CORE
Centre for Ocular Research & Education

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Optometry & Vision Science

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Protocol

EVALUATION OF THE PERFORMANCE OF MONTHLY REPLACEMENT SPHERE LENS DESIGNS IN HABITUAL SOFT CONTACT LENS WEARERS

(STUDY CODENAME: STARFISH)

Sponsor Company:	**CooperVision Inc.**
Sponsor study number:	**EX-MKTG-129**
CORE protocol number:	**P/780/21/CVI**
Version number:	**1.2**
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Document type:	**Study protocol**
Study & data management Institution:	**CORE, University of Waterloo, Canada**

[redacted]

Study locations

1. **Study co-ordination & data management institution** (no clinical visits):

   Lyndon Jones (Director)
   CORE
   School of Optometry & Vision Science
   University of Waterloo
   200 Columbia Street West
   Waterloo, Ontario N2L 3G1
   CANADA

2. **Clinical research conducted at in-practice study sites:**

   It is anticipated that between 4 and 6 sites in the United States of America and/or Canada will be identified and contracted for this study. The details of all sites and all principal Investigators will be included in the study report.

1 DOCUMENT CHANGE HISTORY

Version number	Version date	Author	Description of change(s)
1.0	10sep2021	Jill Woods	Original protocol
1.1	22sep2021	Jill Woods	Updated protocol title, exclusion criteria, power range to be used, retention of study records by sites.
1.2	30sep2021	Doerte Luensmann	Minor administrative changes, payment information removed from sections 5.4.2, 9, 11, near VA measurements added to visits

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Disclaimer

This study will be conducted for research purposes only.

2 INTRODUCTION

As new lenses come to market it is of interest to compare the performance of the new product to the performance of established products. The goal of this study is to compare the performance of Biofinity (Lens A), a SiHy monthly replacement lens from CooperVision Inc., which has successfully been established on the market with TOTAL30 (Lens B), a SiHy monthly replacement lens recently launched by Alcon Inc.

3 OBJECTIVES

To evaluate the clinical performance of two monthly silicone hydrogel contact lenses in habitual wearers of frequent replacement (FRP) lenses when worn for 1-month.

The primary outcome variable for this study is:

- Lens handling on removal (0-10 scale, 0.5 steps) collected in the Day 27 At-Home Subjective ratings.

4 HYPOTHESIS

The null hypothesis is that there will be no difference for lens handling on removal on day 27 between Lens A compared to Lens B, captured in the Day 27 At-home Subjective Ratings form.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

This study is a prospective, bilateral eye, double-masked, randomized, 1-month cross-over, daily-wear design involving two different FRP lens types. Each lens type will be worn for approximately one month, during which participants record their subjective lens-wear experience on several different days at home and during study visits.

5.1.2 RANDOMIZATION

A randomization schedule will determine the order of Lens A and Lens B wear for the first/second month for each participant. Participants will be randomized immediately prior to their first lens dispense.

This randomization schedule will be generated for each site using a web-based program: (www.randomization.com). The lens type that will be worn during the first month is called "Lens

type #1", the lens type dispended for the second month is called "Lens type #2". The final study randomization schedule will be generated by CORE's Database Administrator and provided to the research assistants at each site.

5.1.3 MASKING

At the fitting visit, only the participant will be masked of the lens type, the investigator will know which type is being fit in order to make changes to the lens at this visit if needed.

At both dispense visits, participants and investigators will be masked to the lens type dispensed. In order to achieve this, unmasked study personnel will determine the lens order according to the randomization schedule and will over-labeled the lens packages/foils prior to dispense.

5.2 INVESTIGATIONAL SITES

5.2.1 NUMBER OF SITES

This study will be conducted in between four and six optometry practice sites in the US and/or Canada, depending on their ability to recruit sufficient number of participants. The exact site locations and names of the principal Investigators will be listed in the final study report.

5.2.2 INVESTIGATOR RECRUITMENT

The principal investigator at each site will be required to fulfil the following criteria:

- Is a licensed Optometrist with at least two years of contact lens fitting experience.
- Can demonstrate training in Good Clinical Practice (GCP) by the already trained principal investigator.
- Accepts responsibility for the conduct of the study at their site.
- Has in-office email and either document scanning capabilities or fax.
- Will scan and send all study visit documents to CORE, ideally the same day* as the visit or at most within 2 days of the study visit.
- Is willing to follow the study protocol and to co-operate with the study monitors at CORE.

* Study documents are required as soon as possible because this allows for prompt lens ordering and timely data review, query and entry.

5.3 STUDY POPULATION

5.3.1 SAMPLE SIZE CALCULATION

The sample size calculation was based on "lens handling for removal" using data at 2 weeks from a study comparing MyDay Multifocal (CooperVision) to Dailies Total 1 Multifocal (Alcon Inc) in which participants used a 0-10 scale (10 being best).

A minimum sample size of 60 is required to detect a paired difference between groups of 1.0 unit on a 0-10 scale for "lens handling for removal" with 80% power and alpha 0.05 in a two-tailed t-test. Therefore, up to 66 participants may be dispensed with study products with the goal to complete at least 60.

Difference	Sample Size	Target Power	Actual Power
1	60	0.80	0.805637
1	66	0.84	0.842360
1	79	0.90	0.901677

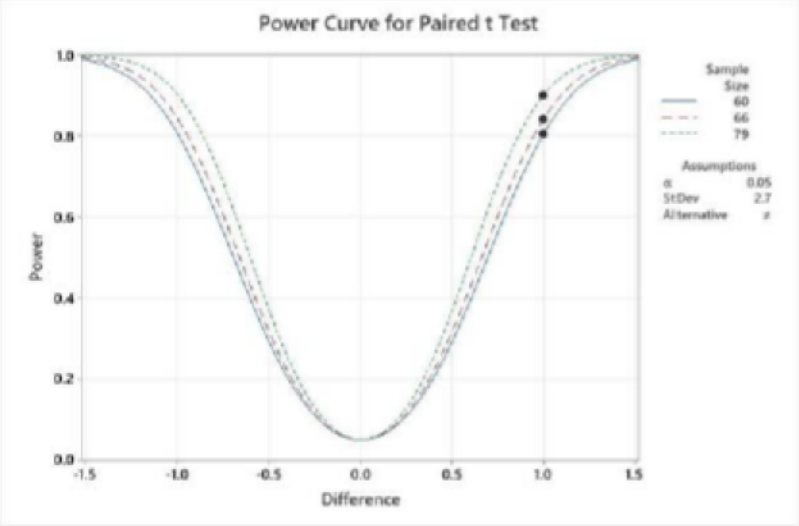

Figure 1: Sample size calculation graph

5.3.2 NUMBER OF PARTICIPANTS

Participants will be recruited using site records, databases and advertising materials (eg. posters, email scripts) approved by the ethics review board. All initial individual-targeted

recruitment activities, such as any direct mailing of recruitment scripts, will be conducted by practice staff that are not directly involved in conducting the research. This separation will reduce any undue influence of the optometrist-patient relationship. This process will also eliminate opportunity for the investigator to access personal health information before any consent for disclosure is provided by the potential participant.

It is anticipated that up to 80 potential participants may attend a Screening visit and up to 65 participants may be randomized and dispensed with study products, with a target of at least 60 completing the study.

5.3.3 INCLUSION AND EXCLUSION CRITERIA

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

1. Is at least 18 years of age and no older than 35 years, and has full legal capacity to volunteer;
2. Has read and signed an information consent letter;
3. Is willing and able to follow instructions and maintain the appointment schedule;
4. Self-reports having a full eye examination in the previous two years;
5. Self-reports spending on most days at least 6 hours cumulative (not necessarily in one single stretch) using digital devices such as a computer, laptop, tablet, e-reader, smart-phone;
6. Has healthy eyes with no health condition or medication that contra-indicate contact lens wear, in the opinion of the investigator;
7. Anticipates being able to wear the study lenses for at least 8 hours a day, 6 days a week;
8. Habitually wears soft frequent replacement contact lenses, for the past 3 months minimum (NOTE: the habitual contact lens brand is restricted such that no more than one third are to be the Biofinity brand (or their equivalent private label brand name) and no more than one third are to be an Alcon brand;
9. Has refractive astigmatism no higher than -0.75DC in each eye;
10. Can be fit and achieve binocular distance vision of at least 20/30 Snellen (Available lens parameters are sphere +6.00 to -6.00D, 0.25D steps).

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

1. Is participating in any concurrent clinical or research study;

2. Has any known active* ocular disease and/or infection that contraindicates contact lens wear;
3. Has a systemic or ocular condition that in the opinion of the investigator may affect a study outcome variable;
4. Is using any systemic or topical medications that in the opinion of the investigator may affect contact lens wear or a study outcome variable;
5. Has known sensitivity to the diagnostic sodium fluorescein used in the study;
6. Self-reports as pregnant, lactating or planning a pregnancy at the time of enrolment;
7. Has undergone refractive error surgery or intraocular surgery.

* For the purposes of this study, active ocular disease is defined as infection or inflammation which requires therapeutic treatment. Mild (i.e. not considered clinically relevant) lid abnormalities (blepharitis, meibomian gland dysfunction, papillae), corneal and conjunctival staining and dry eye are not considered active ocular disease. Neovascularization and corneal scars are the result of previous hypoxia, infection or inflammation and are therefore not active.

The upper age limit of 35years is in place to eliminate the influence of presbyopia (age-related difficulties focusing at close range) on eye strain with extended close work or digital device use.

Pregnant and lactating women are not being excluded from the study due to safety concerns but due to fluctuations in refractive error, accommodation and/ or visual acuity that occur secondary to systemic hormonal changes and water retention. It has further been shown that pregnancy could impact tear production, which could impact dry eye symptoms. Such fluctuations could affect data, thereby negatively affecting study data integrity.

5.4 STUDY MATERIALS

It is anticipated that sites will pre-order the study contact lenses (Lens A and Lens B) for each potential participant prior to them attending for the screening/fit visit. This order will be based on their habitual contact lens power. One commercial pack of 6 lenses will be ordered per eye unless both eyes require the same prescription, when only one 6-pack of lenses will be ordered. This will mean that there will be study lenses on site at the time of the screening visit and unless there are changes required to the prescription, the dispense visit will be able to occur immediately after the screening/fit visit.

Reimbursement to practice sites for study product expenses will be provided by CooperVision after recruitment has been completed and CORE has reconciled the invoices.

CORE will provide all sites with the study paperwork. This will include participant informed consent letters and study data collection forms, product accountability logs and the participant dispensing logs. CORE will train site personnel to complete the forms correctly and provide continued support to answer queries on correct form completion.

[redacted]

5.4.1 LENSES

Both, Lens A and Lens B are cleared by the United States Food and Drug Administration (FDA) and are commercially available in the U.S.

The table below lists the contact lens details for Lens A and Lens B including the lens parameters available for this study.

Table 1: Lens characteristics & parameter to be used

Lens	Lens A (Biofinity)	Lens B (TOTAL30)
Manufacturer	CooperVision	Alcon Inc.
Material	comfilcon A	lehfilcon A
FDA Class	Group 5	Group 5
Sphere power (D)	+6.00 to -6.00 (0.25 steps)	+6.00 to -6.00 (0.25 steps)
Base curve (mm)	8.6	8.4
Diameter (mm)	14.0	14.2

5.4.2 LENS CARE PRODUCTS

It is expected that participants will continue to use their habitual lens care products with the study lenses. This will avoid any potential incompatibility the participants may have with a new care product. Each participant will be compensated for them using their own lens care product for the approximately 2-month study period.

5.4.3 OTHER PRODUCTS

Sodium fluorescein will be used to assess corneal and conjunctival staining.

5.4.4 REWETTING DROPS

Participants will not be encouraged to use rewetting drops; however, those who habitually used rewetting drops will be allowed to continue using their normal drops.

5.4.5 DISPOSING OF STUDY PRODUCTS

At the end of the study, all sites will dispose of all unused products after lens reconciliation has been completed, unless otherwise directed. Worn lenses will be disposed of according to local regulations.

5.4.6 PRODUCT ACCOUNTABILITY

Accountability logs must be kept by each site to include the number of contact lenses received and on hand at the end of the study. All products dispensed to participants must be recorded in participant dispensing logs.

5.5 SCHEDULED AND UNSCHEDULED VISITS

This study has a minimum of 4 scheduled study visits, including the screening visit. There is an option for repeated screening visit if needed.

A scheduled 1-month follow-up visits may only take place when the participant attends wearing the study lenses for at least two hours that day. If this is not the case and the participant is not experiencing any problems with the lenses, the appointment will be rescheduled, ideally within the visit window.

Visits that fall outside of the specified visit windows will be designated as protocol deviations and at the end of the study, the data collected during protocol deviations will be assessed for their suitability to be included in the analysis population.

Table 2 summarizes the scheduled study visits and study codes.

Table 2: Summary of visits

Visit code	Approximate Duration	Visits
0	1.0 hr	Screening & Fit of study lenses
0/R1, 0/R2	As needed	Repeat Visit 0 if needed
1-0	0.75 hr	Dispense Lens type #1 (0-21 days after Visit 0)
2-0	1.25 hr	1-month follow-up Lens type #1 and Dispense Lens type #2 (28-32, incl days after 1-0)
3-0 and exit	1.0 hr	1-month follow-up Lens type #2 (28-32, incl days after 2-0), exit forms & remuneration

Visits 1-0 (Dispense Lens type #1) and 2-0 (Dispense Lens type #2) will count as day 0

Lens type #1 and #2 will be either Lens A or B, as determined by the randomization table.

Participants will complete subjective ratings 'at-home' on days 1, 7, 14, 21 and 27 during each of the two 1-month lens wear periods; anticipated to take a total of 1 hour for all of them. These ratings will be provided to the participants on visits 1-0 and 2-0 and will be returned and reviewed at visits 2-0 and 3-0 respectively.

5.5.1 VISIT 0 SCREENING & FIT VISIT

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

Participants will be assigned a unique alpha-numeric study ID after they sign the consent documentation i.e. before their eligibility for the study has been confirmed. Each site will use a different letter preceding the participant ID number. For example, participant 01 at site T will be T01, and participant 01 at site N will be N01. Ineligible participants will be discontinued from the study.

The investigator will determine participant eligibility using the inclusion and exclusion criteria. The study procedures are outlined below:

1. The participant may attend this visit wearing their spectacles or contact lenses.
2. The participant will be required to read and sign an Informed Consent Form prior to enrollment. When the participant has signed the consent form, the participant will be considered enrolled in the study and will be assigned a study ID.
3. Participant demographics and medical history (age, sex, race, ethnicity, medical conditions, medications, allergies).

4. Contact lens history collected: habitual lens information (including brand name) and wearing habits.

5. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

11. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

c. [redacted]

[redacted]

d. [redacted]

13. The investigator will confirm that the participant meets the eligibility specifications set out in the inclusion criteria and exclusion criteria and is eligible to continue in the study.
14. If the required prescriptions for both lens types are available, the lens Dispense visit (1-0) will occur on the same day, otherwise the correct lens powers will be ordered and the Dispense visit will be scheduled once both lens types are on site (within 0-21 days after Visit 0).

5.5.2 REPEATED SCREENING VISITS (VISIT 0 OR VISIT 0/R1)

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

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

The maximum total number of screenings permitted will be 2, the initial and one repeat screening visit.

5.5.3 VISIT 1-0 DISPENSE LENS TYPE #1

This visit may or may not be immediately subsequent to the screening visit, depending on lens availability but will occur no later than 21 days after Visit 0.

The study procedures are outlined below:

1. Confirm participant's health and medications are unchanged.
2. [redacted]
3. An unmasked study staff will assign the participant to the next available randomization number on the randomization table provided and will prepare a new pair of Lens type #1 by placing strongly adhesive sticker on the lens blister to ensure masking of investigator and participant.
4. [redacted]
5. [redacted]
6. [redacted]
7. Provide and explain to participant the subjective at-home rating forms to be completed on Days 1, 7, 14, 21 and 27 (Note: Day 1 is the day <u>after</u> the dispensing visit). Fill in the days and dates on these forms. Explain the ratings will include:
   - [redacted]

- [redacted]
- [redacted]
- Ease of lens handling for removal (0 – 10 scale, 0.5 steps).
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

8. The participant will be instructed to use their habitual lens care products and to wear the lenses for at least 8 hours a day, 6 days a week.
9. Visit 2-0 will be scheduled 28-32, inclusive, days after Visit 1-0.

5.5.4 VISIT 2-0, 1-MONTH FOLLOW-UP LENS TYPE #1, DISPENSE LENS TYPE #2

Participants will be asked to insert Lens type #1 at least 2 hours prior to the visit. This visit will occur 28-32 days (inclusive) after visit 1-0.

The study procedures are outlined below:

1. [redacted]
2. Review 'at-home' ratings for completeness and legibility.
3. [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
6. [redacted]
   - [redacted]

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

8. [redacted]
9. Visit 3-0 will be scheduled 28-32 days after Visit 2-0.

5.5.5 VISIT 3-0 1-MONTH FOLLOW-UP LENS TYPE #2

Participants will be asked to insert Lens type #2 lenses at least 2 hours prior to the visit. This visit will occur 28-32 days (inclusive) after visit 2-0.

[redacted]

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

[redacted]

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

6. [redacted]

7. [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
   - [redacted]
8. Continue with Study Exit.

5.5.6 STUDY EXIT

The study exit form will be completed when a participant exits the study. This form will be completed either at study completion, or if the participant is discontinued from the study at another time. A study exit form must be completed for all participants who have taken a study ID number. If in the opinion of the investigator post-study follow-up visits are required, the exit form will be completed after the last follow-up visit.

Exit visual acuity will be recorded with either the participant's spectacles, subjective refraction or habitual contact lenses. An exit biomicroscopy assessment will be conducted if not already completed on the same day for a concurrent study visit.

After the exit assessments have been completed, the participant and investigator will complete the study completion and remuneration forms. At this time the participant will be considered as having exited the study.

5.5.7 UNSCHEDULED VISITS

An unscheduled visit is defined as an interim visit requested by the participant or investigator due to an unanticipated problem. Data recorded at these visits will be entered into the database. Only relevant and applicable unscheduled visit information will be included in the final report as deemed necessary.

5.6 STUDY PROCEDURES

Table 3 summarizes the procedures conducted at each visit.

Table 3: Summary of procedures to be conducted at scheduled visits

	0 Screen & Fit of Study Lenses	1-0 Dispense Lens type #1	2-0 1-month follow-up Lens type #1 dispense Lens type #2	3-0 1-month follow-up Lens type #2 and Exit
Consent process	x			
Subject age, sex, race, ethnicity	x			
CL history, brand & lens wear schedule	x		x	x
Digital device use	x		x	x
Health & medication	x	X	x	x
Review any problems with eyes/study lenses		X	x	x
[redacted]	x			x (or with subj. refraction from V 0)
[redacted]	x			
[redacted]	x			
[redacted]	x			
Dispense study CLs		X	x	
[redacted]	x	X	x	x
[redacted]		X	x	x
[redacted]	x	X	x	x
[redacted]			x	x
[redacted]				x
Issue 'at-home' subjective ratings		X	x	
[redacted]			x	x
[redacted]	x	x*	x	x
Study Exit				x

* Not required if visit concurrent subsequent to previous one.

[1] High Contrast High Illumination

5.6.1 STUDY LENS FITTING

Both lens types will be fit according to the manufacturers fitting guide.

5.6.2 [redacted]

[redacted]

5.6.3 [redacted]

[redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

[redacted]

6 MONITORING PROTOCOL ADHERENCE

Adherence to study visit windows, lens wearing schedule, and time windows around other data collection points (i.e. subjective ratings) will be monitored by CORE. Deviations from the study plan as described in the protocol will be reported in the study report. As described in Section 13.4, major protocol deviations will be reported to the Sponsor and Sterling Institutional Review Board within 10 business days of becoming aware of them (as per Sterling Institutional Review Board guidelines).

7 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

There may be no direct benefits to the subjects in this study. Participation in a study may contribute to scientific research information that may be used in the development of new contact lens products. The 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 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 (1) do not represent a potential for serious risk to the health, safety or welfare of the subject, and (2) are not implants, (3) are not used to support or sustain human life, (4) are not of substantial importance in diagnosing, curing, mitigating or treating disease or otherwise prevents impairment of human health.

The two study contact lens types will be worn as per their approved use; on a daily wear, monthly replacement basis. When contact lenses are worn on a daily wear basis there is a small risk of an adverse event compared to not wearing contact lenses. When contact lenses are worn on an extended wear basis, there is a significantly increased risk of an adverse reaction compared with wearing contact lenses on a daily wear basis.

Adverse events and/ or complications in daily wear of soft contact lenses can occur (eg: inflammation and infection). 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 pain, 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 and only current soft lens wearers will be recruited for this study.

A dye (fluorescein) normally used for eye examinations is being used in this study. Although rare, it is possible to have an allergic reaction to the dye. Participants will be asked if they have a known allergy or sensitivity to fluorescein.

The assessments conducted in this study are routine clinical procedures and they include 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. Patients will be monitored frequently until the end of the study to reduce the occurrence of adverse or potential adverse events. Patients will be given instructions from their investigator regarding early symptoms and signs of adverse events.

8 ADVERSE EVENTS

An 'adverse event' refers to any undesirable clinical occurrence in a participant, 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, Table 4.

A number of conditions may result in temporary suspension until resolution. These include corneal infiltrates, corneal staining, limbal injection, bulbar injection or tarsal conjunctival abnormalities.

Table 4: Classification of types of adverse event

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 study 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 reporting details, plus examples, are provided in Table 5.

Table 5: Contact lens adverse event classification, coding and reporting guide

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	For all serious AEs: Notify sponsor as soon as possible, **within 24 hours;** ORE reporting will be **within 24 hours** 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 days**; ORE reporting as per requirements
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)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO **1**11980 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 participant 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**; ORE 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	

8.1 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.

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 participant may be managed at the practice or referred to another eye care practitioner 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 participant must be followed until resolution or no further change is anticipated and/or referred for further care with the appropriate health care professional and/or recorded as being under appropriate health care as per investigator's discretion. A written report will be 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 participant's participation will be reported to CORE's lead study coordinator (details below) and also to the sponsor (details below) within 24 hours of the investigator becoming aware of the event.

The site's Principal Investigator will also report the event to Sterling IRB within 10 business days of becoming aware of the Serious or Unanticipated event, using the Reportable Events Form. All fatal or life-threatening events will be reported immediately to the IRB.

Significant and Non-Significant Adverse Events will be reported to CORE's lead study coordinator and the sponsor as soon as possible, but no later than 5 working days after becoming aware of it.

[redacted]

[redacted]

Details of all adverse events will be included in the study report.

9 DISCONTINUATION FROM THE STUDY

Participants may be discontinued at the discretion of the investigator or sponsor in consideration of participant safety or protocol compliance, or at discretion of the participant. Participants discontinued from a study will be reimbursed per visit for their active involvement in the study (including the initial screening visit and all lens fitting visits). Upon discontinuing, a participant will be offered the option of their data being withdrawn from future statistical analysis. The following is a list of possible reasons for discontinuation from the study:

- Screening failure: Participants will be discontinued if they do not meet the inclusion and exclusion criteria outlined in section 5.2.3.

- Unacceptable performance with products to be used in study: Participants may be discontinued if they are unable to achieve acceptable comfort and /or vision with the study products.
- Positive slit lamp finding: Participants 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 participant experiences an adverse event during the study they may be discontinued based on the clinical judgement of the investigator.
- Symptoms: If the participant has persistent symptoms, they may be discontinued based on the clinical judgement of the investigator.
- Disinterest, relocation or illness: The participant may choose to discontinue due to reasons within or beyond their control.
- Violation of protocol or non-compliance: The participant 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 participant 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 participant may remain an active participant (at the discretion of the investigator) after stopping topical ocular medication following resolution of the ocular condition).
- Lost to follow-up: The participant will be discontinued if they cannot be contacted and do not return to complete the final study exit, and if the investigator has made a reasonable effort to contact the participant for a final study visit.
- Premature termination of the study by the sponsor, CORE or Sterling IRB.

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

When a participant chooses to discontinue from the study, they will be given the opportunity to withdraw their data from the statistical analysis. This choice will be captured on the discontinuation form.

All discontinuations including their reasons will be included in the final report.

10 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 CORE and the sponsor **within 24 hours** of the investigator becoming aware of the malfunction. STERLING IRB would also be notified within 10 business days of any device malfunction that may contribute to a *Serious Adverse Event*.

Other defective lenses should be reported to CORE as soon as possible.

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as complaints or device malfunctions.

11 STUDY COMPLETION AND REMUNERATION

At the last scheduled protocol visit a study completion form will be completed, which requires the signatures of both the participant and the investigator. Participants will also be provided with a letter of appreciation.

Once their involvement in the study is complete, participants will be informed about receiving feedback following study completion in the Letter of Appreciation.

Participant remuneration will be provided at the end of their study involvement.

12 STATISTICAL ANALYSIS AND DATA MANAGEMENT

12.1 STATISTICAL ANALYSIS

All data will be analyzed by CORE at the University of Waterloo. Unmasked data analysis will be conducted using Statistica 10, Statsoft or other suitable software. Descriptive statistics will be provided on demographic data (age, gender, refractive error distribution, etc.). Table 6 lists the primary and other outcome variables and anticipated statistical procedures.

[redacted]

Comparisons will be made between the study lenses for the variables measured at the 1-month visits. Additionally, the subjective ratings completed on days 1, 7, 14, 21 and 27 with each study lens will be compared. [redacted]

[redacted]

Additional analysis may be conducted.

[redacted]

12.2 DATA MANAGEMENT

Data will be collected and written on paper forms which will be provided to each site by CORE. Each site will be instructed to send completed study forms to CORE using a secure file share system operated by the University of Waterloo called Sendit which uses 128bit (or 256bit) SSL encryption. The sites will receive their individual accounts and passwords.

The site will endeavour to send the scanned forms to CORE **on the same day as the study visit** or a maximum of two days after the study visit.

Within CORE, data will be entered into a REDCap database developed and tested specifically for this study and accessible only to trained, authorised users. A data management plan will be developed to describe the data handling in more detail, including the personnel involved.

Data from this study will be retained by CORE for a minimum of 25 years on a password-protected server. After 25 years, data will be disposed of in accordance with the guidelines laid

out by the University of Waterloo. More details regarding storage procedures are provided in section 15.7 and also in CORE SOP014 Clinical data management.

At the completion of the study CORE will provide a copy of the study database in Excel format to the sponsor when requested. Data will typically be sent using Sendit. This system provides a secure way to transfer files when email is not appropriate, whether because of file size, file type or concerns over security. Sendit includes features such as password protection, a restricted time period for download, IP logging and email notification of download. Files may be encrypted prior to transmission at the request of the sponsor. Using this method means that data files are only stored on University of Waterloo servers during the transfer.

12.3 COMMENTS ON SOURCE DOCUMENTS

Data analysis will not be conducted on comments which have been recorded in the source documents. Only relevant and applicable comments will be included in the final report as deemed necessary by CORE's Lead Coordinator.

13 PROTOCOL & OTHER TRAINING

All study personnel will be required to complete training prior to their involvement in the study. Records of training will be kept at CORE. This will include training by CORE on the study protocol, study procedures, informed consent procedures, and on the randomization and participant masking procedures, as well as training for Good Clinical Practice.

All site Principal Investigators and co-investigators will provide CooperVision Inc with a scan of their curriculum vitae, license to practice optometry and evidence of professional indemnity insurance.

14 STUDY MONITORING

Each site will provide regular status reports to CORE. Status reports will include:

- These may include but are not limited to participant enrollment status, cases of discontinuation etc.
- Details of all protocol deviations, adverse events, device malfunctions.
- Reports of unintended events.

CORE will collate the site updates and provide frequent status reports to the study sponsor.

Study monitoring visits to the sites may be conducted by CORE, the sponsor, or sponsor's designate, throughout the study and will be scheduled in conjunction with the Principal

Investigator at each site. In addition, study records may be inspected by the sponsor, the sponsor's designate, Sterling Institutional Review Board, and by regulatory authorities in Canada and the United States, namely Health Canada and the United States Food and Drug Administration (FDA); however, they will not be permitted to take away any records containing identifiable personal information.

Study data review and data monitoring will be conducted by CORE personnel. To improve data integrity, data entry will be conducted by two people and the entries will be compared. Data queries will be reported to the site within 5 working days of receipt of initial data. A response resolving the query will be expected from the site within 5 working days of receipt of the query.

All adverse events and protocol deviations will be reviewed by the site Principal Investigator and CORE's Lead Coordinator. All serious adverse events and major protocol deviations will be reviewed by the site Principal Investigator and CORE's Director and/or Head of Clinical Research.

15 STUDY MANAGEMENT

15.1 STATEMENT OF COMPLIANCE

This clinical study is designed to be in compliance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for Good Clinical Practice (GCP), with the University of Waterloo's Guidelines for Research with Human Participants and with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, 2nd Edition.

- Declaration of Helsinki
- ICH E6 - International Conference on Harmonisation; Good Clinical Practice
- http://iris.uwaterloo.ca/ethics/human/guidelines/index.htm
- http://iris.uwaterloo.ca/ethics/human/ethicsReview/UWStatement.htm
- http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

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

15.2 ETHICS REVIEW

This protocol will be submitted to and reviewed through the Sterling Institutional Review Board. Notification of ethics clearance of the application is required prior to the commencement of the study.

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 Institutional Review Board: Sterling Institutional Review Board; Telephone number: (888) 636-1062 and email address: info@sterlingirb.com.

15.3 CLINICAL TRIAL REGISTRATION

CooperVision will register this study with clinical trials.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. They will maintain the information on that site.

15.4 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.

15.4.1 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 participants.

The following are examples of protocol deviations that must be reported to the Sterling Institutional Review Board:

- Changes in procedures initiated to eliminate immediate risks/hazards to participants;
- Enrollment of participants 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.

15.4.2 MINOR PROTOCOL DEVIATIONS

Many protocol deviations which are caused by or originate with research participants are considered minor, and normally are not reported to the Sterling Institutional Review Board unless these result in increased risk to the participant(s). The following are examples of protocol deviations that are considered minor and do not require reporting to the Sterling Institutional Review Board :

- Logistical or administrative aspects of the study (e.g., study participant 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).

15.4.3 REPORTING AND DOCUMENTING PROTCOL DEVIATIONS

Major protocol deviations must be reported to the Sterling Institutional Review Board within 10 business days of the deviation occurring (or its discovery) using the Reportable Events Form. To facilitate timely reporting to the sponsor, all sites must notify CORE of a major protocol deviation as soon as possible.

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

15.5 PREMATURE TERMINATION OF THE STUDY

The sponsor, CORE or Sterling Institutional Review Board may terminate the study at any time for any reason.

15.6 STUDY PARTICIPANT RECORDS

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

- Unique study acronym and/or code;
- Participant ID;
- Date enrolled;
- Confirmation by investigator that participant met eligibility criteria;
- Confirmation that participant received a signed and dated copy of informed consent;
- Exit date;

- Investigator's signature confirming study exit.

An enrolment log will be maintained at each site which will list all participants who attended for a screening visit.

15.7 RETENTION OF STUDY RECORDS AND DATA

When the study has been completed, all sites will send electronic copies of the study product accountability and dispensing logs to CORE for review. Each site should retain the original consent documents and the study data collection forms documentation for ten years following the close of the database in case data queries arise during the analysis and report writing stages unless instructed otherwise. CORE may request that these originals be sent to them for storage and study data collections forms may be sent to the sponsor for storage.

Records and data from this study will be retained at CORE for a minimum of 25 years. Details regarding storage procedures are given in CORE SOP014 Clinical data management.

16 REPORT

A report will be sent to the sponsor by CORE according to terms described in the study contract.