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Protocol

PERFORMANCE EVALUATION OF TWO SILICONE HYDROGEL TORIC LENS DESIGNS IN HABITUAL SOFT CONTACT LENS WEARERS

(STUDY CODENAME: TIGER)

Sponsor Company:	**CooperVision Inc.**
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[redacted]

Study Personnel

1 DOCUMENT CHANGE HISTORY

Version number	Version date	Author	Description of change(s)
1.0	03May2023	Jaya Dantam	Original protocol
2.0	30May2023	Doerte Luensmann	Updates to the inclusion/ exclusion criteria, other administrative changes. Information no lens care products added.
3.0	31May2023	Doerte Luensmann	Updates to study variables (near VA) other administrative changes.

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Disclaimer

This study will be conducted for research purposes only.

2 INTRODUCTION

It is anticipated that more than 40% of contact lens wearers would benefit from a contact lens that corrects astigmatism, but this target is not reached in most countries.[1] 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 toric (Lens A), a silicone hydrogel monthly replacement lens from CooperVision Inc., which has successfully been established on the market with TOTAL30 for astigmatism (Lens B), a SiHy monthly replacement lens recently launched by Alcon Inc.

3 OBJECTIVES

To compare the clinical performance of Biofinity toric versus Total 30 for astigmatism in habitual lens wearers, when worn for 1-month each.

The primary outcome variable:

- Ease of handling for lens removal (0 - 100) reflecting a typical day in the past month, collected at the 1-month in-office visits

The secondary outcome variable:

- Distance Visual Acuity (Snellen converted to logMAR) for study lenses determined at the 1-month in-office visits

Other outcome variables:

- Lens fit: centration, lens orientation, post blink movement at 1-month follow-up
- Subjective ratings:
  - At-home questionnaires [collected on Days 7, 14 and 27 (study CL)]
  - In-office experience ratings - after lens insertion [collected at lens dispense visit (study CL)]
  - In-office experience ratings – a typical day in the past week [collected at screening (habitual CL) and 1-month follow-up visits (study CL)]
  - In-office satisfaction ratings – a typical day in the past week [collected at screening (habitual CL) and 1-month follow-up visits (study CL)]
  - In-office agreement ratings– a typical day in the past week [collected at screening (habitual CL) and 1-month follow-up visits (study CL)]
  - In-office preference ratings collected at exit visit (study CL)

4 HYPOTHESIS

The null hypothesis is that there will be no difference for the primary outcome variable between Lens A compared to Lens B.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

This study will be conducted at several optometry practices in the US and Canada. This study is a prospective, bilateral eye, subjected-masked, randomized, 1-month cross-over, daily-wear design involving two different silicone hydrogel toric lens types. Each lens type will be worn bilaterally for approximately one month, during which participants record their subjective lens-wear experience on three different days. Additional measures will be collected during in-office 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 fit to make changes to the lens at this visit if needed. Strongly adhesive stickers will be placed on the packages/foils to mask the participant to the lens brand. At both dispense visits, participants will be masked to the lens type dispensed. The 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 at approximately 5 optometry practice sites within the United States and Canada.

5.2.2 INVESTIGATOR RECRUITMENT

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

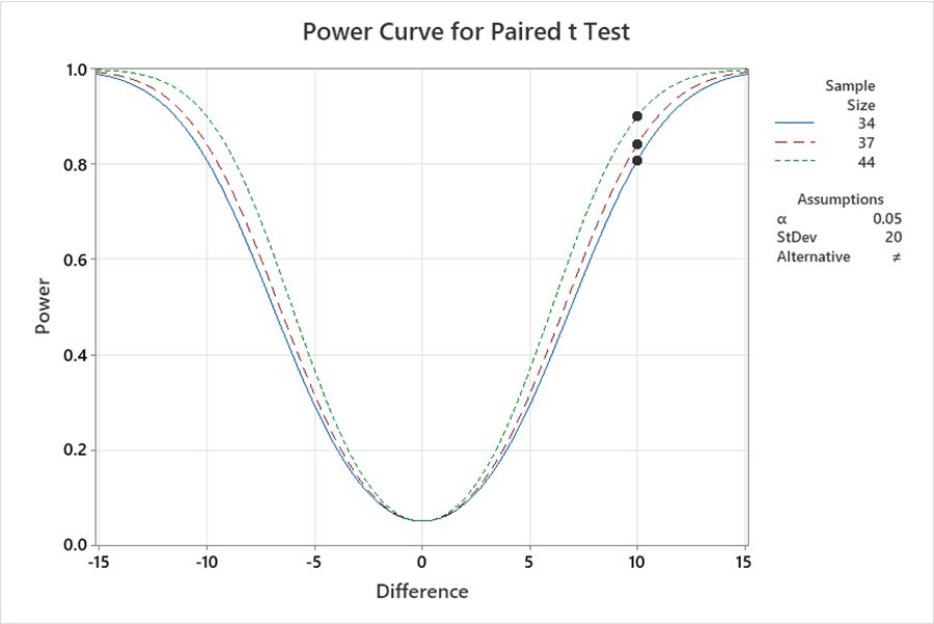
- Is a licensed Optometrist with at least two years of contact lens fitting experience.
- Can demonstrate training in Good Clinical Practice (GCP).
- Accepts responsibility for the conduct of the study at their site.
- Has in-office email and document scanning capabilities.
- Will scan and send all study 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 timely data review, query and entry.

5.3 STUDY POPULATION

5.3.1 SAMPLE SIZE CALCULATION

The sample size calculation was based on a recent study comparing Biofinity sphere and Total30 sphere; the data for subjective responses for ease lens handling for lens removal when reflecting in a typical day, collected at the 1-month visits: standard deviation of 2.0 (0 - 10 scale) was transformed to a standard deviation of 20 for using a 0 - 100 scale for this study. 90% power is achieved with a minimum sample size of 44 participants.



Therefore, up to 48 participants will be dispensed with study products with the goal to complete at least 44.

5.3.2 NUMBER OF PARTICIPANTS

Participants will be recruited using site records and databases where consent for contact about research has been provided. There will also be general advertising materials (e.g. posters, social media posts) and all these, including email scripts, will be 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 60 potential participants may attend a Screening visit and at least 48 participants will be randomized and dispensed with study products, with a target of at least 44 completing the study. Each site will dispense study products to approximately 10 participants.

5.3.3 INCLUSION AND EXCLUSION CRITERIA

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

1. Is between 18 and 39 years of age (inclusive) and has full legal capacity to volunteer;
2. Has read and signed an information consent letter;
3. Self-reports having a full eye examination in the previous two years;

4. Anticipates being able to wear the study lenses for at least 8 hours a day, 6 days a week;
5. Is willing and able to follow instructions and maintain the appointment schedule;
6. Habitually wears of toric soft contact lenses binocularly.
    a. No more than 1/3 of the participants should be wearing daily disposable soft toric lenses;
    b. the remaining 2/3+ of the participants must be planned frequent replacement soft toric lens wearers as follows^:
        i. TOTAL30 for Astigmatism: maximum of 3 (~10%) (no target percentage)
        ii. Biofinity toric: maximum of 13 (~40%) (PLUS a target of minimum 10 (~30%))
        iii. Air Optix for Astigmatism (inclusive of +Hydraglyde): maximum of 10 (~30%) (PLUS a target of minimum 7 (~20%))
        iv. ULTRA for Astigmatism: maximum of 5 (~15%) (no target percentage)
        v. Acuvue Vita for Astigmatism: maximum of 3 (~10%) (no target percentage)
        vi. Acuvue Oasys for Astigmatism: maximum of 10 (~30%) (no target percentage)
        vii. Other brands of frequent replacement: maximum of 7 (~20%) (no target percentage)

7. Has refractive astigmatism of at least -0.75DC but no more than -2.75DC in each eye that is correctable with a soft toric lens with a cylinder power of no greater than -2.25DC;
8. Is ammetropic and requires a spectacle spherical component of +8.00 to -10.00D inclusively;
9. Can be fit and achieve binocular distance vision of at least 20/32 Snellen with the available lens parameters (see Table 1).

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 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.

^*These recommended percentages are reasonable estimates of market shares in the U.S. Exceptions may be permitted after discussion with the study monitor or sponsor to target the anticipated habitual lens distribution across all sites.*

**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.*

#*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 the secondary outcome data, thereby negatively affecting study data integrity.*

5.4 STUDY MATERIALS

Sites will be provided (if needed) with a trial kit of Lens A and will source their own trial kit or order trial lenses in the required parameters of Lens B. The sites will use these trial kits/lenses to fit Lens A and Lens B lenses to determine the optimal lens power. The final lens prescription has to be tested on eye and commercial boxes of Lens A and B will be ordered through the site's normal commercial route (Lenses from the fitting sets will not be used for dispensing). In case, the same prescription is worn on both eyes, a single 6-pack will be ordered to be split between both eyes.

Reimbursement to practice sites for study product expenses will be provided by CooperVision, after CORE has reconciled the invoices and the product accountability and dispensing logs.

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. and Canada.

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 toric)**	**Lens B (Total30 for Astigmatism)**
Manufacturer	CooperVision	Alcon
Material	comfilcon A	lehfilcon A
FDA Class	Group 5	
Sphere power (D)	+8.00D to +6.50D (0.50D) +6.00D to -6.00D (0.25 steps) -6.50D to -10.00D (0.50D)	
Cylinder powers (DC)	-0.75, -1.25, -1.75, -2.25	
Axes (steps)	10º to 180º (10º steps)	10º to 180º (10º steps)
Base curve (mm)	8.7	8.6
Diameter (mm)	14.5	14.5

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. Participants who habitually use a daily disposable lens or use a care regimen that is not suitable with the use of the study lenses, will be provided with OptiFree Puremoist with Hydraglyde (Alcon). The sites will source commercial bottles of this care product and reimbursement will be provided by CooperVision, after CORE has reconciled the invoices and the product accountability and dispensing logs.

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 return all unused products to CORE, unless otherwise directed. Worn lenses will be disposed of by participants and at the sites according to local regulations.

5.4.6 PRODUCT ACCOUNTABILITY

Accountability logs are completed to record all study products that were used for each participant, which includes products used during the visits and those dispensed to and returned by each participant.

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 visit 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 3 summarizes the scheduled study visits and study codes.

Table 2: Summary of visits

Visit code	Approximate Duration	Visit Description
0	2 hrs	Screening, Habitual baseline (collect in-office ratings for subjective experience, satisfaction and agreement questions) & Fitting of study lenses
0/R1, 0/R2	As needed	Repeat Visit 0 if needed
1-0	0.75 hr	Dispense Lens type #1 (0-28 days after Visit 0); collect in-office subjective ratings after 10 mins of lens insertion; provide at-home diaries
2-0	1.5 hr	1-month follow-up Lens type #1 (28-32 days after 1-0); review at-home diaries; collect in-office ratings for subjective experience, satisfaction and agreement questions for Lens type#1 Dispense Lens type #2; collect in-office subjective ratings after 10 mins of lens insertion; & Provide at-home diaries
3-0 and exit	1.5 hr	1-month follow-up Lens type #2 (28-32 days after 2-0); review at-home diaries; collect in-office ratings for subjective experience, satisfaction and agreement questions for Lens type#2; collect preference ratings between Lens type#1 and Lens Type#2 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.

[redacted]

5.5.1 VISIT 0 SCREENING & FITTING 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 P will be P01, and participant 01 at site L will be L01. 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 is expected to insert their habitual contact lenses at least 2 hours before attending the visit.
2. The participant will be required to read and sign an Informed Consent Form (Appendix 1) 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, medical conditions, medications, allergies).
4. Contact lens history (habitual lens information and wearing habits).
5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]).
9. [redacted]
10. The participant removes their habitual contact lenses.

11. [redacted].
12. [redacted]
13. [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
14. [redacted]
15. The investigator will fit both study lenses (Lens A and Lens B) using trial lenses following to the manufacturers fitting guidelines.

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

[redacted]

16. [redacted]
17. 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.
18. Schedule dispense visit (0-28 days after Visit 0) and order both study lens types in the final prescriptions (only lenses from commercial 6-pack boxes are used for dispensing) – see section 5.4 for details.

5.5.2 REPEATED SCREENING VISITS (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. Required study lenses 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 3, the initial and two repeat screening visits.

5.5.3 VISIT 1-0 DISPENSE LENS TYPE #1

This visit may or may not be subsequent to the screening visit, depending on lens availability (only lenses from commercial 6-pack boxes are used for dispensing) but will occur no later than 28 days after Visit 0 (or 0/R1). Participant to attend this visit wearing spectacles if this visit is scheduled on a different day as Visit 0 (or 0/R1).

The study procedures are outlined below:

1. Confirm participant's health and medications are unchanged.
2. [redacted]
3. [redacted]
4. [redacted]
5. [redacted]
6. Assess lens fit (refer to the described procedure in visit 0)
7. [redacted]

[redacted]

8. [redacted]
9. [redacted]
10. [redacted]
11. Confirm that Visit 2-0 is scheduled 28-32 days after this 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 arrive having worn Lens type #1 for 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. Confirm participant's health and medications are unchanged.
2. [redacted].
3. [redacted]
4. [redacted]

5. [redacted]
6. [redacted]:
7. [redacted]
8. Assess lens fit:
   - [redacted]
9. The participant will remove the lenses
10. [redacted]
    - [redacted]
11. [redacted]
12. Confirm that Visit 3-0 has been scheduled 28-32 days after this Visit 2-0.

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

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

The study procedures are outlined below:

1. Confirm participant's health and medications are unchanged.
2. [redacted]

3. [redacted]
4. [redacted]
5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]
9. Assess lens fit:
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
10. The participant will remove the lenses.
11. [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
12. 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 after the last study visit, or if the participant is discontinued from the study at another time, complete also an unscheduled visit form. 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, 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 4 summarizes the procedures conducted at each visit.

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

	0 Screen Fit & order study CL	1-0 Dispense first study lens	2-0 1-month follow-up first study lens, dispense second study lens	3-0 1-month follow-up second study lens	Exit
Consent process	x				
Subject age & sex	x				
CL history and/or lens wear schedule	x		x	x	
Health & medication	x	x	x	x	

	0 Screen Fit & order study CL	1-0 Dispense first study lens	2-0 1-month follow-up first study lens, dispense second study lens	3-0 1-month follow-up second study lens	Exit
Review any problems with eyes/study lenses		x	x	x	
[redacted]	x				x (or V1 subj. refraction result)
[redacted]	x				
[redacted]	x				
Study lens fitting	x				
Dispense study CLs		x	x		
[redacted]	x	x	x	x	
[redacted]	x	x	x	x	
[redacted]	x		x	x	
[redacted]	x		x	x	
[redacted]				x	
[redacted]	x		x	x	
[redacted]		x	x		
[redacted]			x	x	
[redacted]	x	x	x	x	x (unless completed at concurrent visit)
Study completion and Exit					x

[1] High Contrast High Illumination

5.6.1 STUDY LENS FITTING

Both lens types will be fit according to the manufacturers fitting guide, using the vertex-corrected spectacle refraction as a guide.

5.6.2 [redacted]

[redacted]

[redacted]

5.6.3 LENS FIT ASSESSMENT

Post-blink movement (0-4 descriptive scale, 1 step)

0 insufficient, unacceptable movement
1 minimal, but acceptable movement
2 optimal movement
3 moderate, but acceptable movement
4 excessive, unacceptable movement

Lens centration (1-4 descriptive scale, 1 step)

1 perfectly centred
2 slightly decentred
3 markedly decentred but corneal coverage
4 unacceptable decentration showing corneal exposure

Rotation of the inferior toric mark: three response options, two with degrees to be measured by estimation or slit-lamp protractor:

i. optimal (ie. toric mark stabilizes exactly at 6 o'clock)
ii. toric mark stabilizes to rest nasal to the 6 o'clock position; include the number of degrees from 6 o'clock position
iii. toric mark stabilizes to rest temporal to the 6 o'clock position; include the number of degrees from 6 o'clock position

Overall lens fit acceptability:

- Is the lens fit clinically acceptable? Yes / No

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 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.

All lenses used in this study are IDE exempt under 21 CFR 812.2(c)2.The two study contact lens types will be worn as per their approved use; on a daily wear basis with monthly replacement. 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 (e.g.: 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

See CORE SOP012 for a description of all adverse events, including management and reporting. 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 5.

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 6.

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:
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)	Notify sponsor as soon as possible, **within 24 hours;** ORE reporting will be **within 24 hours** as per requirements
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 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 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 ocular adverse events may be managed at the practice, or the participant may be 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 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 the occurrence.

[redacted]

[redacted]

[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 for their active involvement in the study (including the initial screening visit and all lens fitting visits) as per the information on the consent letter. 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 chose 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 24 hours 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 paid as per site contract and approved consent letter.

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 14.0, Statsoft or other suitable software. Descriptive statistics will be provided on demographic data (age, gender, refractive error distribution, etc.). Table 7 lists the primary and other outcome variables and anticipated statistical procedures.

Visual acuity results will be converted to LogMAR for analysis purposes.

Comparisons will be made between the study lenses for the variables measured at the 1-month visits. Additionally, the subjective ratings completed on days 7, 14 and 27 with each study lens will be compared. A binomial test will be used to analyze the results for the count data of subjective preferences and experience responses. Where relevant, the number of “no preference” responses will be evenly distributed to the two options on the basis they would be equally likely to choose either.

For assessments conducted for each eye separately, the right eye will be used for analysis. If a general difference is found (paired t-test / Wilcoxon matched pairs) between OD and OS, a comment will be provided.

Where appropriate, data may be presented as both mean or median and as counts by ‘bucket’ groups.

Additional analysis may be conducted.

Table 6: Statistical procedures

Variable	Analysis	Statistical test
[redacted]	Comparison between study lenses and time points	Freidman ANOVA Wilcoxon matched pairs test
[redacted]	Comparison between study days and/or between contact lenses per time point.	Freidman ANOVA Wilcoxon matched pairs test RMANOVA
Demographics, *lens fit variables*	Descriptive stats	One or more: mean, median*, mode, standard deviation, minimum, maximum, frequency count

* For non-parametric data only

12.2 DATA MANAGEMENT

Data will be collected and written on paper forms which will be provided to each site by CORE.

Each site is required to submit completed study forms via a secure file-sharing system hosted on a University of Waterloo SharePoint site. Each site will be provided with their own account and password to access the designated folder for uploading files. Users will be required to log in with their provided credentials to deposit their files securely.

The site will endeavour to provide 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 Co-ordinator.

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 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:

- The number of participants screened, enrolled, and randomized (i.e. assigned a study ID number), discontinued and completed.
- Details of all protocol deviations, adverse events, device malfunctions.
- Reports of unintended events.

CORE will collate the site updates and regular 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 one person and a second person will visually compare the data entry to the source documents. 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 will be reported to the sponsor. All serious adverse events and major protocol deviations will be reviewed by the site Principal Investigator and CORE's Lead Co-ordinator before reporting to the sponsor and to Sterling Institutional Review Board as per their policies.

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 Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guidelines for Good Clinical Practice
- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2018)
- https://uwaterloo.ca/research/office-research-ethics/research-human-participants

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. All protocol deviations must be reported to CORE's lead study coordinator (see section 8.3).

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 Sterling IRB:

- 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

Protocol deviations caused by or which originate with research participants are considered minor, and normally are not reported to Sterling IRB 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 ORE:

- 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 and the sponsor within 10 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 (see contact details in section 8.3) 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 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 the original study product accountability and dispensing logs, and enrolment logs to CORE. 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. 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

Data will be analysed at CORE and a report will be sent to the sponsor according to terms described in the study contract.

17 REFERENCES

1. Luensmann D, Schaeffer JL, Rumney NJ, et al. Spectacle prescriptions review to determine prevalence of ametropia and coverage of frequent replacement soft toric contact lenses. Cont Lens Anterior Eye 2018;41:412-20.