall. Frequencies and percentages will be presented for categorical variables such as sex, age group, race, and ethnicity. 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 [REDACTED]  
[REDACTED] Unless otherwise specified, effectiveness evaluations will use the FAS as the

primary analysis set, except for those relating to lens fitting. [REDACTED]  
[REDACTED]



### **12.4.1 Analysis of Primary Effectiveness Endpoint(s)**

The primary objective is to evaluate the percentage of LID226397 contact lenses with axis orientation within  $\pm 30$  degrees from the  $90^\circ$  axis (ideal location), 10 min after lens insertion, at the dispense visit.

The primary endpoint is the percentage of LID226397 contact lenses with axis orientation, recorded as deviations from  $90^\circ$  axis, between  $-30$  and  $+30$  degrees, inclusive, assessed at the dispense visit, 10 min after lens insertion.

#### **12.4.1.1 Statistical Hypotheses**

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



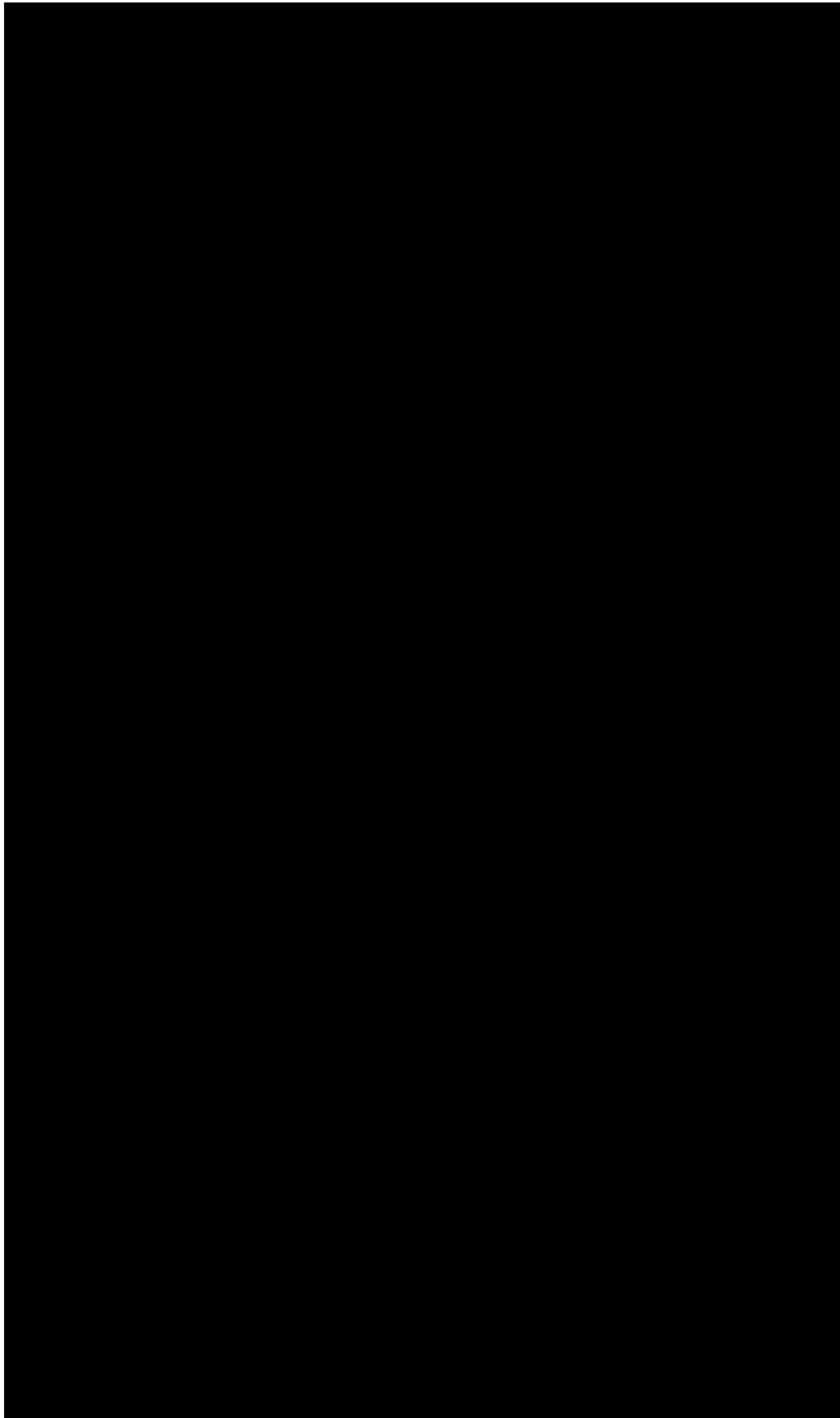
### 12.4.1.2 Analysis Methods

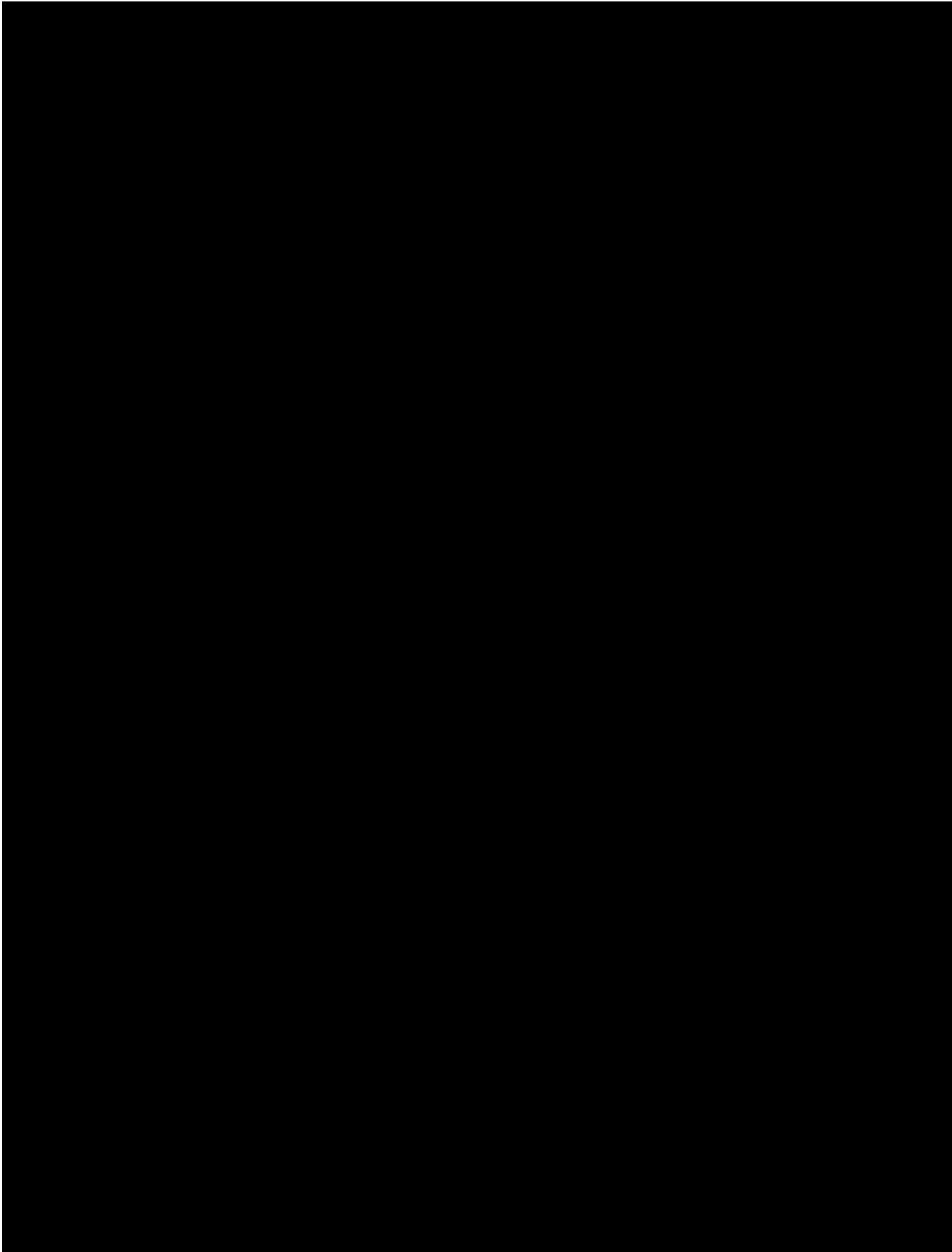
Frequencies and percentages will be provided, [REDACTED]

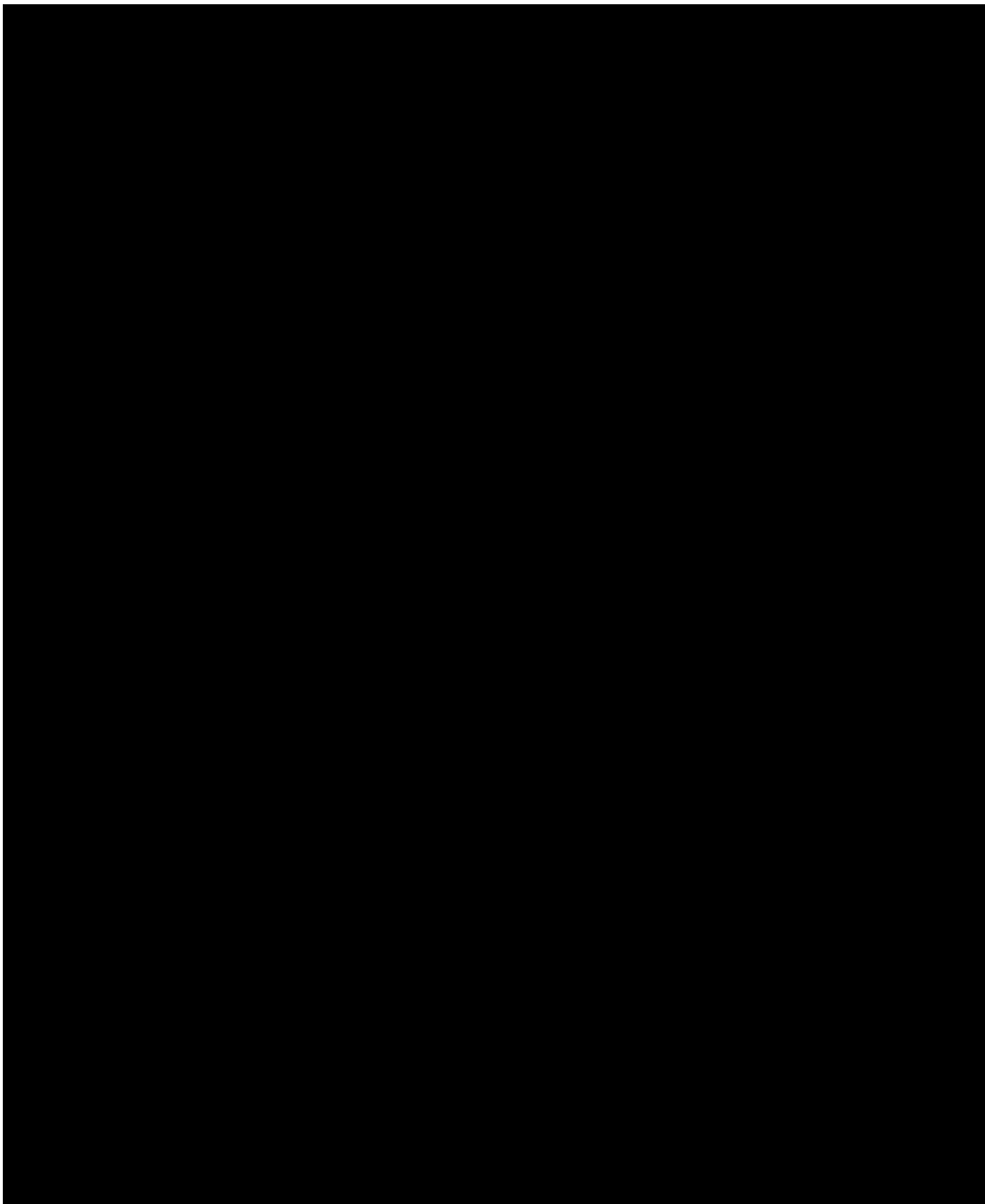
[REDACTED]

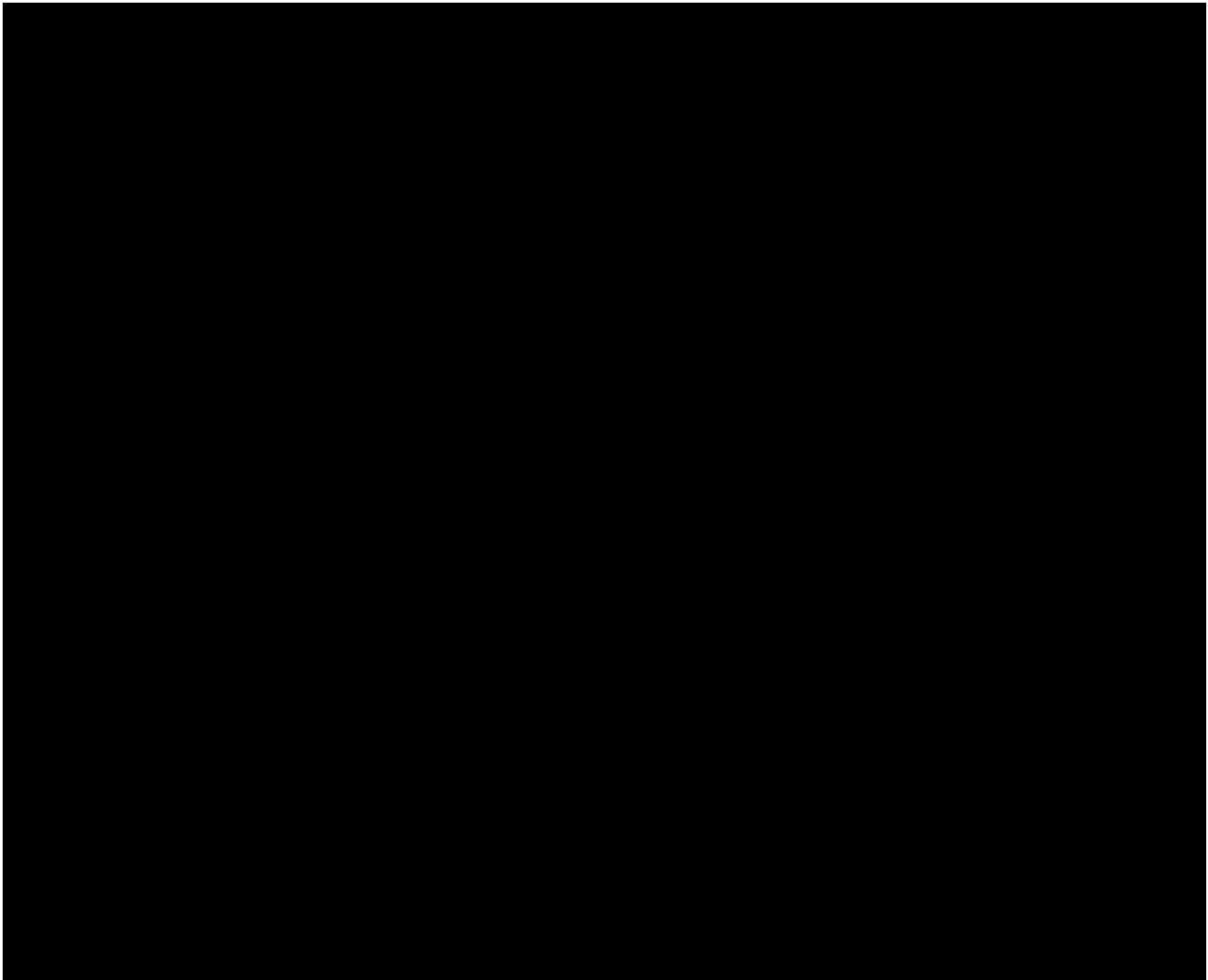
[REDACTED].

[REDACTED]









## **12.5 Handling of Missing Data**

All data obtained in evaluable subjects/eyes will be included in the analysis. No imputation for missing values will be carried out for 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 adverse events as well as the other listed parameters.

All AEs occurring from the time a subject signs informed consent to study exit will be accounted for in the reporting. Safety analyses will be conducted using the safety analysis set on a treatment-emergent basis. Descriptive summaries (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, frequencies and percentages of eyes that experience an increase of  $\geq 2$  grades from baseline (last assessment prior to study lens exposure) to any subsequent visit within the same period will be presented. A supportive listing will be generated which will include all biomicroscopy data from all visits within the same period for those eyes experiencing the increase.

Two listings for device deficiencies, prior to exposure to study contact 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.



## **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. For this study, the principal investigator and sub-investigators must be eye care professionals appropriately licensed to diagnose and treat subjects with the condition under study and be able to dispense contact lenses.

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.

The sponsor must be supervised by the investigator or designee to ensure the sponsor presence or activities do not bias the outcome of the study, affect the quality of the research data, and/or compromise the rights and welfare of the subject. The sponsor will not intervene with the standard of care provided to study subjects or make safety-related decisions or assessments.

### **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 Good Clinical Practices; international and national regulations, laws and guidelines; ISO 14155; 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
- 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 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 will be provided for test product and Package Insert for the control product, any periodic safety updates, and all other information as required by local regulation and/or the IRB/IEC. Any additional requirements imposed by the EC 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 informed consent form. The subject must be provided an opportunity to ask questions of the investigator, and if required by local regulation, other qualified personnel. The investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with the IP and the study, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and must be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also must be told that their records may be accessed by appropriate authorities and sponsor-designated personnel. The investigator must keep the original, signed copy of the consent (file in subject's medical records) and must provide a duplicate copy to each subject according to local regulations.

The investigator must have a defined process in case a subject would like to withdraw their consent (s). The investigator is the designated contact point for any such withdrawals.

The investigator must have a defined process in case a subject would like to exercise any of their rights under applicable Data Protection laws. The investigator is the designated contact point for any such requests.

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
- US FDA Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses
- 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

### **15.2 Scientific and Other References**

- Young G, Chalmers RL, Napier L, Hunt C, Kern J. Characterizing contact lens-related dryness symptoms in a cross-section of UK soft lens wearers. *Contact Lens Anterior Eye*. 2011 Apr;34(2):64-70.
- Investigator's Brochure for Mercury Toric Contact Lenses for Daily Wear. IB for CLN109-C001 V3.0. V-CLN-0042048.
- US FDA Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses
- Acuvue Oasys Brand Contact Lenses Package Insert. Package Insert for CLN109-C001 V1.0. V-CLN-0176412



