FINAL

Performance of Two Toric Silicone Hydrogel Contact Lenses

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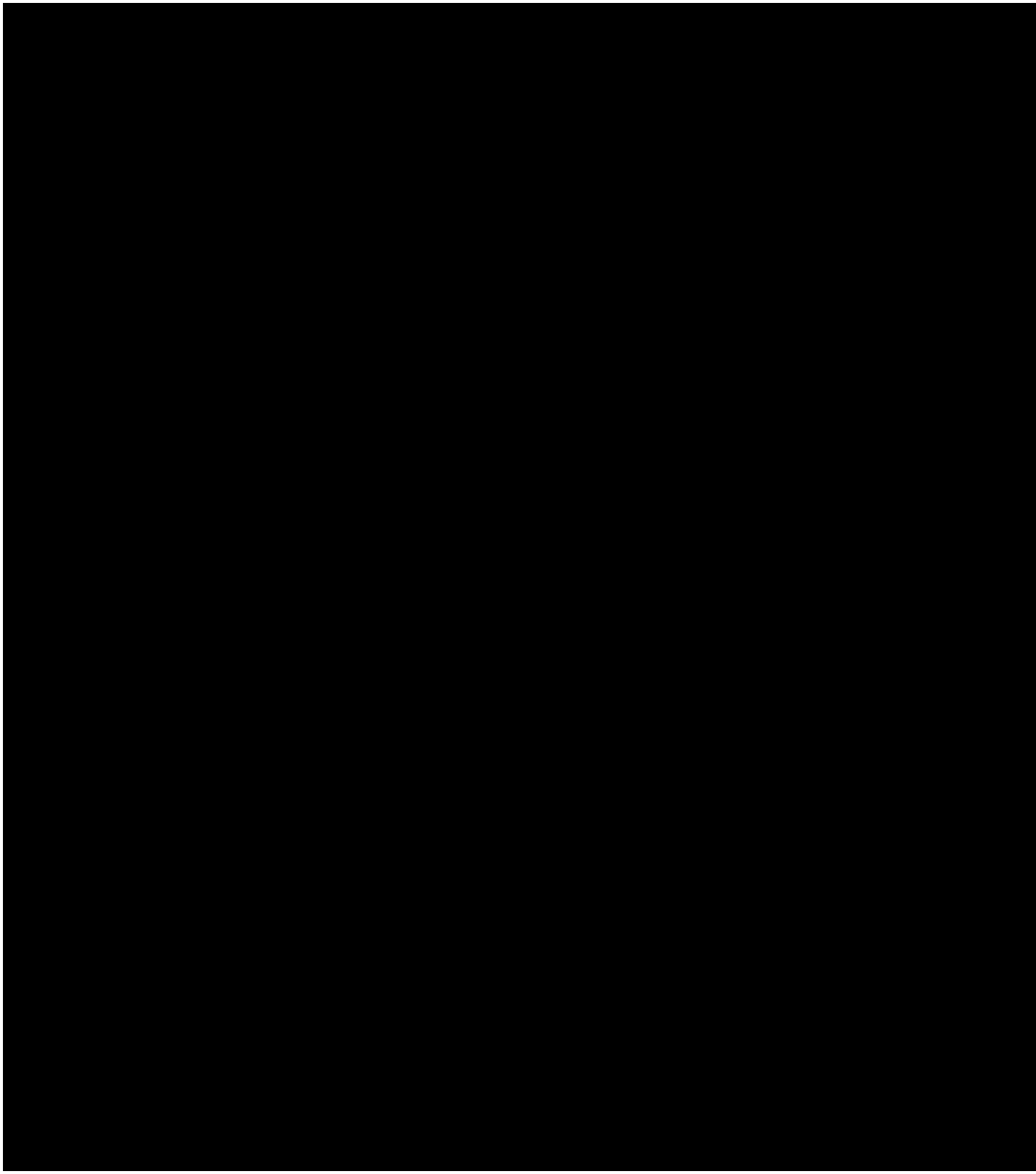
[redacted]

Revision History

Document number	Date	Comments
EX-MKTG-128	08/16/2021	First draft (v 1.0)
EX-MKTG-128	08/18/2021	Second draft (v 2.0)
EX-MKTG-128	08/19/2021	FINAL



Protocol Synopsis

Protocol Number	EX-MKTG-128
Title	Performance of Two Toric Silicone Hydrogel Contact Lenses
Name of Device(s) and (by USAN material)	Miru 1 month Menicon toric lens (Asmofilcon A), Avaira Vitality™ toric (fanfilcon A)
Indications for Use	**Approved for use:** • Asmofilcon A. (Daily wear) • fanfilcon A. (Daily wear) **Indication for use in this study:** • 1 month of daily wear
Study Design	Single-site, prospective, randomized, double masked, cross-over, 1-month daily wear study. This study will evaluate the Avaira Vitality™ toric when compared to the Miru 1month Menicon toric lens after 1-month of daily wear.
Purpose	Evaluate the clinical performance and subjective acceptance of two toric silicone hydrogel contact lenses after 1-month of daily wear.
Study Duration	The anticipated timeline for this study is as follows: • Patient enrolment and completion: Sept 20th - Nov 30th, 2021 • Visits: V1: (BL/trial fit/lens order), V2: (Dispense P1), V3: (2-week visit P1), V4: (1-month visit P1/dispense P2), V5: (2-week visit P2), V6: (1-month visit P2/study exit).
Patient Population	Adapted soft contact lens wearers with astigmatism that provide written informed consent and meet protocol entry criteria.
Sample Size	Target enrollment is **38 subjects** and completion of **33 in** total.
Center Destination (Mexico)	National Autonomous University of Mexico. Av. de los Barrios no. 1, Los Reyes Iztacala, Tlalnepantla Edo. de México. Código Postal 54090 (México).
Number of Centers	Single-Center
Patient Follow-up	Patients enrolled in this study will be followed up after the lens dispensing session: • Follow-up: 2 weeks and 1 month for each lens pair
Primary outcome variable	• Lens handling (insertion and removal)
[redacted]	[redacted]

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1 Introduction

The utilization of soft toric contact lenses has increased significantly over the past few years. Toric contact lens wearers demand two things from their contact lenses, great comfort, and excellent vision. CooperVision's Avaira Vitality™ toric uses a third generation silicone hydrogel material which makes the lens inherently wettable with no surface treatments and uses naturally wettable building blocks to improve compatibility between silicone and hydrophilic domains. This combined with the higher water content of Avaira Vitality™ toric ensures a high performing, comfortable lens.

Menicon recently launched its Miru 1month lens family in the U.S. market, a monthly replacement silicone hydrogel lens in spherical, toric, and multifocal designs. Miru 1month toric Menicon is a monthly replacement silicone hydrogel contact lens manufactured in asmofilcon A material that has a water content of 40%. It uses both MeniSilk and NanoGloss technologies. The Miru 1month toric Menicon uses a unique double vertical asymmetric Thin Zones called Visiostable design™. The unique asymmetric vertical Thin Zones matches the eyelids natural asymmetric coverage of the cornea, harnessing the natural lid force, optimizing centration, and preventing rotation. A lens designed to work with the eyes for clear, comfortable vision

Therefore, CooperVision is interested in evaluating the clinical performance of the Avaira Vitality™ toric and Miru 1month toric Menicon lenses when existing wearers of hydrogel toric lenses are refitted with these lenses over 1 month of wear.

2 Study Objective

The aim of this prospective study is to evaluate the clinical performance and subjective acceptance of two toric silicone hydrogel contact lenses after 1-month of daily wear.

Primary outcome variable:

- Lens handling ratings (ease of insertion & removal. 0 -10 scale)

[redacted]

- [redacted]

[redacted]

[redacted]

[redacted]

3 Study Hypothesis

3.1 Study Hypothesis

- Null hypothesis (Ho): There is no difference between the Avaira Vitality™ toric and Miru 1month toric Menicon lenses in subjective lens handling ratings.
- Alternative hypothesis (H1): There is a difference between the Avaira Vitality™ toric and Miru 1month toric Menicon lenses in subjective lens handling ratings.

4 Study Design

This is a 38-subject, prospective, randomized, double masked, (investigator and participant), bilateral, 1 month cross-over study comparing the handling characteristics, (insertion & removal), of asmofilcon A toric lenses against fanfilcon A silicone hydrogel toric lenses (table 1). It is anticipated that this study will involve up to 6 scheduled visits: At the first visit, (V1), subject's habitual toric lenses will be evaluated and then re-fitted with both study lenses [redacted] At the second visit, (V2), the first pair of study lenses, (e.g., asmofilcon A or fanfilcon A toric lenses), will be dispensed. After 2 -weeks of daily wear, subjects will return for a third evaluation, (V3), and a 4-week visit will be scheduled. At the 4-week visit, (V4), pair 1 will be evaluated and then pair 2 dispensed. Next, a 2-week, (V5), and 4-week visits, (V6) will be scheduled. At visit 6, subjects will exit the study. [redacted]

5 Investigational Sites

5.1 Number of Sites

This will be a single center investigational site in Mexico City. (Target 38 subjects).

5.2 Investigator Recruitment

This study will be conducted at the School of Optometry Clinic; National Autonomous University (UNAM) Mexico City. The Investigators will be required to fulfil the following criteria:

- Licensed Optometrist with at least two years of contact lens fitting experience.
- Experienced Investigators who will be trained in Good Clinical Practice (GCP) by the principal investigator.
- In-office email or fax.
- Willingness to follow the study protocol and to co-operate with the study monitors.

This clinical study is designed to be in conformance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for Good Clinical Practice (GCP) and all the applicable local guidelines.

6 Ethics Review / Statement of Compliance

6.1 Relevant Standards / Guidelines

This implementation document has been developed in accordance with the following:

- ISO 14155 Clinical Investigation of Medical Devices for Human Subjects, Parts 1 & 2, 2011.
- ICH Harmonized Tripartite Guideline for Good Clinical Practice E6, 1996.
- Declaration of Helsinki
- COFEPRIS Applicable Guidelines

6.2 Institutional Review Board

This study will be conducted in accordance with Institutional Review Board regulations (U.S. 21CFR Part 56.103) or applicable IEC regulations. Copies of all IRB/IEC correspondence with the investigator/sponsor will be kept on file. The study will commence upon approval from the following Ethics Committee: Comisión de Ética de la FESI. Avenida de los Barrios no. 1, Los Reyes Iztacala, Tlalnepantla Edo. de México. CP 54090. Telephone number 56-23-12-20 and email address jrjf@unam.mx.

6.3 Clinical Trial Registration

This study will be registered with clinicaltrials.gov in accordance with section 801 of the Food and Drug Administration (FDA) Act which mandates the registration of certain clinical trials of drugs and medical devices.

6.4 Informed Consent

Informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is carried out.

7 Potential Risks and Benefits to Human Subjects

There may be direct benefits to the subjects in this study such as improved vision, comfort, convenience, and cosmetic advantage. Participation in a study may contribute to scientific research information that may be used in the development of new contact lens products. In addition, subjects will receive an examination of the front part of their eyes and may have the opportunity to try a different type of soft contact lenses and/or different lens care products at no cost to them. The contact lens materials used in this study are commercially available as daily or extended wear. This study will investigate participants' wearing schedule intended for daily wear (NOT extended wear) similar to the average wearing time of 10-16 hours for daily wear lenses.

This study is considered to be a non-significant risk study based on United State Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines because the study devices used as intended in this study (daily wear) don't represent a potential for serious risk to the health, safety or welfare of the subject, and (2) it is not an implant, (3) it is not used to support or sustain human life, (4) it is not of substantial importance in diagnosing, curing, mitigating or treating disease or otherwise prevents impairment of human health, (5) does not present a potential for serious risk to the health, safety or welfare of the subject (Appendix 2).

Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The incidence of infection due to day-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. This risk is assumed by 35-million Americans who currently wear contact lenses.

Routine clinical procedures including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and contact lens fitting will be used. In addition, high magnification imaging of the lens fit may be made using 35 mm or digital cameras, in vivo confocal microscopy, and/or specular microscopy. Patients will be monitored every two weeks until the end of the study to reduce if not eliminate the occurrence of adverse or potential adverse events. Patients will be given instructions from their ECP regarding early symptoms and signs of adverse events and their contact information.

8 Materials and Methods

8.1 Participants

Approximately **38 habitual** soft toric contact lens wearers will be enrolled. Each subject will be required to attend up to **six** scheduled study visits over a period of approximately two months.

Each subject will be given a unique ID number. Additionally, all subjects must meet the study inclusion and exclusion criteria listed below.

Inclusion criteria

A person is eligible for inclusion in the study if he/she:

- A person is eligible for inclusion in the study if he/she:
- Is between 18 and 40 years of age (inclusive)
- Has had a self-reported visual exam in the last two years
- Is an adapted soft contact lens wearer
- Is not a habitual wearer of either study lens
- Has a contact lens spherical prescription between +4.00 to - 10.00 (inclusive)Best corrected visual acuity of 20/30 or better in either eye
- Have contact lens prescription of no less than -0.75D of astigmatism and no more than -2.25 D in both eyes.
- Can achieve best corrected spectacle distance visual acuity of 20/25 (0.10 logMAR) or better in each eye.
- Can achieve a distance visual acuity of 20/30 (0.18 logMAR) or better in each eye with the study contact lenses.
- Has clear corneas and no active ocular disease
- Has read, understood and signed the information consent letter.
- Patient contact lens refraction should fit within the available parameters of the study lenses.
- Is willing to comply with the wear schedule (at least 5 days per week, > 8 hours/day assuming there are no contraindications for doing so).
- Is willing to comply with the visit schedule

Exclusion Criteria

A person will be excluded from the study if he/she:

- A person was excluded from the study if he/she:
- Has a CL prescription outside the range of the available parameters of the study lenses.
- Has a spectacle cylinder less than -0.75D or more than -2.50 D of cylinder in either eye.
- Has a history of not achieving comfortable CL wear (5 days per week; > 8 hours/day)
- Has contact lens best corrected distance vision worse than 20/25 (0.10 logMAR) in either eye.
- Presence of clinically significant (grade 2-4) anterior segment abnormalities
- Presence of ocular or systemic disease or need of medications which might interfere with contact lens wear.
- Slit lamp findings that would contraindicate contact lens wear such as:
    - Pathological dry eye or associated findings
    - Pterygium, pinguecula, or corneal scars within the visual axis
    - Neovascularization > 0.75 mm in from of the limbus

- Giant papillary conjunctivitis (GCP) worse than grade 1
- Anterior uveitis or iritis (past or present)
- Seborrheic eczema, Seborrheic conjunctivitis
- History of corneal ulcers or fungal infections
- Poor personal hygiene
- Has a known history of corneal hypoesthesia (reduced corneal sensitivity)
- Has aphakia, keratoconus or a highly irregular cornea.
- Has Presbyopia or has dependence on spectacles for near work over the contact lenses.
- Has undergone corneal refractive surgery.
- Is participating in any other type of eye related clinical or research study.

8.2 Study Materials

8.2.1 Contact lens

All subjects will be trial fitted and, if suitable, dispensed the Avaira Vitality™ toric and Miru 1month toric lenses. The study toric lenses and solutions will be provided by the Sponsor. Details of the contact lenses are shown in Table 1.

Table1: Study lenses

	Avaira Vitality™ toric	Miru 1month Menicon toric
Manufacturer	CooperVision	Menicon
Material	fanfilcon A	asmofilcon A
WC %	55%	40%
Base Curve	8.5 mm	8.6 mm
Lens Diameter	14.5 mm	14.0 mm
Lens Powers Sphere	+4.00 to – 10.00	+4.00 to -10.00
Lens Power Cylinder	-0.75, -1.25, - 1.75, -2.25	-0.75, -1.25, - 1.75, -2.25
Axis cylinder	10 degrees to 180 degrees in 10 degree steps	10 degrees to 180 degrees in 10 degree steps
Wearing schedule	Daily wear	Daily wear

8.2.2 Contact Lens care

OPTI-FREE® PureMoist® multipurpose disinfecting solution and lens cases (Alcon, Fort Worth, TX) will be provided to all subjects for care and maintenance of the contact lenses during the study.

8.2.3 Storage of Study Medications/Treatments

There are no unapproved investigational products used in this study requiring special storage accommodations.

8.2.4 Clinical Supply Inventory

There are no unapproved investigational products used in this study requiring special inventory requirements.

8.2.5 Disposal of Consumables

This study dispenses consumables (lenses) to participants for use during the study. Study lenses worn for the full 1-month of daily wear by participants will be collected at the last visit and destroyed.

8.2.6 Masking and Control of Study Materials

The study contact lenses will be **masked to BOTH, the subject and investigator**. Study lenses will be transferred, by an assistant, out of their packaging to unmarked new contact lens cases filled with unpreserved sterile saline just prior to dispensing to maintain subject masking of the study lenses.

8.2.7 Ordering and Accountability of Study Materials

The study lenses and solutions will be provided by the sponsor. If additional lenses are required, the study sponsor will re-supply the investigator as requested.

8.3 Visit Schedule and Procedures

8.3.1 Visit 1: Baseline and fitting visit (screening and enrollment)

The following evaluations will be performed to assess eligibility according to the Inclusion and Exclusion Criteria at the baseline visit only:

- The subjects should attend the first visit wearing their habitual contact lenses and having worn them that day for at least 2 hours prior to the visit. If they are not wearing their lenses, please reschedule the visit.
- The subject will be required to read and sign an Informed Consent Form prior to enrolment. When the subject has signed the consent form, the subject will be considered to be enrolled on to the study.
- The person explaining the consent and Investigator should also sign the consent form. Provide the subject with a copy and keep the original in the subject's paper chart or scan into the subject's electronic medical record (EMR) file.
- The subject is assigned with a Subject ID number. Subjects must be enrolled sequentially.

- Full anterior segment ocular health will be established.
-

Visit 1a: Baseline habitual lenses

- Details of current lens:
  - Brand (no more than three subjects in any study lens brand allowed)
  - Power(s)
  - Replacement schedule (daily, 2-week, monthly)
  - Lens age (days).

The following baseline measurements and assessments will be recorded:

- [redacted]
- [redacted]
- [redacted]
- Habitual lens subjective binocular ratings
  - [redacted]
  - Handling (insertion & removal, 0-10 scale)
  - [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

[redacted]

- Complete the eligibility checklist.
- If at this point the subject is found to be ineligible, then complete an Exit form and exit the subject from the study.

Visit 1 b: Trial fitting visit

If eligible, complete the Enrolment Log and identify the test lens [redacted] The subjects will undergo a trial fit in both eyes with both study lenses (e.g., Avaira Vitality Toric and Miru 1month Menicon toric, according to manufacturer's fitting guides) to ensure optimization of the lens parameters needed to provide the best distance visual acuity. Re–order final lens if appropriate. If the lenses are not suitable to be dispensed, then the subject will be discontinued and an Exit form will be completed.

8.3.2 Visit 2: Dispense pair 1

- Data is only collected on the final pair of study lenses dispensed after the power has been assessed and if needed corrected.

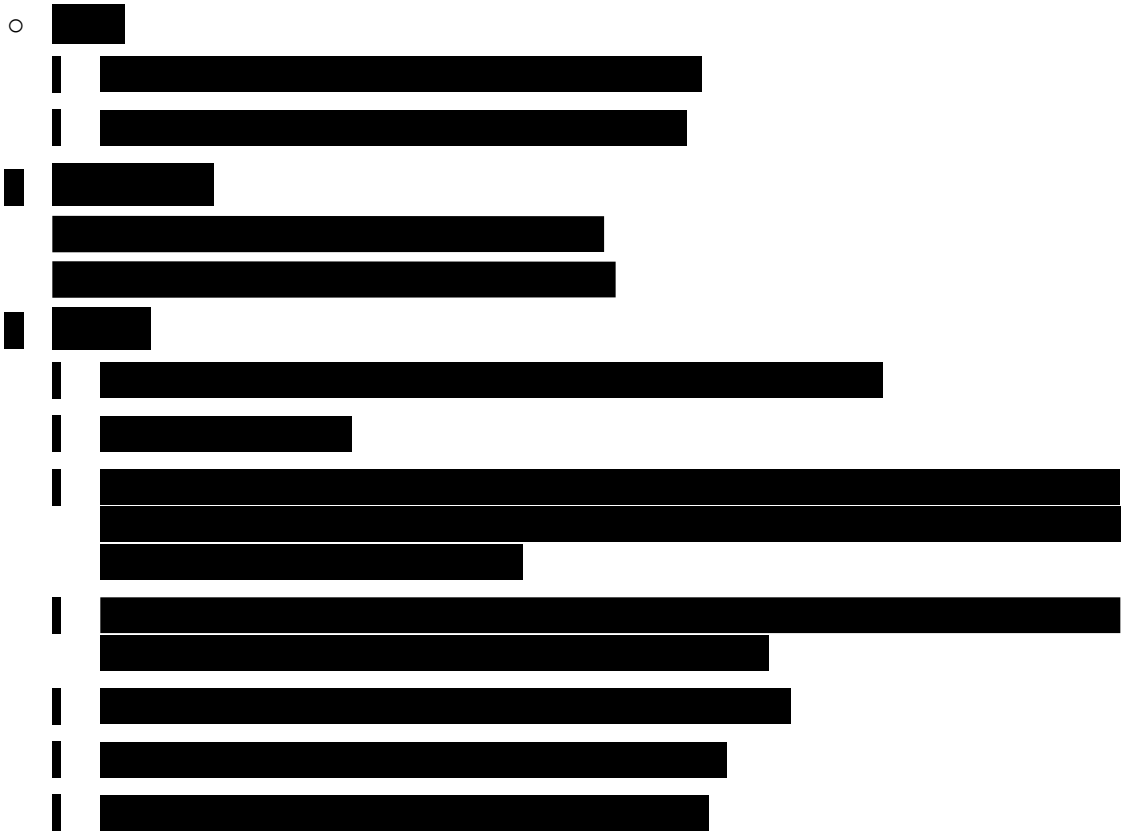
- Record the parameters of the lenses, [redacted] on the Dispensing CRF [redacted]
- [redacted]
  - [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- Lost or damaged study lenses may be replaced. Note which lens was replaced, date of replacement and reason for replacement on the Lens Replacement Log, [redacted]
- The subject will be instructed to wear the lenses on a daily wear basis, (at least 40 hours per week), until the 2-weeks follow-up appointment, unless they experience a problem which warrants lens removal.
- The Investigator or a clinical assistant will review instructions and warnings for lens wear, when to remove lenses, and other important issues with the participant.

- Participants, who appear unable or unwilling to follow instructions to a degree that, in the Investigator's opinion, jeopardises the participant's wellbeing or the validity of the study, will be discontinued. The reason for discontinuation will be documented.
- The subject will be discharged and asked to return for a follow-up visit (V2) after 1-month.

8.3.3 Visit 3: 2-week follow-up pair 1

The 2-week follow-up visit will be scheduled one month **(14 ± 2 days)** from the initial lens dispensing date. The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible, within the visit window.

- The following clinical test variables will be recorded on the Follow-Up Visit CRF:
  - [redacted]
  - Subjective Assessments
    - [redacted]
    - Handling (insertion & removal, 0-10 scale)
    - [redacted]
    - [redacted]
    - [redacted]

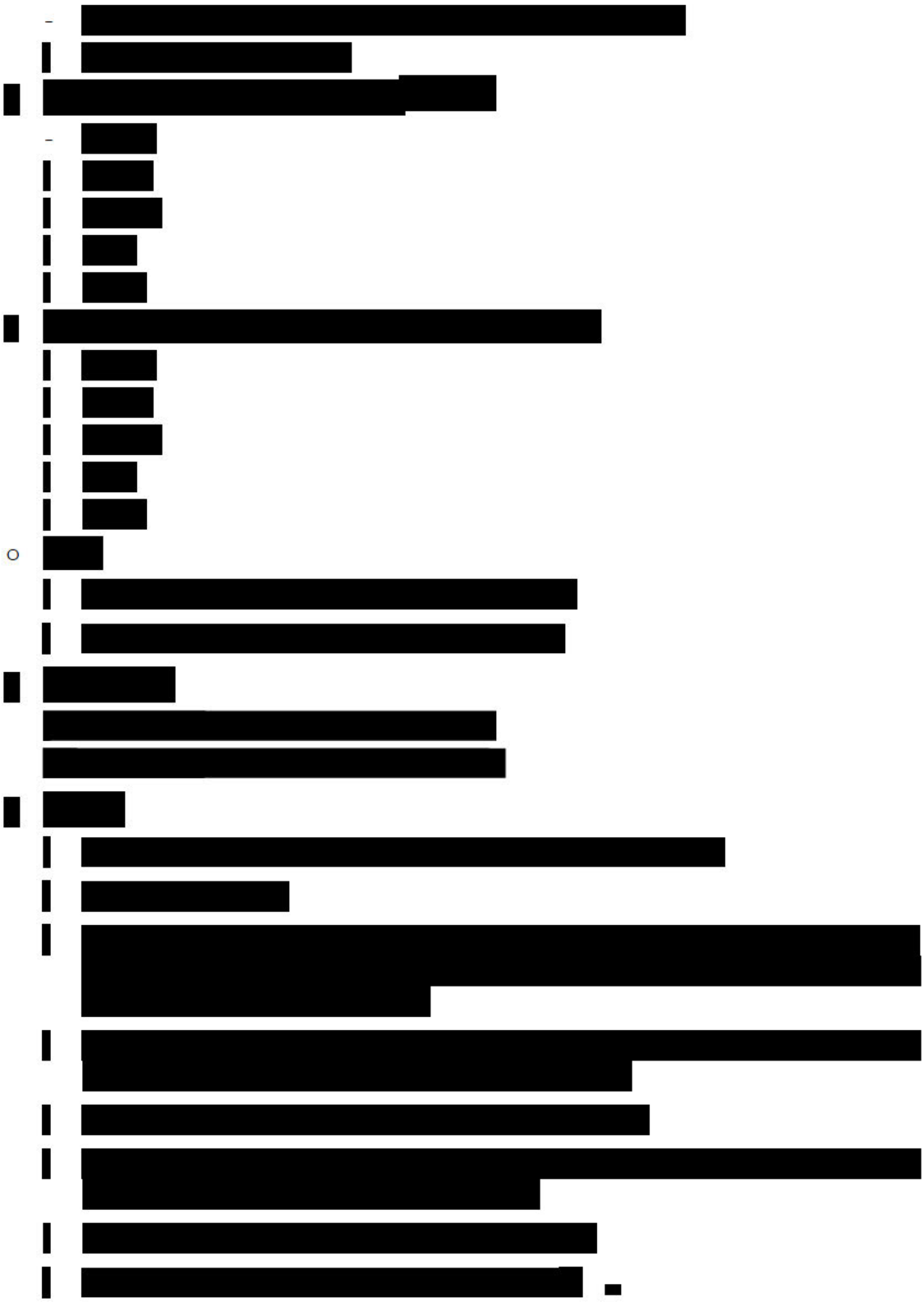


8.3.4 Visit 4: 1-month follow-up pair 1/dispenses pair 2

The 1-month follow-up visit will be scheduled one month **(28 + 2 days)** from the initial lens dispensing date. The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible, within the visit window.

Visit 4a: Lens evaluation pair 1

- The following clinical test variables will be recorded on the Follow-Up Visit CRF:
  - Subjective Assessments
    - Handling (insertion & removal, 0-10 scale)



Visit 4b: Dispense pair 2

The study subjects will undergo a trial fit in each eye with the second pair of study lenses.

- The performance of the second pair of study lenses should be assessed after 10-15 minutes settling time and the same variables as those collected on *visit 2* (section 8.3.2) will be assessed.

8.3.5 Visit 5: 2-week follow-up pair 2

The 2-week follow-up visit will be scheduled one month (14 + 2 days) from the initial lens dispensing date. The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible, within the visit window. The same variables as those collected on section **8.3.3** will be assessed at this visit.

8.3.6 Visit 6: 1-month follow-up pair 2 / Exit

Visit 6a: Lens evaluation pair 2

The 1-month follow-up visit for pair 2 will be scheduled one month **(28 ± 2 days)** from the initial lens dispensing date for pair 2. The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible, within the visit window. The same variables as those collected on section **8.3.4** will be assessed at this visit.

Visit 6b: Study exit

- The Study Exit Form must be completed when a subject exits the study. This will occur either at study completion, i.e., at Visit 3, or if the subject is discontinued from the study at another time. If there are records entered into the clinics own patient chart system the exit date should be recorded on these source documents.
- A Study Exit Form must be completed for all subjects who have taken a study ID number. Post-study follow-up visits will be scheduled if the Investigator judges this is necessary.
- At the study Exit Visit the following measurements are taken:
  - [redacted]
  - [redacted]
  - [redacted]

- Post-study follow-up requirement (Y/N). If yes, the reason and date of the follow-visit must also be recorded.

- If the subject is being exited due to discontinuation, further details need to be recorded on the exit form.

9 Adverse Event Reporting

9.1 Adverse Response Definitions

Adverse Event (AE): An AE refers to any untoward medical occurrence (sign, symptom or disease) in a trial subject that does not necessarily have a causal relationship with the study device. AEs may be classified as 'unanticipated adverse device effects,' 'serious AEs,' 'significant AEs,' or 'non-significant AEs,' as defined below.

Classification	Definition
Serious Adverse Event	Those events that are life-threatening, or result in permanent impairment of a body function, or permanent damage to a body structure or necessitate medical (therapeutic) or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
Unanticipated Adverse Device Effect	Adverse events in a clinical trial that were not previously identified in the protocol in terms of nature, severity, or degree of incidence. An Unanticipated Serious Adverse Device Effect is an unanticipated adverse event that is serious in nature and caused by or associated with the device and is considered reportable.
Significant Adverse Event	Those non-serious adverse events that occur with contact lens usage that are not sight-threatening but are usually symptomatic and may warrant therapeutic management and /or temporary or permanent discontinuation of contact lens wear.
Non-Significant Adverse Events	Those less severe non-serious adverse events that occur with contact lens usage that are not sight-threatening, may or may not be symptomatic and may warrant palliative management, such as ocular lubricants or temporary interruption of contact lens wear.

AE classification, coding (for reporting to the sponsor) and examples are provided in the following table of Contact Lens Adverse Event Classification and Reporting:

Code	Condition	Potential AE Classification	Reporting
01	Presumed infectious corneal ulcer	SERIOUS	Notify sponsor as soon as possible, **within 24 hrs;** IRB
02	Permanent loss of ≥2 lines of best spectacle corrected visual acuity (BSCVA)	SERIOUS	

03	Corneal injury that results in permanent opacification within central cornea (6mm)	SERIOUS	reporting as per requirements
04	Neovascularization within the central 6mm of cornea	SERIOUS	
05	Uveitis or Iritis	SERIOUS	
06	Endophthalmitis	SERIOUS	
07	Hyphema	SERIOUS	
08	Hypopyon	SERIOUS	
09	Persistent epithelial defect	SERIOUS	
00	Other serious event	SERIOUS	
11	Peripheral non-infectious ulcer (outside central 6mm)	SIGNIFICANT	Notify sponsor as soon as possible, within 5 working days; IRB reporting as per requirements
12	Symptomatic corneal infiltrative events	SIGNIFICANT	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	SIGNIFICANT	
14	Any temporary loss of ≥2 lines BSCVA for ≥2wks	SIGNIFICANT	
15	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (i.e. moderate staining)	SIGNIFICANT	
16	Corneal neovascularization ≥ 1.0mm to 1.5mm vessel penetration (if 2 Grade change from baseline)	SIGNIFICANT	
17	Any sign and/or symptom for which subject is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	SIGNIFICANT	
10	Other significant event	SIGNIFICANT	
21	Conjunctivitis: bacterial, viral, allergic	NON-SIGNIFICANT	
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (if 2 Grade change from baseline)	NON-SIGNIFICANT	
25	Asymptomatic corneal infiltrative events	NON-SIGNIFICANT	
26	Localized allergic reaction	NON-SIGNIFICANT	
27	Contact dermatitis	NON-SIGNIFICANT	
28	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended	NON-SIGNIFICANT	
20	Other non-significant sign and/or symptom	NON-SIGNIFICANT	

Normal or adaptive symptoms

Transient symptoms such as end-of-day dryness, lens awareness, itching or burning or other discomfort may occur with contact lens wear and may occasionally reduce wearing time. ***These***

are not reported as adverse events unless they are unexpected in nature, severity or rate of occurrence.

9.2 Procedures for Adverse Events

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the subject may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the test device or a result of other factors.

An Adverse Event Form will be completed for each adverse event. If both eyes are involved, a separate Adverse Event Form will be completed for each eye. Whenever possible, the adverse event will be photo-documented.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The subject must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

9.3 Discontinuation from the Study

All discontinuations will be fully documented on the appropriate CRF Exit and Adverse Event forms as needed. Participants will be followed until resolution (in most instances) and are free of the ophthalmic insert related complications or other ocular pathology. When possible study lenses involved in an Adverse Event will be returned to the sponsor in a new tightly sealed contact lens case, and labeled with the subject identification and stored in Unisol non-preserved saline.

9.4 Reporting Adverse Events

All potential **Serious and Unanticipated Adverse Device Effects** that are related or possibly related to subject participation in the investigation will be reported to the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the EC/IRB as soon as possible (by fax, mail/delivery, phone, or email), but within 10 business days of becoming aware of the problem. *All fatal or life threatening events will be reported immediately to the IRB.*

Significant and Non-Significant Adverse Events will be reported to the sponsor as soon as possible, but no later than 5 working days after the occurrence. [redacted]

10 Statistical Analysis and Sample Size

10.1 Statistical analysis

Summary statistics will be produced (e.g., mean, standard deviation). Differences between lenses will be compared using Paired t-tests. Paired t-tests /analysis of variance for normal (interval/continuous) data, Wilcoxon's signed ranks test for non-normal (ordinal) data, chi-squares test for nominal data. A Binomial test will be used to evaluate lens preference questions. All participants who were evaluated will be used in the analysis. In the event of missing data, individual data points will be excluded in the analysis and not extrapolated from the collected data.

10.2 Sample size

Figure 1 shows the sample size determination for a paired t-test, (alpha=0.05), in order to detect a difference in mean subjective handling scores between lenses. Assuming a standard deviation of 1.2, a sample size of about 33 completed subjects provides 90% power to detect a difference in subjective handling ratings of 0.7 points on a 0 - 10 scale. In order to account for potential subject dropouts or AEs, 10%-15% should be added to the sample size. Therefore, 38 subjects should be enrolled with the aim to complete 33.

11 Data Quality Assurance

11.1 Study monitoring

A site visit or discussion may be conducted during the course of the study as appropriate. Prior to final data freeze, a close-out visit/discussion may be warranted to check for accuracy and completeness of records. The sponsor or sponsor's representatives will be authorized to gain access to the source documentation for the purposes of monitoring and auditing the study.

11.2 Record keeping

Detailed records of all study visits will be made using the electronic Case Report Forms (CRFs).

11.3 Record retention

Following study completion, data will be available in electronic and/or paper format for audit, sponsor use, or subsequent analysis. The original clinical raw data (including completed CRFs and Informed Consent forms) will be retained according to guidelines set forth in the general work agreement with the site. The Sponsor will be notified and consulted if ever the files are to be destroyed. In the event that this implementation document is indicated for design verification and validation purposes, as indicated on the title page, all original raw data forms and completed CRF's will be forwarded to the sponsor at completion of the final report.

11.4 Data Entry / Data Management

Data will be entered into an electronic spreadsheet. Study staff will only be able to modify the data file via password entry. The investigators will be responsible for the data integrity, and complete data entry for each visit as well as the take home questionnaires. The investigator will send the data collected to the study sponsor within 5 business days after the last subject completes the final visit.

11.5 Confidentiality

This study is confidential in nature. All information gathered during this study is proprietary and should be made available only to those directly involved in the study. Information and reports arising from this project are the property of the sponsor.

All records will also be handled in accordance with HIPAA (1996).

11.6 Publication

The investigators will not be permitted to publish or present at scientific meetings results obtained from the clinical study without prior written consent from the sponsor.

[redacted]

APPENDIX 1 – STATEMENT OF INFORMED CONSENT

APPENDIX 2- STUDY TIMELINE *

TASK	Aug-2021	Sept-2021	Oct-2021	Nov-2021	Dec-2021	Jan-2022
Generate study Protocol.	Aug 16 - 19					
Protocol EC submission.	Aug 19-20					
Protocol EC approval.	Sept 20th					
First Subject First Visit (FSFV).		Week of Sept 20th				
Last Subject Last Visit (LSLV).				Week of Nov 30th		
Study report.					Dec 15th.	

**This timeline is subject to change depending on COVID-19 situation, participant enrollment, lens power availability, and study progress.*

APPENDIX 3-LENS RANDOMIZATION

APPENDIX 4 – LENS REPLACEMENT LOG

Date	Investigator Initials	Subject Initials	Visit Just Prior to Lens Replacement	Number of Days Lens was Worn prior to Replacement	Lens Replaced (check one)	Reason
Click here to enter a date.					☐ Right ☐ Left ☐ Both	
Click here to enter a date.					☐ Right ☐ Left ☐ Both	
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Click here to enter a date.					☐ Right ☐ Left ☐ Both	

APPENDIX 5 – GRADING SCALES

GRADING & MEASUREMENT SYSTEM

Variable	Assessment Method	Grading/Measurement System
Wearing Times		
Average # of days lenses worn in a week	Enter the number of days lenses are worn during the week.	Days per week
Average Daily Wearing Time	Typical time of day when lenses inserted and removed.	Time of day to nearest half hour
Average # of hours of wear per day	Enter the number of hours lenses are worn per day.	Hours per day
Average Comfortable Wearing Time	Typical time of day when subject first experiences lens awareness or irritation.	'Does CL comfort deteriorate during wear?' (tick-box). If yes, record time of day to nearest half hour when first aware of lenses
Typical Removal Time	Typical time of day when subject removes the lens.	Time of day to nearest half hour
Subjective Assessments (Questions asked by the investigator and recorded)		
Comfort, dryness, handling, lens fit, vision satisfaction.	Assessed by subject on a 0-10 scale.	0-10 scale Comfort: (10= can't feel) Dryness: (10=no dryness) Handling: (10=very easy) Fit stability (10=very stable) * Vision: (10=very satisfied)
Vision Quality	Assessed by subject on a 0-10 scale.	Vision quality: (10=Excellent vision, totally sharp)
Night Vision Quality	Assessed by subject on a 0-10 scale.	Vision quality: (10=Excellent vision, totally sharp)
Vision Stability	Assessed by subject on a 0-10 scale.	Vision stability: (10=perfectly stable, not fluctuating, changing)
Satisfaction	Subject's assessment of various symptoms on a 4-point Likert scale.	1. Completely satisfied 2. Somewhat satisfied 3. Somewhat dissatisfied 4. Completely dissatisfied
Preference	Subject's preference for one of two contact lenses.	Forced choice: Study lenses or Habitual
Vision		
Distance VA – High contrast	Measured using Snellen or logMAR chart.	Snellen or logMAR visual acuity (VA) to nearest letter.

Variable	Assessment Method	Grading/Measurement System
Lens Surface assessed using slit lamp		
Front Surface Wettability	Lens surface viewed with a slit lamp, white diffuse light and broad beam under low-medium magnification.	0 – 4 0=poor 4=excellent
Lens surface deposits assessed using the slit-lamp		
Front Surface Deposits	Lens surface deposits viewed with a slit lamp, white diffuse light and broad beam under low-medium magnification.	0 Clean, no deposits 1 5 or less small deposits (<0.1 mm) 2 > 5 deposits of <0.1 mm size or film covering 25-50% of surface 3 Deposits of between 0.1 and 0.5 mm or film covering 50-75% of surface 4 Deposits of 0.5 mm or larger or film covering more than 75% of surface
Lens Fit- assessed using slit lamp		
Lens Centration	Lens centration will be recorded by degree and direction in the primary position.	0 Centered - optimal 1 Decentered slightly 2 Substantially decentered (≥0.5mm) If decentered, direction(s) will be recorded as: Superior, Inferior, Nasal, Temporal
Corneal Coverage	Assessed in primary gaze.	Y Yes, full corneal coverage at all times N No, incomplete corneal coverage
Post-Blink Movement	Assessed immediately after the blink - lower lid to be depressed only if necessary, for observation.	0 Insufficient, unacceptable movement 1 Minimal, but acceptable movement 2 Optimal movement 3 Moderate, but acceptable movement 4 Excessive, unacceptable movement
Lens orientation in primary position of gaze	Slit lamp, with 10x magnification. Nasal mislocation is recorded as (+) and temporal as (-)	Mislocation of the axis mark on the lens relative to the 6 o'clock position, zero rotation, measured in degrees.
Overall stability	Slit lamp, with 10x magnification.	(0–4 scale), where 0=very poor, 4= excellent
Rotational recovery in degrees after 60 seconds	Slit lamp, with 10x magnification.	Lens ability to return to its original position measured 60 seconds after manually rotating the lens 45^0 degrees temporally. Rotational recovery (RR) is assessed by manually rotating the lens 45° temporally from the primary gaze orientation (PGO) and allowing one minute (60 seconds) for the lens to recover. The absolute difference between the position of the lens following the recovery period and the PGO is taken as the measure of interest.

Variable	Assessment Method	Grading/Measurement System
Overall Fit Acceptance	Assessed by the Investigator based on lens fit alone (i.e., not comfort or vision).	0 Should not be worn 1 Borderline but unacceptable 2 Min. acceptable, early review 3 Not perfect but OK to dispense 4 Perfect
Biomicroscopy		
Limbal & Bulbar Hyperemia	Assessed using slit lamp with white light, low-medium magnification. (Use Brien Holden Vision Institute grading scales for reference) ½ grades recorded.	0 NONE: No injection present 1 VERY SLIGHT 2 SLIGHT 3 MODERATE 4 SEVERE
Lower palpebral hyperemia	Assessed using slit lamp with white light, low-medium magnification. (Use Brien Holden Vision Institute grading scales for reference) ½ grades recorded.	0 NONE: No injection present 1 VERY SLIGHT 2 SLIGHT 3 MODERATE 4 SEVERE
Corneal Infiltrates	Assessed using slit lamp with diffuse white light, low-medium magnification.	0 NONE: No infiltrates 1 TRACE: One faint peripheral infiltrate that does not stain. 2 MILD: A few mild infiltrates 3 MODERATE: Multiple dense infiltrates 4 SEVERE: Marked infiltrates with overlying staining.
Other Slit Lamp Findings	This section is intended to capture less commonly observed clinical entities such as conjunctival infection, EKC, corneal ulcers, lens adhesions, and recurrent erosions. The complication should be identified, described and graded by severity using the 0-4 scale.	0 None 1 Trace 2 Mild 3 Moderate 4 Severe

APPENDIX 6– CRF's / UNSCHEDULED VISIT & ADVERSE EVENT FORM