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Centre for Ocular Research & Education

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Protocol

Performance evaluation of different daily disposable contact lenses in habitual lens wearers who report frequent use of digital devices (STUDY CODENAME: SUN)

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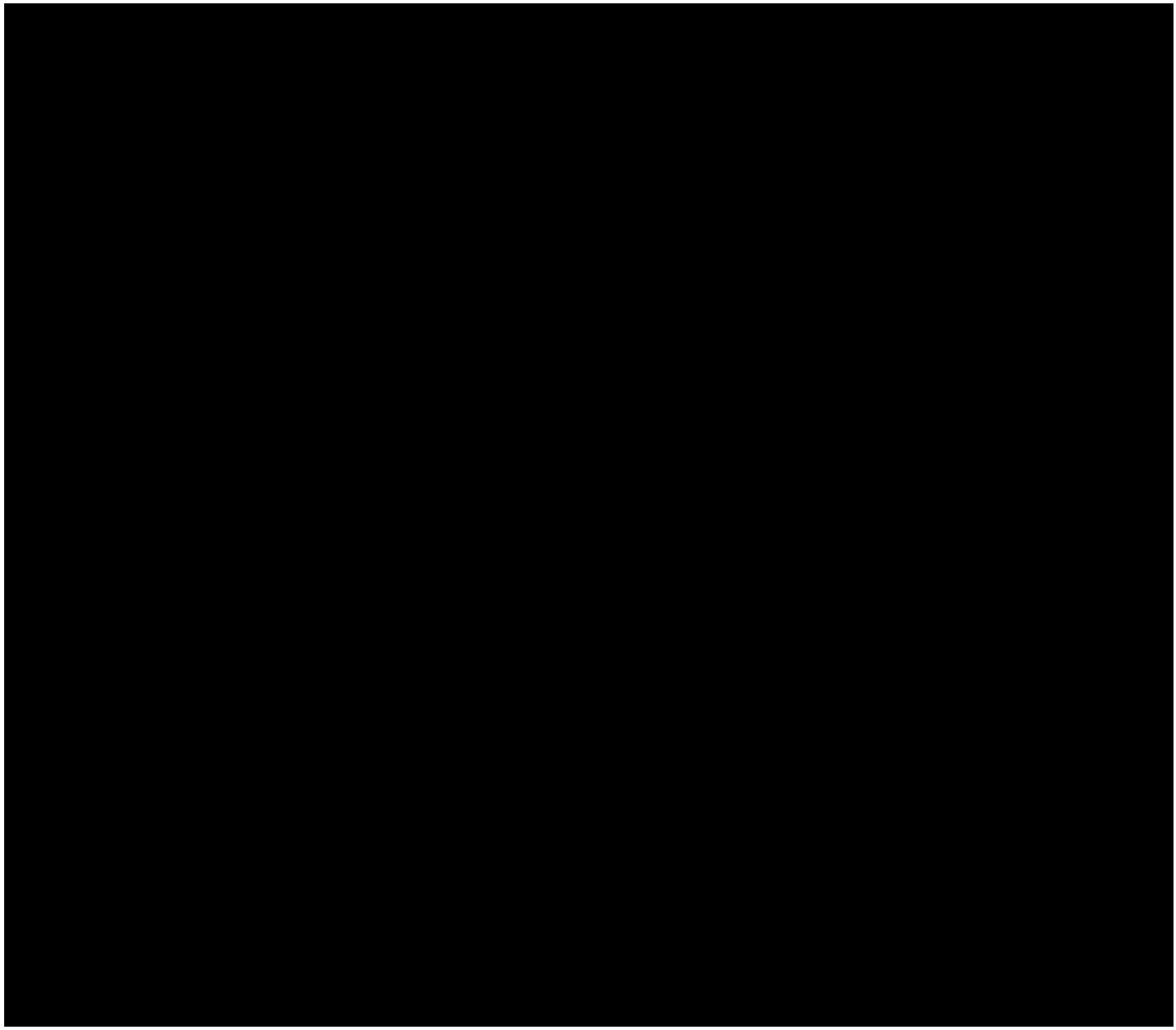

1 DOCUMENT CHANGE HISTORY

Version number	Version date	Author	Description of change(s)
1.0	12Dec2022	Doerte Luensmann	Original protocol
1.1	14Dec2022	Doerte Luensmann	Multiple administrative changes
1.2	09Jan2023	Doerte Luensmann	Sample size calculation added
1.3	24Jan2023	Doerte Luensmann	Computer Vision Syndrome Questionnaire (CVS-Q) added
1.4	06Feb2023	Doerte Luensmann	Lens order procedure updates
1.5	23Feb2023	Doerte Luensmann	Inclusion criteria updated (5.3.3): Participant age range 18-35 years (inclusively)

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Confidentiality

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Disclaimer

This study will be conducted for research purposes only.

2 INTRODUCTION

Daily disposable (DD) contact lenses are popular choices today and are frequently recommended by eye care professionals, as this avoids the use of a lens cleaning product and with the goal to reduce symptoms of dryness and discomfort.[1] As a result, DD lenses account for 45% of all soft lens fits today.[2]

DD lenses were mainly available in hydrogel materials in the past, however, more and more new high oxygen-permeable silicone hydrogel (SiHy) DD lenses are becoming available today.

The goal of this study is to compare the performance of MyDay Energys, a SiHy DD lens from CooperVision Inc., which has successfully been established on the market, with ACUVUE OASYS MAX 1-Day, a DD SiHy lens recently launched by Johnson & Johnson Inc.

3 OBJECTIVES

To evaluate and compare the performance of MyDay Energys (CONTROL) (CooperVision Inc.) and ACUVUE OASYS MAX 1-Day sphere (TEST) (Johnson & Johnson Inc.) in existing soft lens (CL) wearers over one week of wear.

The primary outcome variable for this study is:

- Lens handling on removal collected on Day 6 on the at-home ratings (0-100 scale).

4 HYPOTHESIS

The null hypothesis is that there will be no difference for lens handling on removal on Day 6 (At-home ratings, 0-100 scale) between CONTROL compared to TEST lens.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

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

5.1.2 RANDOMIZATION

A randomization schedule will determine the order of CONTROL and TEST CL wear for the first/second week 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: (for example www.randomization.com). The lens type that will be worn during the first week is called "Lens type #1", the lens type dispensed for the second week is called "Lens type #2". The final study randomization schedule will be generated by CORE's Database Administrator and provided to the unmasked research assistants at each site.

5.1.3 MASKING

This study will be double masked i.e. participants and investigators will be masked to the lens type dispensed. In order to achieve this, unmasked research assistants will determine the lens order according to the randomization schedule (see section 5.1.2) and will over-label the lens packages/foils prior to dispense by placing strongly adhesive stickers on the packages/foils to mask the participant and investigator to the lens brand. At the fitting visit both lens types will be fit, but only the participant can be masked to the lens type during this process because the investigator needs to know which type is being fit in order to follow the fitting guide when making changes to the lens. During the lens wear phases both investigators and participants will be masked.

5.2 INVESTIGATIONAL SITES

5.2.1 NUMBER OF SITES

This study will be conducted at approximately 4 optometry practice sites in the USA.

5.2.2 INVESTIGATOR RECRUITMENT

The principal investigator at each site will undergo qualification by CooperVision oversight personnel and among other requirements they will be required to fulfil the following criteria:

- Is a licensed eye care professional 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 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 a 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 at removal” using historical data at 1 week in which participants used a 0-100 scale (100 being best).

A sample size of 64 is required to detect a mean difference in “handling at removal” of 10 units on a 0 to 100 scale using a standard deviation of the paired differences of 24.2 with 90% power and alpha 0.05 in a two-tailed t-test. Therefore, up to 73 participants will be dispensed with study products with the goal to complete at least 64.

Power and Sample Size (handling on removal (0-100)

Paired t Test
Testing mean paired difference = 0 (versus ≠ 0)
Calculating power for mean paired difference = difference
α = 0.05 Assumed standard deviation of paired differences = 24.2

Results

Difference	Sample Size	Target Power	Actual Power
10	48	0.80	0.800662
10	54	0.84	0.846406
10	64	0.90	0.902344

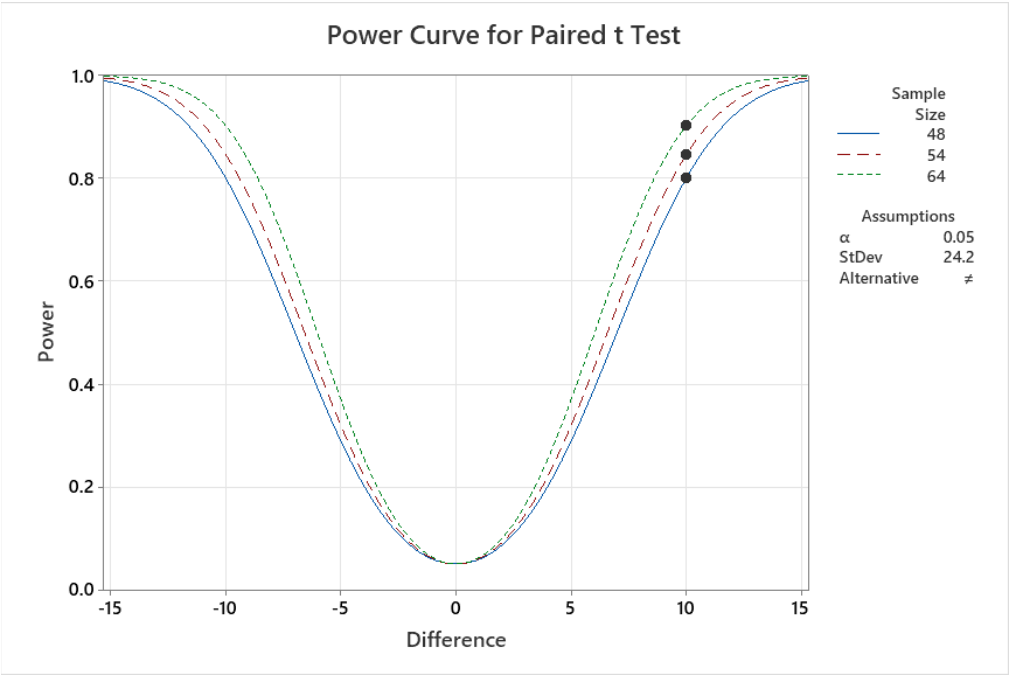

Figure 1: Sample size calculation graph

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 73 potential participants may attend a Screening visit and up to 70 participants may be randomized and dispensed with study products, with a target of at least 64 completing the study.

5.3.3 INCLUSION AND EXCLUSION CRITERIA

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

1. Is between 18 and 35 years of age (inclusively) 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. 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;
5. Anticipates being able to wear the study lenses for at least 8 hours a day, 7 days a week;
6. Is willing and able to follow instructions and maintain the appointment schedule;
7. Habitually wears soft contact lenses, for the past 3 months minimum;
    a. No more than 1/3 of participants should be habitual wearer of MyDay or MyDay Energys
    b. No more than 1/3 of participants should be habitual wearer of ACUVUE® OASYS MAX 1-Day or ACUVUE® OASYS 1-Day.
8. Has refractive astigmatism no higher than -0.75DC in each eye;
9. Can be fit and achieve binocular distance vision of at least 20/30 Snellen (Available lens parameters are sphere -1.00 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 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.

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

Each site will be provided with an inventory of the CONTROL lens which will be used for fitting and dispensing the CONTROL lens.

For the TEST lens, the clinical sites will pre-order two packs of 30 CL in each prescription in the range -1.00 to -6.00 inclusively in 0.25D steps for the use in this study. These lenses will be used for fitting and dispensing the TEST lens. Reimbursement to practice sites for study product expenses for the TEST lens will be provided by CooperVision, after 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 study lenses 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 both study lenses including the lens parameters available for this study.

Table 1: Lens characteristics & parameter to be used

Lens	CONTROL (MyDay Energys)	TEST (ACUVUE OASYS MAX 1-Day)
Manufacturer	CooperVision	Johnson & Johnson
Material	stenfilcon A	senofilcon A
FDA Class	Group 5	Group 5
Sphere power (D)	-1.00 to -6.00 (0.25 steps)	-1.00 to -6.00 (0.25 steps)
Base curve (mm)	8.4	8.5
Diameter (mm)	14.2	14.3

5.4.2 OTHER PRODUCTS

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

5.4.3 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.

5.4.4 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.

5.4.5 PRODUCT ACCOUNTABILITY

Accountability logs are to be 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-week 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	Visits
0	1.5 hr	Screening & Fitting of study lenses
0/R1, 0/R2	As needed	Repeat Visit 0 if needed
1-0	0.5 hr	Dispense Lens type #1 (0-28 days after Visit 0)
2-0	1.0 hr	1-week follow-up Lens type #1 and Dispense Lens type #2 (7-10 days after 1-0)
3-0 and exit	1.0 hr	1-week follow-up Lens type #2 (7-10 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 Test or Control CL, as determined by the randomization table.

Participants will complete subjective ratings 'at-home' on days 1, 3 and 6 during each of the two 1-week lens wear periods; anticipated to take a total of 30 minutes. These ratings will be provided to the participants on visits 1-0 and 2-0 respectively and will be returned and reviewed at visits 2-0 and 3-0 respectively.

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 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 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 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. The participant removes their habitual contact lenses.
8. [redacted].
9. [redacted]
10. [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
    - [redacted]
11. After a minimum 5-minute washout time after fluorescein insertion, the participant will be fit with the study lenses.
12. The investigator will fit both study lenses (CONTROL and TEST) using the pre-ordered or provided lenses following the manufacturers fitting guidelines.

    Trial fitting of both study lenses:

a. The contact lens power will be chosen based on the vertex-corrected spectacle refraction.
b. The contact lenses will be provided to participants in a manner that does not unmask the participant as described in Section 5.1.3.
c. The participant will insert the lenses, allow to settle for at least 10 minutes.
d. [redacted]
e. [redacted]
f. If any changes are made to the lens power, the above procedures (b to e) will be repeated.

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 additional fitting lenses need to be ordered to determine the final lens power, schedule a re-screening visit. Both study lenses have to be tested on eye in the final power before any of the study lens types can be dispensed.
15. Ensure sufficient lenses are available for dispense in the final prescription with each lens type (minimum 12 pairs) before proceeding with Visit 1.0 (Dispense visit).

5.5.2 REPEATED SCREENING VISITS (VISIT 0/R1 OR VISIT 0/R2)

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. [redacted]

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 subsequent to the screening visit, depending on lens availability but will occur no later than 28 days after Visit 0. If this visit occurs on a different day as the screening visit, participant should attend this visit wearing spectacles.

The study procedures are outlined below:

1. Confirm participant's health and medications are unchanged.
2. [redacted]
3. After a minimum 5-minute washout time after fluorescein insertion, participant to insert Lens type #1 according to the randomization table. Ensure that both investigator and participant are fully masked to the study lens type.
4. [redacted]
5. [redacted]
6. [redacted]
7. Provide and explain to participant the subjective at-home rating forms to be completed on Day [redacted] 6 (Note: Day 1 is the day <u>after</u> the dispensing visit). Fill in the days and dates on these forms.
8. The participant will receive lens supply and will be instructed to wear the lenses for at least 8 hours a day, 7 days a week.
9. Visit 2-0 will be scheduled 7-10 days after Visit 1-0.

5.5.4 VISIT 2-0, 1-WEEK 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 7-10 days (inclusive) after visit 1-0.

The study procedures are outlined below:

1. Confirm participant's health and medications are unchanged.
2. Review 'at-home' ratings for completeness and legibility.
3. [redacted]
4. [redacted]
7. The participant will remove the lenses.
8. [redacted]
9. Continue with the lens dispense for Lens type #2 as described in visit 1-0 starting at point #3 to #8.
10. Visit 3-0 will be scheduled 7-10 days after Visit 2-0.

5.5.5 VISIT 3-0 1-WEEK 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 7-10 days (inclusive) after visit 2-0.

The study procedures are outlined below:

1. Confirm participant's health and medications are unchanged.
2. Review 'at-home' ratings for completeness and legibility.
3. [redacted]
4. [redacted]
5. [redacted]

7. [redacted]
8. The participant will remove the lenses.
9. [redacted]
10. 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.

[redacted]

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 of study Lenses	1-0 Dispense Lens type #1	2-0 1-week follow-up Lens type #1 dispense Lens type #2	3-0 1-week follow-up Lens type #2 and Exit
Consent process	x			
Subject age & sex	x			
CL history and/or lens wear schedule	x		x	x
[redacted]	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	x
[redacted]			x	x
[redacted]				x
Issue 'at-home' subjective ratings		x	x	
Collect & review 'at home' ratings			x	x
[redacted]	x	x*	x	x
Study Exit				x

* Not required if visit concurrent subsequent to previous one.

[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 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 habitual lens and the two study contact lens types will be worn as per their approved use; on a daily wear, daily disposable 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

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: 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 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 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 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, CORE and the sponsor.

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 the occurrence. Each site's Principal Investigator will report the event to the IRB as per IRB requirements (by fax, mail/delivery, phone, or email).

[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 choses 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 (usually in weekly study updates).

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.

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 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-week visits. Additionally the subjective ratings completed on days 1, 3 and 6 with each study lens will be compared for differences and equivalence. 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 and as counts by ‘bucket’ groups.

Additional analysis may be conducted

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 Co-ordinator.

13 PROTOCOL & OTHER TRAINING

All study personnel will be required to complete training prior to their involvement in the study. 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. Additional training and site qualification may be required as indicated by the sponsor.

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 provide 2-weekly 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 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 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.

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 major (significant) protocol deviations:

- 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

The following are examples of protocol deviations that are typically considered minor:

- 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 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 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.

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.