CooperVision™

PROTOCOL

DAILY DISPOSABLE DISPENSING CLINICAL TRIAL OF NEPTUNE LENS AGAINST MYDAY LENS

Sponsor Study Code:	CV-16-60
Version Number:	2.3
Implementation document Date:	31 AUG 2016
Sponsor Company:	CooperVision, Inc.
Study Category:	Design Validation
Clinical Sites:	CORL, Indiana University TOSI, University of Houston

Protocol Sponsor: [redacted] Date [redacted]

[redacted]

Site Principal Investigator: [redacted] Date: [redacted]

[redacted]

Site Principal Investigator: [redacted] Date: [redacted]

[redacted]

TABLE OF CONTENTS

1 Introduction

CooperVision is evaluating the clinical performance of MyDay 1-Day lenses (Neptune test lenses) [redacted]

2 Study Objective

The purpose of this study is to investigate the overall clinical performance of the Neptune daily disposable silicone hydrogel lens (test) compared to the MyDay lens (control).

This is a study to validate the performance of Neptune lenses when worn on a daily disposable wear modality over 1 month (for each lens).

The primary variables of interest are:

- Comfort (subjective ratings)
- Vision (logMAR, high and low illumination, and subjective ratings)
- Anterior ocular health (corneal staining, conjunctival staining and hyperemia)

Secondary variables are:

- Lens fit performance
- Handling (subjective ratings)
- Lens surface wettability and deposit resistance

[redacted]

- Dryness

[redacted]

3 Study Design

This will be, prospective, multicenter, double-masked, randomized, bilateral, 1 month cross-over, dispensing study comparing the Neptune test lens against the MyDay control lens with a study duration of approximately two months.

Each subject will be randomized to wear either the test or control as a matched pair first and subjects will be randomized based on the order in which the subject is enrolled and qualified into the study.

Both test and control lenses will be used in a daily disposable lens wear modality for one (1) month. It is anticipated that this study will involve 5 scheduled visits:

- Visit 1: Enrollment/ Screening/ Baseline/Fitting/Dispensing of first pair of lens
- Visit 2: 1-week follow-up visit (Day 7±3)
- Visit 3: 4-week follow-up visit for the first pair and dispensing visit of the second pair of contact lenses (Day 28±4)
- Visit 4: 1-week follow-up visit of second pair (Day 7±3 from dispense of second pair)
- Visit 5: 4-week follow-up for the second pair and exit visit (Day 28±4 from dispense of second pair)
- Subjective questionnaires will be collected at the following timepoints:
  - Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) at baseline,
  - Dispensing/visit 1: Baseline and dispensing questionnaires,
  - Visits 2 and 4: One week questionnaire, and
  - Visits 3 and 5: One month questionnaire

Visits that fall outside of the specified visit windows or repeat visits within the window will be classified as unscheduled visits for analysis purposes.

4 Ethics Review / Statement of Compliance

4.1 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
- ICH Harmonized Tripartite Guideline for Good Clinical Practice
- Declaration of Helsinki

4.2 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 conduct of this study will occur at two sites, TOSI at the University of Houston and CORL at Indiana University. The conduct of this study will be approved for each site by an Institutional Review Board prior to commencement.

4.3 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.

5 Clinical Trial Registration

This study will be registered in the clinical trials registry (www.ClinicalTrials.gov or equivalent) by the study sponsor.

[redacted]

7 Materials and Methods

7.1 Subjects

This study will recruit at two clinical sites, The Ocular Surface Institute (TOSI) at the University of Houston, and the Clinical Optics Research Lab (CORL) at Indiana University. Up to 70 participants will be dispensed across both sites with the aim of completing study products to 60 participants across both sites.

Potential participants will be identified from the investigators' clinic database records and/or will be actively recruited by advertisements circulated at the investigational sites as approved by the appropriate IRB.

There are no provisions for replacing subjects who are discontinued from the study.

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:

- Has had a self-reported oculo-visual examination in the last two years.
- Is at least 18 years of age and has full legal capacity to volunteer.
- Has read and understood the information consent letter.
- Is willing and able to follow instructions and maintain the appointment schedule.
- Is correctable to a visual acuity of 20/40 or better (in each eye) with their habitual vision correction or 20/20 best-corrected.
- Must achieve 20/30 or better (in each eye) with study lenses
- Requires spectacle lens powers between -0.75 and -6.50 diopters sphere (0.25D steps).
- Has no more than 0.75 diopters of refractive astigmatism.
- Currently wears soft contact lenses.
- Have clear corneas and no active ocular disease.
- Has not worn lenses for at least 12 hours before the examination

Exclusion Criteria

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

- Has never worn contact lenses before.
- Has any systemic disease affecting ocular health.
- Is using any systemic or topical medications that will affect ocular health.
- Has any ocular pathology or severe insufficiency of lacrimal secretion (moderate to severe dry eyes) that would affect the wearing of contact lenses.

- Has persistent, clinically significant corneal or conjunctival staining using sodium fluorescein dye.
- Has any clinically significant lid or conjunctival abnormalities, active neovascularization or any central corneal scars.
- Is aphakic.
- Has undergone corneal refractive surgery.
- Is pregnant, lactating, or planning a pregnancy at the time of enrolment (by verbal confirmation at the screening visit).
- Have taken part in any other contact lens or care solution clinical trial or research, within one week prior to starting this study.

7.1.1 Repeated Screenings

In some circumstances a repeated screening may need to be scheduled. Examples include, but are not limited to:

a) Incomplete information available at time of screening to determine eligibility (e.g. current lens brands worn, history from current eye care practitioner etc.)
b) Study procedures unable to be completed in time scheduled for visit;
c) Study products not available at the time of the screening visit;
d) A transient health condition which may affect the eye(s) (e.g. a common cold, active allergies, fatigue etc.)
e) The short term use of medications (e.g. antibiotics, antihistamines etc.)
f) Reassessment of baseline ocular conditions (e.g. corneal and/or conjunctival staining, scars etc.)

The maximum total number of screenings permitted will be 3.

7.2 Number of Sites

The study will be take place at two sites.

The College of Optometry at the University of Houston within The Ocular Surface Institute (TOSI), and Indiana University School of Optometry within The Clinical Optics Research Lab (CORL).

These sites were selected based on the experience of the site investigator and staff in conducting clinical trials, the availability of potential study participants, and the interest of the site in performing the trial. A site investigator agreement and financial disclosure document will be in place prior to commencement of the trial.

The investigators and the sites are listed in Appendix 1.

7.3 Study Materials

7.3.1 Contact lens

This study has one investigational silicone hydrogel contact lens, and one comparator silicone hydrogel contact lens.

[redacted]

Details of the Neptune (test) and MyDay (control) study lenses are shown in Table 1. The lenses used in this study will be provided by the Sponsor. Details of the contact lenses are shown in Table 1: Study lenses

	Neptune (test)	MyDay (control)
Manufacturer	CooperVision	CooperVision
Material	stenfilcon A	stenfilcon A
EWC (%)	54%	54%
BOZR (mm)	8.4	8.4
Diameter (mm)	14.2	14.2
Sphere power (D)	-1.00D to -6.00D	-1.00D to -6.00D

Table 1: Study lenses

7.3.2 Contact Lens care

No contact lens care is required for this study as lenses are to be worn for a single day only.

7.3.3 Contact lens dispensing

The lenses will be inserted directly from the blister pack. The use of saline for rinsing prior to insertion is permitted if necessary. Saline will not be dispensed during the study.

Subjects will not be encouraged to use rewetting drops; however, those who habitually used rewetting drops will be allowed to continue using their normal drops. Rewetting drop use will be recorded at each visit.

7.3.4 Storage of Lenses and Lens Care Solutions

The study materials must be stored in a secured area. All lenses and lens care solutions should be stored at controlled room temperature (59-86°F).

7.3.5 Clinical Supply Inventory

The investigator must keep an accurate accounting of the study product during the study. A detailed inventory must be completed for study supplies. The study supplies are to be used in

accordance with the implementation document by subjects who are under the direct supervision of an investigator.

In the event that lenses need to be replaced due to damage/defects before the next scheduled visit, only the damaged/defective lenses will be replaced. A log of lens replacement will be recorded by the site.

7.3.6 Disposal of Consumables

This study dispenses consumables (lenses) to subjects for use during the study. Subjects will be instructed to dispose of worn lenses (both test and control lenses) daily, but retain the foils of all used lens packs and return them at their next study visit. Lenses worn for the scheduled visits will be collected from the subjects and they may be either returned to the Sponsor or disposed. The study lenses (Test and Control) worn by subjects will be collected in plastic lens cases stored in non-preserved saline solution. The control lenses will be sent for destruction and test lenses will be returned to CooperVision at the end of the study unless the investigator is otherwise directed in writing by the study Sponsor for analysis; sponsor to advise closer to the time.

Lenses with product observations (e.g. moderate lens deposits), product defects, or product quality complaints will be collected and returned to CooperVision at the completion of the study. All unworn lenses will be collected from each study subject.

7.3.7 Masking and Control of Study Materials

The contact lenses coding will be masked to both the investigators and subjects as much as possible. A computer generated randomization scheme (Appendix 2) will be used and will be provided to an unmasked member of staff at the study site(s). Study investigators will remain masked to the randomization schedule until the study is completed and the database is locked.

The contact lenses coding will be masked to both the investigator and subject. If standard labelling does not sufficiently mask the study material then over labelling will be performed. However the safety information on the outer package label of the contact lens will not be covered and shall be clearly visible.

Under normal circumstances, the mask will not be broken until all subjects have completed the study and the database is finalized. Otherwise, the mask should be broken only if a specific emergency treatment or course of action would be dictated by knowing the treatment status of the subject. In such cases, the investigator may contact CVI in an emergency to request this information. In the event the mask is broken, the sponsor must be informed as soon as possible. The date, time, and reason for the unmasking must be documented.

7.3.8 Ordering and Accountability of Study Materials

The Neptune test lenses and the MyDay control lenses will be provided by the Sponsor.

The investigator must complete an accurate accounting of the study product at the completion of the study. A detailed inventory must be completed for study supplies. All unused and used materials will be returned to the Sponsor at the end of the study unless the investigator is otherwise directed by the study Sponsor.

7.4 Visit Schedule and Procedures

Prior to lens insertion biomicroscopy (including corneal and conjunctival staining) will be completed at the screening assessment. When possible, the screening will be combined with the baseline assessment.

The investigator should confirm with the subject that they are able to attend the follow-up visits within the visit window before enrolling them in the study.

A scheduled follow-up visit of lens assessment/s may only take place when the subject attends wearing the study lenses. If this is not the case and the subject is not experiencing any problems with the lenses, the appointment will be rescheduled, ideally within the visit window unless they are experiencing difficulty.

Visits that fall outside of the specified visit windows will be counted as unscheduled visits for analysis purposes.

In addition to the screening visit, subjects will attend four visits (not including any unscheduled visits) and will wear the test or control lenses according to the study design.

The test lenses will be worn for one month (24-32 days) and the control lenses will be worn for one month (24-32 days). Lens assessment visits will occur with each pair of lenses.

There will be a minimum of five scheduled visits as follows:

Visit 1: Baseline/Screening/Dispensing Pair 1 (Day 0)

Visit 2: One week follow up for Pair 1 (Day 7±3)

Visit 3: One month follow up for Pair 1/Dispensing Pair 2 (Day 28±4)

Visit 4: One week follow up for Pair 2 (Day 7±3 from dispensing 2)

Visit 5: One month follow up for Pair 2/Exit visit (Day 28±4 from dispensing 2)

At the completion of the four week period of wear with the first pair of lenses there will be a washout period of 10 minutes where subjects wear their spectacles, followed by a dispense and assessment of the second pair of lenses. At the completion of the last visit, subjects will exit the study.

7.4.1 Baseline Visit

Procedures to be Performed

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

- The patient is expected to attend the baseline visit not wearing their habitual contact lens products.
- 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.
- Subject demographics and medical history (age, sex, race and ethnicity, medical conditions, medications, allergies)
- Contact lens history (own lens information, rewetting drop use, and wear time)

[redacted]

- Baseline visual acuity with spectacles or spectacle refraction (logMAR).
- Auto refraction/auto keratometry: Horizontal and Vertical K readings (D)
- Sphero-cylindrical refraction (D), and best sphere refraction (D) & monocular & binocular distance visual acuity (high contrast) (logMAR)
- Slit lamp biomicroscopy will be assessed according to the approved study biomicroscopy CRF (Appendix 3).
- The investigator will confirm that the patient meets the criteria set out in the inclusion criteria, and is eligible to continue in the study.

[redacted]

- The subject will be assigned a randomization ID and the first pair of contact lenses (either test or control) will be selected according to the randomization table (Appendix 2).

- Initial contact lens power chosen based on vertexed, spherical equivalent obtained from refraction. When the desired power is not available, subjects can be fitted with lenses within +/-0.25 of their required contact lens powers. The uncorrected amount will be kept the same for both test and control/s.
- The lenses will be inserted by the subject from the blister pack as described in 7.3.3.
- The lens fit will be assessed for fit acceptance (acceptable or not acceptable) and absence of lens defects. If the fit is acceptable and there are no defects, the subject will be allowed to sit for 10 minutes to allow for the lenses to settle.
- Monocular over refraction will be done to determine if a different power is needed.

  The endpoint of this over refraction will be the minimum minus (-) correction that gives best visual acuity (but not to the point that letters start to shrink in size). A lens change will be implemented if over-refraction dictates. The replacement lens will be allowed to settle.
- Change lens prescription to that noted by over-refraction, if needed.
- Monocular and binocular logMAR visual acuity (4M) will be recorded with high contrast letters under high and low room illumination*.

  [redacted]

  *[redacted]
- The subject will be asked to give subjective ratings after lens settling on:

  [redacted]
  - Comfort (0-10 scale)
  - Dryness (0-10 scale)

  [redacted]
- Monocular lens surface and fit will then be assessed and graded according to the CVI grading scales.
- The lens assessments will include:
  - Lens wettability (0-4 scale)
  - [redacted]
  - [redacted]
  - Lens deposition (0-4 scale) and type of deposit

- Overall lens fit acceptance (0-4 scale)

- The subject will be instructed to wear the study lenses for at least 8 hours per day, maximum of 16 hours per day and a minimum of 5 days per week.
- Subjects will be provided contact lenses for wear until the next scheduled visit.
- At end of visit the subject will be reminded to return for the next scheduled visit of the first pair.

7.4.2 Visit 2: Assessment of pair #1 - One-week visit (Day 4 to Day 10)

Subjects will be asked to wear lenses **within the first four (4) hours after lens insertion** prior to the visit appointment. Subjects who attend without wearing lenses for the specified period will be rescheduled.

- 

- The subject will be asked to give subjective ratings over the last week on:

  - Comfort (0-10 scale)
  - Dryness (0-10 scale)
  - 

[redacted]

- Monocular and binocular logMAR visual acuity (4M) will be recorded with high contrast letters under high and low room illumination.
- Monocular lens surface and fit will then be assessed and graded according to the CVI grading scales. The assessments will include:

  [redacted]

  - Lens wettability (0-4 scale)

  [redacted]

  - Lens deposition (0-4 scale), and type of deposit

  [redacted]

  - Overall lens fit acceptance (0-4 scale)

- The lenses will be removed and retained.
- Slit lamp biomicroscopy will be carried out for the signs outlined in Appendix 3 and in accordance with the current CooperVision grading scales. Grades will be scored to the nearest 0.1 unit in the best judgement of the investigator. Corneal staining will be graded for five regions (central, superior, temporal, inferior and nasal) as well as an 'overall' grade. The predominant type of corneal staining present will also be recorded.
- The same pair of contact lenses will be re-inserted.

7.4.3 Visit 3: One month visit of pair #1 (Day 24 to Day 32)/Dispensing pair #2

Subjects will be asked to wear lenses for **within four (4) hours of lens insertion** *prior to the visit appointment.*

[redacted]

- The subject will be asked to give subjective ratings since the last visit on:

  [redacted]

  - Comfort (0-10 scale)
  - Dryness (0-10 scale)

  [redacted]

- Monocular and binocular logMAR visual acuity (4M) will be recorded with high contrast letters under high and low room illumination.
- Monocular lens surface and fit will then be assessed and graded according to grading scale.

  [redacted]

  - Lens wettability (0-4 scale)

  [redacted]

  - Lens deposition (0-4 scale), and type of deposit

  [redacted]

  [redacted]

[redacted]

- Overall lens fit acceptance (0-4 scale)

- The lenses will be removed and retained.
- Slit lamp biomicroscopy will be assessed according to the CVI approved study biomicroscopy CRF.
- There will be a 10 minutes wash-out before insertion of pair 2.
- Procedures of lens assessment and dispense will be repeated as detailed in section Table 2 for Baseline visit / Dispensing Pair #1.
- *Lens powers of the second pair will be matched with the first pair if possible.*
- The same procedures will be followed for pair 2 as in section 7.3.1.
- The contact lenses will be provided by a study coordinator/technician to maintain masking of the investigator. The lenses will be inserted by the subject from the blister pack after the label is removed by the study coordinator/technician.

Procedure will be repeated as detailed in the Dispensing/Follow up visit for pair 2 for the five week and 2 month visits, sections 7.3.2 and 7.3.3.

7.4.4 Visit 5: Final Visit/Study Exit

Procedures will be repeated as detailed in the Follow up visit section 7.3.3.

- The subject will be asked to give subjective ratings since the last visit on:

[redacted]

- Comfort (0-10 scale)
- Dryness (0-10 scale)

[redacted]

- The lenses will be removed by the subject and retained.
- Slit lamp biomicroscopy assessment will be conducted according to the CV approved study biomicroscopy CRF, using fluorescein
- Exit visual acuity will be performed with habitual glasses (logMAR).
- The subject will be discharged and will sign the exit statement.

7.4.5 Summary of Visits and Procedures

Table 2 summarizes the visits and procedures for the study.

Table 2: Visits and procedures

	Baseline	Dispensing Lens Pair 1	Follow Up Lens Pair 1	Dispensing Lens Pair 2	Follow Up Lens Pair 2	Exit
Informed consent	✓					
Meet inclusion/exclusion criteria	✓					
History at baseline	✓					
LogMAR VA with spectacles or refraction	✓					✓
Auto-refraction & keratometry	✓					
Sphero-cylindrical refraction	✓					
LogMAR Visual Acuity	✓	✓	✓	✓	✓	✓
Sphero-cylindrical refraction	✓					
Slit lamp examination	✓		✓		✓	✓
Insert Lenses		✓		✓		
Over Refraction		✓		✓		
Fit Evaluation		✓	✓	✓	✓	
HIHC, LIHC VA OD, OS, OU (4m)	✓	✓	✓	✓	✓	
Subjective Ratings	✓	✓	✓	✓	✓	
Lens Removal & Storage			✓		✓	
Study exit						✓

8 Adverse Event Reporting

8.1 Adverse Event Definitions

An 'adverse event' refers to any undesirable clinical occurrence in a subject, whether it is considered to be device-related or not. Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' 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.
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.
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.

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

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	Notify sponsor as soon as possible, **within 24 hours;** IRB reporting as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		
11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working**
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	

14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	**days**; IRB reporting as per requirements
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	
17	Any sign and/or symptom for which subject is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	
10	Other significant event	
Non-significant Adverse Events		
21	Conjunctivitis (bacterial, viral or allergic)	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	
23	Asymptomatic corneal infiltrative events	
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	

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 in the investigator's opinion they are unexpected in nature, severe or have a high rate of occurrence.***

This clinical study will also ascertain subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as Adverse Events.

8.2 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.

8.3 Reporting Adverse Events

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to subject participation 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 IRB as soon as possible (by fax, mail/delivery, phone, or email). 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.

8.4 Discontinuation from the Study

A subject's study participation may be discontinued at any time if, in the opinion of the sponsor or the investigator it is in the best interest of the subject. All discontinuations will be fully documented on the appropriate study forms and the Discontinuation Form will be completed.

Subjects will be discontinued at the discretion of the investigator, sponsor or subject. The following is a list of possible reasons for discontinuation from the study:

- Screening failure: Subjects will be discontinued is they do not meet the inclusion and exclusion criteria outlined in section 4.2.1.
- Unacceptable performance with products to be used in study: Subjects may be discontinued if they are unable to achieve acceptable comfort and /or vision with the study products.
- Positive slit lamp finding: Subjects may be permanently discontinued from the study depending on the severity of the condition and on the judgement of the investigator.
- Adverse event: If a subject experiences an adverse event during the study they may be discontinued based on the clinical judgement of the investigator.
- Symptoms: If the subject has persistent symptoms they may be discontinued based on the clinical judgement of the investigator.
- Disinterest, relocation or illness: The subject may choose to discontinue due to reasons within or beyond their control.

- Violation of protocol or non-compliance: The subject will be discontinued if they are unable or unwilling to follow the protocol specified visit schedules and/or study procedures.
- Instillation of topical ocular medication: The subject will be discontinued if they elect to use a topical ocular medication during the study unless that topical ocular medication is prescribed for a limited duration (less than two weeks) to treat a transient condition; in this case the subject may remain an active subject (at the discretion of the investigator) after stopping topical ocular medication following resolution of the ocular condition).
- Lost to follow-up: The subject will be discontinued if they cannot be contacted and does not return for a final exit visit, and if the investigator has made a reasonable effort to contact the subject for a final study visit.
- Premature termination of the study by the sponsor, the clinical sites or the Office of Research Ethics at the sites.

A discontinuation form will be completed, which requires the signatures of both the subject and the investigator except where the subject is lost to follow-up in which case only the signature of the investigator is required.

9 Device Malfunctions

A device malfunction means the failure of the device to meet its performance specification or otherwise perform as intended. *Any defective lens that is likely to cause or contribute to a Serious Adverse Event should be reported to the Principal Investigator and the sponsor* ***within 24 hours*** *of the investigator becoming aware of the malfunction.*

Other defective lenses should be reported to the Sponsor as soon as possible.

10 Statistical Analysis

10.1 Sample Size Calculation

A sample size of 60 completing subjects is sufficient to detect a mean difference of 10 (0 – 100) in subjective ratings and 30% difference in ocular health incidents assuming α=0.05 and a power of 80% (Table 3). Approximately 70 subjects will be enrolled assuming the dropout rate of 10% to 15%. This calculation is based on two sites completing a specific number of subjects to give a total of 60 completed subjects.

Table 3: Sample Size Calculations

	Subjective responses	Ocular Health
Difference between pairs	10	-
SD between pairs	15	-
Comparison Proportion (p1)	-	40%
Baseline Proportion (p2)	-	10%
Sample size of completion	60	
Type I (α)	5%	
Power (1-β)	80%	

10.2 Statistical Analysis

Statistical analysis and report writing will be performed by the sponsor. De-identified data will be provided to the sponsor by each site for the sponsor to perform the analyses. Each site will only have access to the data collected at their site.

Statistically analyses will be conducted on all randomized subjects who have successfully completed the study without a protocol deviation that may be regarded as impacting the assessments of primary hypothesis. The overall type I error rate will set at α=5% level. All primary hypotheses must be met in order to satisfy the objective of the study.

Descriptive statistics will be generated at baseline/dispense and each follow up visits (e.g. mean, SD). In each case, Noninferiority will be concluded if the low limit of 95% confidence interval of difference in subjective response is above the low bound: -10. Paired testing, ANOVA, or mixed linear model may also be used for additional analysis on selected variables. Binomial test was used to analysis the results for the count data of subjective preferences; the number of "no preference" were evenly distributed to the two options on the basis they would be equally likely to choose either. A p-value less than or equal to 0.050 will be regarded as statistically significant.

11 Data Quality Assurance

11.1 Study monitoring

Site qualification of the investigative site has been completed to ensure that the site facility is adequate, personnel are qualified and resources are satisfactory to conduct clinical studies for the Sponsor. The protocol will be reviewed by the investigators prior to enrollment of the first subject. This will involve an overview of the protocol, which includes information on study objectives, inclusion and exclusion criteria, study visits and adverse event reporting. Data

collection forms will also be reviewed and this will provide an opportunity to discuss any questions.

Central study monitoring will involve regular study updates from the clinical site to the sponsor. The updates will include the number of subjects enrolled, the number eligible, the number completed and whether there have been any unscheduled visits, discontinuations, significant or serious adverse events or major protocol deviations. These updates will be provided weekly.

A site visit 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 Sponsor Responsibilities

The Sponsor is responsible for the selection of the Investigator and study site, and should also select and appoint a monitor. The Sponsor has the ultimate responsibility for monitoring. The Sponsor is to supply and keep an up-to-date signed protocol and protocol amendments, and provide devices which are the Subject of the clinical investigation.

The sponsor should ensure: appropriate information is provided to the Investigators to conduct the clinical trial; that deviations are reviewed with the Investigator as needed and included in the final report. Adverse events are reported by the Investigator, and the sponsor in turn will then notify their applicable regulatory authorities, and other investigators as appropriate. The Sponsor is to maintain Sponsor-specific clinical trial documentation as required by the regulatory authorities and to ensure the Investigator is aware of their record keeping responsibilities.

11.3 Investigator Responsibilities

The Investigator is responsible for ensuring subject safety and data quality by: protocol compliance, adherence to GCP and local regulatory requirements, and the Declaration of Helsinki. The Investigator should be appropriately qualified and legally entitled to practice, and be trained in the proper method of obtaining informed consent.

The Investigator must have the appropriate resources to conduct the clinical trial, be familiar with the protocol and agree to adhere to it, support monitoring and auditing activities, communicate with the Sponsor regarding any clinical trial issues or need for protocol modifications, make the necessary arrangements to ensure proper conduct and completion of the clinical trial, and ensure the protection and welfare of the subject, including arranging any emergency treatment as needed.

The Investigator must ensure written IRB approval is received prior to the start of the clinical trial, that the IRB and Sponsor is kept informed of the clinical trial progress, including serious/adverse

events and deviations as required by them, and that any changes to the protocol are notified to the IRB and review written approval prior to implementation.

The Investigator must try to ensure adequate subject recruitment; that all necessary and appropriate information is given to potential subjects to ensure informed consent; is taken and documents; and that clinical records indicate the subject is enrolled in a clinical trial. The Investigator must ensure that clinical trial subjects are provided with emergency contact details along with a procedure to follow in the case of an emergency, and that clinical trial subjects are kept informed as pertinent new information becomes available that may affect their decision to participate.

The Investigator has primary responsibility for the accuracy, legibility and security of all clinical investigation data, documents and subject records at the Investigator site during and after the clinical trial. CRFs are to be signed by the Investigator, and any alterations to data are to be by authorized personnel, initialed and dated by same or, in the instance of electronic data, an audit trail must be in place, with no obstruction of the original data.

The Investigator must ensure that data be kept for the minimum time as specified by this protocol, test product must be accounted for (the quantity of the devices received must be reconciled with the quantities of the device used, discarded or returned), and must also be responsible for the supervision and assignment of duties to all responsible for the conduct and evaluation of the clinical trial for the Investigator center involved.

11.4 Record keeping

Detailed records of all study visits will be made using the Case Report Forms (CRFs). All data recorded on forms will be in ink. Any corrections to the forms will be initialed and dated at the time they are modified.

Study subject records will be completed to comply with GCP guidelines. Records will contain:

- Unique study acronym and/or code;
- Subject ID;
- Date enrolled;
- Confirmation by investigator that subject met eligibility criteria;
- Confirmation that subject received a signed and dated copy of informed consent;
- Exit date;
- Investigators signature confirming study exit.

11.5 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 investigative site guidelines, but as a minimum for 3 years. The Sponsor will be notified and consulted if ever the files are to be destroyed. In the event that this protocol is indicated for design verification and validation purposes, as indicated on the title page, copies of all original raw data forms and copies of completed CRF's (with personal identifiers removed) can be forwarded to the sponsor after completion of the final report, at the sponsor's request.

12 Protocol Deviations

Protocol deviations are unanticipated or unintentional changes to a study after it has received prior sponsor approval and ethics clearance. Protocol deviations can be major or minor.

12.1 Major protocol deviations

Major protocol deviations may impact the research protocol, information consent document or other study materials, usually cannot be anticipated ahead of time and are often necessary to ensure the safety and welfare of the subjects.

The following are examples of protocol deviations that must be reported to the ORE/IRB:

- Changes in procedures initiated to eliminate immediate risks/hazards to subjects;
- Enrollment of subjects outside the protocol inclusion/exclusion criteria whether agreed to or not by the sponsor;
- Medication / device / intervention errors (i.e. incorrect drug or dosage of drug / incorrect contact lens(es) dispensed / incorrect care system dispensed);
- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design;
- Information consent documentation violations: no documentation of informed consent; incorrect version of, or incomplete, informed consent documentation used.

12.2 Minor protocol deviations

Protocol deviations caused by or which originate with research subjects are considered minor, and normally are not reported to the ORE/IRB unless these result in increased risk to the subject(s). The following are examples of protocol deviations that are considered minor and do not require reporting to the ORE/IRB:

- Logistical or administrative aspects of the study (e.g., study subject missed appointment, change in appointment date);
- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would not impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

12.2.1 Reporting and documenting protocol deviations

Major protocol deviations must be reported to the ORE/IRB according to its guidelines.

All protocol deviations (major and minor) occurring during the study will be documented and included in the final report.

13 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 approximately 5 business days after the last subject completes the final visit. In addition, a full one month dataset will be provided to the sponsor at the sponsor's request. Investigators will be masked for the interim analysis.

13.1 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).

[redacted]

14 Study Costs

CVI will compensate the investigator and the Subjects for their time and participation in this voluntary study.

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.

15 Study Report

The sponsor will author the study report.