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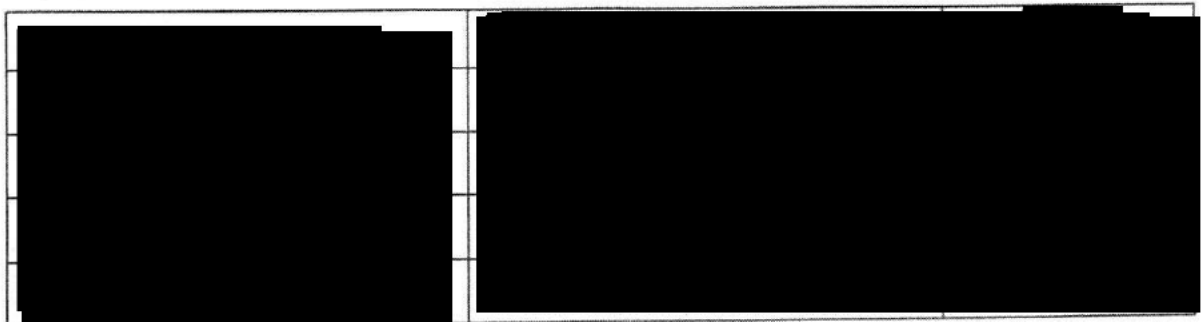
Protocol

COMPARING THE PERFORMANCE OF 1 DAY MULTIFOCAL CONTACT LENSES

(STUDY CODENAME: MANGO)

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Study Personnel

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[REDACTED]	[REDACTED]

Study locations

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



[REDACTED]

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

Site code	Principal Investigator, email	Practice address
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[REDACTED]	[REDACTED]	[REDACTED]
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Disclaimer

This study will be conducted for research purposes only.

2 INTRODUCTION

Multifocal contact lenses provide correction for vision at near as well as in the distance. This segment of the contact lens market has been slowly growing as more products become available.

CooperVision is interested in comparing the performance of their newly developed daily disposable (DD) MyDay® Multifocal (Lens A) contact lens to patients' habitual multifocal lenses and to the competitor product DAILIES TOTAL1® Multifocal (Lens B). Of particular interest is the comparison of handling the lenses, which includes insertion and removal to and from the eye. Ease of lens handling is critical in a presbyopic population who require specific prescription for seeing well up close.

3 OBJECTIVES

The objective of the study is to compare the lens handling and performance of Lens A to habitually worn multifocal contact lenses and to the competitor Lens B.

The primary outcome variable for this study is:

- Subjective at-home ratings of 'Lens handling for insertion', using a 0-10 scale, collected on Day 13.

4 HYPOTHESIS

The null hypothesis is that there will be no difference between the at-home subjective ratings of 'Lens handling for insertion', collected on Day 13 for Lens A compared to Lens B.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

This is a prospective, randomized, participant-masked, crossover, bilateral dispensing study conducted at up to 5 clinical practice sites in the United States, listed on page 3. Each lens type will be worn for up to 3 weeks. The lens prescription of each lens type will be optimized after 3-7 days wearing experience, prior to starting a 2-week wear period.

5.1.2 RANDOMIZATION

Participants will be wearing their habitual lenses during the first 2-week phase, followed by a randomized order of Lens A and Lens B lens wear.

A randomization schedule will be generated for each site using a web-based program to determine the order of Lens A and Lens B lens wear: (www.randomization.com). 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

Participants will wear their habitual lens with an optimized prescription during the first Phase, followed by a masked lens wear using Lens A and Lens B. Lens packages/foils will be over-labeled with strongly adhesive stickers to mask the participant to the lens brand.

It is not possible for the study investigators to be masked because of the need to follow the specific lens fitting guide during the lens prescription optimization visit (Visits 0, 2-1, 3-1).

5.2 INVESTIGATIONAL SITES

5.2.1 NUMBER OF SITES

This study will be conducted at 5 optometry practice sites, listed on page 3 of this document.

5.2.2 INVESTIGATOR RECRUITMENT

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

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

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

5.3 STUDY POPULATION

5.3.1 SAMPLE SIZE CALCULATION

The sample size was calculated using lens handling data from a previous study comparing Lens A against lens B (CooperVision, data on file). In that study a 0-100 scale was used, not the 0-10 used in this study. As a way of compensating for fewer step sizes in the 0-10 scale, a target difference of 5 units on the 0-100 scale was chosen as a meaningful clinical differences in 0-100 subjective responses.

Using the 0-100 scale data described above for 'lens handling for insertion', where the data showed a standard deviation of 12.7 and when applying requirements of 80% power and alpha 0.05 in a two-tailed t-test, a minimum sample size of 53 participants is recommended in order to detect a mean difference of 5 units.

To account for dropout, up to 60 participants may be randomized and dispensed with study product in total, with the target of at least 53 completing the study.

Note: this study will use a subjective rating scale of 0-10, integer steps.

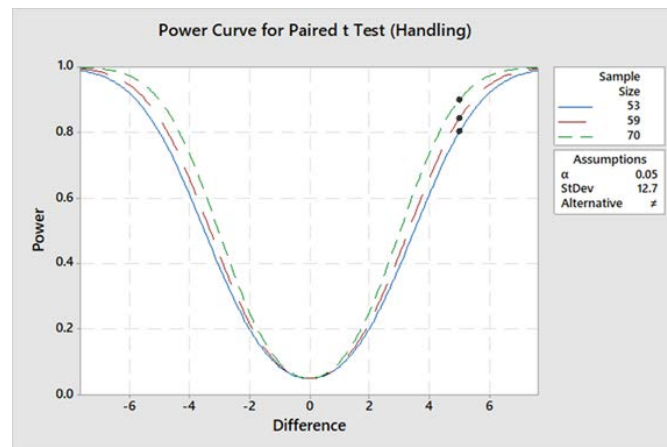


Figure 1: Sample size calculation graph

5.3.2 NUMBER OF PARTICIPANTS

Participants will be recruited using site records, databases and advertising materials (eg. posters, email scripts) approved by the ethics review board. All initial individual-targeted recruitment activities, such as any direct mailing of recruitment scripts, will be conducted by practice staff that are not directly involved in conducting the research. This separation will reduce any undue influence of the optometrist-patient relationship. This process will also

eliminate opportunity for the investigator to access personal health information before any consent for disclosure is provided by the potential participant.

It is anticipated that up to 80 potential participants may attend a Screening visit and up to 60 participants may be randomized and dispensed with study products, with a target of 53 completing the study.

5.3.3 INCLUSION AND EXCLUSION CRITERIA

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

1. Is at least 42 years of age 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, 5 days a week;
5. Is willing and able to follow instructions and maintain the appointment schedule;
6. Habitually wears multifocal soft contact lenses, for the past 3 months minimum;
7. Has refractive astigmatism no higher than -0.75DC;
8. Is presbyopic and requires a reading addition of at least +0.75D and no more than +2.50D;
9. Can be fit and achieve binocular distance vision of at least 20/30 Snellen (or +0.20 logMAR) which participants also deem to be 'acceptable', with the available study lens parameters (sphere +4 to -6; near addition or LOW, MEDIUM, HIGH).

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

1. Is participating in any concurrent clinical or research study;
2. Habitually wears one of the study contact lenses;
3. Has any known active* ocular disease and/or infection that contraindicates contact lens wear;
4. Has a systemic condition that in the opinion of the investigator may affect a study outcome variable;
5. Is using any systemic or topical medications that in the opinion of the investigator may affect contact lens wear or a study outcome variable;
6. Has known sensitivity to the diagnostic sodium fluorescein used in the study;
7. Self-reports as pregnant, lactating or planning a pregnancy at the time of enrolment;
8. 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.

Age ≥ 42 years is an inclusion criteria because presbyopia is unlikely in persons aged < 42 years and, if present, may not be due solely to presbyopic changes representative of the wider population.

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. 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

Habitual lenses: The optimized prescription of the habitual lenses will be determined by the investigator and the clinical site will order a new lens supply to the participant (6-pack for frequent replacement MF lenses, 30-pack for daily disposable MF lenses. If the participant wears the same prescription in both eyes, only one box will be ordered). If applicable, the clinic site will also supply the participant with a new bottle of their habitual care regimen including a new lens case.

Lens A and Lens B: CooperVision will provide each site with a small trial kit of Lens A lenses. Sites will source their own trial kit of Lens B. The sites will use these trial kits to fit Lens B and Lens A lenses to determine the optimal lens power. Once the final lens has been determined, the site will order a pack of 30 lenses for each eye with each lens type. Lens B will be ordered through the site's normal commercial route. CORE will coordinate the Lens A lens orders for each participant upon receipt of the lens order form, which is part of the study visit pack. If the optimization visit determines a different prescription is needed, a new lens supply will be ordered as described previously.

Reimbursement to practice sites for study product expenses will be provided by CooperVision at the end of the study, 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.

The primary contact for study products at CORE is:



5.4.1 LENSES

Lens A is cleared by the by the United States Food and Drug Administration (FDA) and is not yet commercially available in the U.S.

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

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

Table 1: Lens characteristics & parameter to be used

Lens	Lens A	Lens B
Manufacturer	CooperVision	Alcon
Material	stenfilcon A	delefilcon A
FDA Class	Group 5	Group 5
Sphere power (D)	+4.00 to -6.00 (0.25 steps), -	+4.00 to -6.00 (0.25 steps)
ADD power (D)	High, Medium, Low	Hi , Med, Lo
Base curve (mm)	8.4	8.5
Diameter (mm)	14.2	14.1

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 must be kept by each site to include the number of contact lenses received and returned to CORE (where relevant). All products dispensed to participants must be recorded in participant dispensing logs.

5.5 SCHEDULED AND UNSCHEDULED VISITS

This study has a minimum of 12 scheduled study visits, including the screening visit, though some visits may be scheduled concurrently on the same day. There is an option for repeated screening and lens fitting visits as needed.

A scheduled follow-up visit may only take place when the participant attends wearing the study lenses for at least two hours. 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.

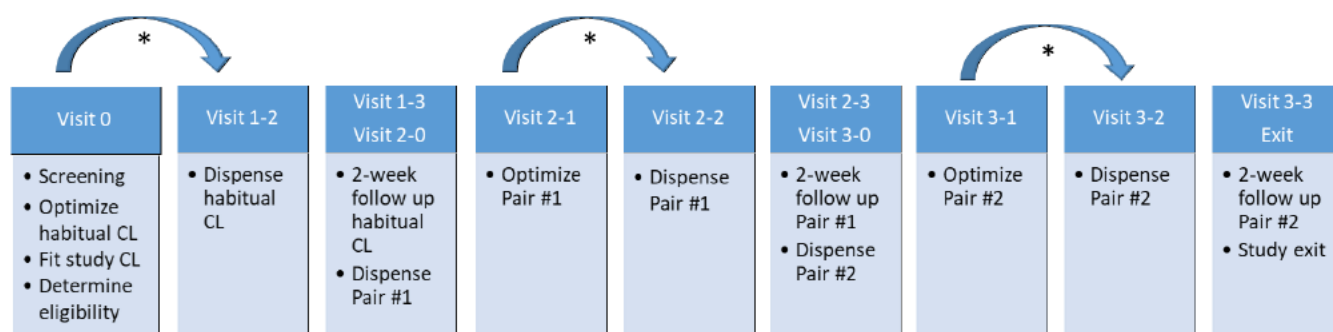
Visits that fall outside of the specified visit windows will be designated as protocol deviations and at the end of the study, the data collected during protocol deviations will be assessed for their suitability to be included in the analysis population.

Table 3 summarizes the scheduled study visits and study codes.

Table 2: Summary of visits

Visit code	Approximate Duration	Visits
0	2 hr	Screening & Optimize habitual lens type & Fitting of study lenses
0/R1, 0/R2	As needed	Repeat Visit 0 if needed
Phase 1		
1-2	0.5 hr	Dispense optimized habitual lenses (Phase 1, 0-10 days after Visit 0)
1-3	0.5 hr	2-week follow-up habitual lenses (Phase 1, 14-16 days after 1-2)
Phase 2		
2-0	0.5 hr	Dispense Pair #1 (Phase 2, same day as 1-3)
2-1	0.5 hr	Optimize Pair #1 (Phase 2, 3-7 days after 2-0)
2-2	0.5 hr	Dispense (optimized) Pair #1
2-3	0.5 hr	2 week follow-up Pair #1 (Phase 2, 14-16 days after 2-2)
Phase 3		
3-0	0.5 hr	Dispense Pair #2 (Phase 3, same day as 2-3)
3-1	0.5 hr	Optimize Pair #2 (Phase 3, 3-7 days after 3-0)
3-2	0.5 hr	Dispense (optimized) Pair #2
3-3	0.5 hr	2 week follow-up Pair #2 (Phase 3, 14-16 days after 3-2)
EXIT	0.25 hr	Exit VA, exit forms & remuneration

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



*Visits could be subsequent on same day if CL power is unchanged

Participants will complete subjective ratings 'at-home' on day 13 during each of the three 2-week lens wear periods (phases); anticipated to take a total of 20 minutes per phase. These ratings will be provided to the participants on visits 1-2, 2-2, and 3-2 respectively and will be returned and reviewed at visits 1-3, 2-3 and 3-3 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 W will be W-01, and participant 01 at site Z will be Z-01. 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 multifocal contact lenses at least 2 hours before attending the visit and if available bring an additional (new) pair of lenses. (If participant habitually wears daily disposable MF lenses, ask if a 2-week supply is available. All habitual lenses used during the study will be replaced at no charge to the participant.)
2. The participant will be required to read and sign an Informed Consent Form prior to enrollment. When the participant has signed the consent form, the participant will be considered enrolled in the study and will be assigned a study ID.
3. Participant demographics and medical history (age, sex, race, ethnicity, medical conditions, medications, allergies).
4. Contact lens history (habitual lens information and wearing habits).
5. [REDACTED]
6. [REDACTED]
7. The participant removes their habitual contact lenses.
8. [REDACTED]
9. [REDACTED]
10. [REDACTED]

11. [REDACTED]

[REDACTED]

13. The investigator will fit both study lenses (Lens A and Lens B) using fitting sets following to 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. [REDACTED]
- g. If any changes are made to the lens power, the above procedures (b to f) will be repeated.

14. 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.

15. If the habitual lens prescription is unchanged and the participant was able to bring in an extra (new) pair of habitual lenses to the visit, continue with Visit 1-2, otherwise order lenses for participant and schedule Visit 1-2.

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. 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 1-2 DISPENSE HABITUAL MF LENSES

This visit may or may not be subsequent to the screening visit, depending on lens availability.

Participant to attend this visit wearing spectacles.

Procedures as follows:

1. Confirm participant's health and medications are unchanged.

2. [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

- d. [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
3. [REDACTED]
[REDACTED]
4. After lenses have settled for at least 10 minutes continue with assessments
5. [REDACTED]
6. [REDACTED]
[REDACTED]
7. [REDACTED]
8. Provide and explain to participant the subjective at-home rating forms to be completed on Day [REDACTED] 13 (Note: Day 1 is the day after the dispensing visit). Fill in the days and dates on these forms. Explain the ratings will include:
[REDACTED]
[REDACTED]
- c. Ease of lens handling for insertion onto eyes (0 – 10 integer scale);
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
- k. Ease of lens handling for removal from eyes (0 – 10 integer scale);
[REDACTED]
[REDACTED]
[REDACTED]
9. The participant will receive lens supply (if applicable) and will be instructed to wear the lenses for at least 8 hours a day, 5 days a week.
10. Visit 1-3 will be scheduled.

5.5.4 VISIT 1-3, 2-WEEK FOLLOW-UP HABITUAL LENSES

Participants will be asked to insert habitual lenses at least 2 hours prior to the visit.

This visit will occur 14-16 days (inclusive) after visit 1-2.

1. Confirm participant's health and medications are unchanged.
2. [REDACTED]
3. Review 'at-home' ratings for completeness and legibility.
4. [REDACTED]
5. [REDACTED]
6. [REDACTED]
7. The participant will remove the lenses.
8. [REDACTED]
9. Continue with visit 2-0.

5.5.5 VISIT 2-0 DISPENSE PAIR #1

This visit is subsequent to Visit 1-3.

1. [REDACTED]
2. After lenses have settled for at least 10 minutes continue with assessments
3. [REDACTED]

4. [REDACTED]
5. [REDACTED]
6. The participant will receive a 1-week lens supply and will be instructed to wear the lenses for at least 8 hours a day, 5 days a week.
7. The participant will be scheduled to return for Visit 2-1.

5.5.6 VISIT 2-1 OPTIMIZE PAIR #1

Participants will be asked to insert study lenses at least 2 hours prior to the visit.

This visit will occur 3-7 days (inclusive) after visit 2-0.

1. Confirm participant's health and medications are unchanged.
2. [REDACTED]
6. If lens power changes are required, and required lens power is not on site, the lens/es will be ordered and assessed at an additional visit. If the required lens power is on site, participant will remove lens(es) from the eye and insert the new fitting lens(es) on eye.
 - a. Allow settling time of 10 minutes before evaluation of vision [REDACTED] to assess the final lens power needed.
8. Remove lenses
9. [REDACTED]

e. [REDACTED]

[REDACTED]

7. If no power change is needed or if a 2-week supply of optimized lenses are available on site continue with visit 2-2, otherwise order the lenses and schedule Visit 2-2. If new lenses need to be ordered, participants will be allowed to wear habitual MF lenses in the meantime.

5.5.7 VISIT 2-2 DISPENSE (OPTIMIZED) PAIR #1

This visit may be conducted immediately following Visit 2-1 (if no prescription change is needed) or can be scheduled after Visit 2-1.

Participant to attend this visit wearing spectacles.

Procedures as follows:

1. Confirm participant's health and medications are unchanged.

2. [REDACTED]

[REDACTED]

b. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

3. [REDACTED]

[REDACTED]

[REDACTED]

4. After lenses have settled for at least 10 minutes continue with assessments

5. [REDACTED]

[REDACTED]

8. [REDACTED]

9. [REDACTED]
10. Provide and explain to participant the subjective at-home rating forms to be completed on Day [REDACTED] 13 (Note: Day 1 is the day after the dispensing visit). Fill in the days and dates on these forms. Explain the ratings will include:
- a. [REDACTED]
 - b. [REDACTED]
 - c. Ease of lens handling for insertion onto eyes (0 – 10 integer scale);
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
 - k. Ease of lens handling for removal from eyes (0 – 10 integer scale);
[REDACTED]
 - m. [REDACTED]
 - n. Report of any unusual symptoms or problems with lenses.
11. The participant will receive a 2-week lens supply and will be instructed to wear the lenses for at least 8 hours a day, 5 days a week.
12. The participant will be scheduled to return for Visit 2-3.

5.5.8 VISIT 2-3, 2-WEEK FOLLOW-UP PAIR #1

Participants will be asked to insert study lenses at least 2 hours prior to the visit.

This visit will occur 14-16 days (inclusive) after visit 2-2.

Assessments of lens Pair #1 will be conducted as described for habitual lenses at visit (Visit 1-3).

[REDACTED]
[REDACTED]

5.5.9 VISIT 3-0, DISPENSE PAIR #2

This visit is subsequent to Visit 2-3.

Assessments of Pair #2 will be conducted as described for habitual lenses at visit (Visit 1-3).

5.5.10 VISIT 3-1 OPTIMIZE PAIR #2

Participants will be asked to insert study lenses at least 2 hours prior to the visit.

This visit will occur 3-7 days (inclusive) after visit 3-0.

Assessments of Pair #2 will be conducted as described for Pair #1 at visit (Visit 2-1).

5.5.11 VISIT 3-2 DISPENSE (OPTIMIZED) PAIR #2

This visit may be subsequent to Visit 2-1 (if no prescription change is needed) or is scheduled after Visit 2-1.

Assessments of Pair #2 will be conducted as described for Pair #1 at visit (Visit 2-1).

5.5.12 VISIT 3-3, 2-WEEK FOLLOW-UP PAIR #2

Participants will be asked to insert study lenses at least 2 hours prior to the visit.

This visit will occur 14-16 days (inclusive) after visit 3-2.

Assessments of Pair #2 will be conducted as described for habitual lenses at visit (Visit 1-3).

[REDACTED]

[REDACTED]

[REDACTED]

After all assessments and questionnaires are completed, the participant will be unmasked [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

5.5.13 EXIT VISIT

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.



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.

5.5.14 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 CL fit	1-2 Disp. Optim. hab. CL	1-3 2-week follow- up hab. CL	2-0 Disp. Pair #1	2-1 Optim. Pair #1	2-2 Disp. Optim. Pair #1	2-3 2-week follow- up Pair #1	3-0 Disp. Pair #2	3-1 Optim. Pair #2	3-2 Disp. Optim. Pair #2	3-3 2-week follow- up Pair #2	Exit
Consent process	x											
Participant age & sex, race & ethnicity	x											
CL history and/or lens wear schedule	x		x		x		x		x		x	

	0 Screen CL fit	1-2 Disp. Optim. hab. CL	1-3 2-week follow- up hab. CL	2-0 Disp. Pair #1	2-1 Optim. Pair #1	2-2 Disp. Optim. Pair #1	2-3 2-week follow- up Pair #1	3-0 Disp. Pair #2	3-1 Optim Pair #2	3-2 Disp. Optim. Pair #2	3-3 2-week follow- up Pair #2	Exit
Health & medication	x	x	x	x	x	x	x	x	x	x	x	
Review any problems with eyes/study lenses		x	x	x	x	x	x	x	x	x	x	
[REDACTED]	█								█			█
[REDACTED]	█											
[REDACTED]	█											
[REDACTED]	x											
[REDACTED]	x				x				x			
Dispense study CLs*		x		x		x		x		x		
[REDACTED]	X (except intern VA)	x	x	x	x	x	x	x	x	x	x	
Study CL fit assessment		x	x	x	x	x	x	x	x	x		
[REDACTED]			█				█				█	
[REDACTED]											x	
Issue 'at-home' subjective ratings		x				x				x		
Collect & review 'at home' ratings			x				x				x	
[REDACTED]	x	x	x	x	x	x	x	x	x	x	x	
Study completion and Exit												x

* Additional lenses may be dispensed at scheduled or U/S visits if there is lens defect, or lens damage or if there is a valid reason (e.g. lenses dropped or misplaced etc.)

** Not required if visit concurrent subsequent to previous one.

¹ High Contrast High Illumination

5.6.1 STUDY LENS FITTING

Both lens types will be fit according to the manufacturers fitting guide, using the vertex-corrected spectacle refraction as a guide. Learnings from the first lens fit will not be applied to the second lens fit because it is of interest to determine how many lenses were needed to achieve the final lens prescription.

5.6.2 [REDACTED]

[REDACTED]

5.6.3 [REDACTED]

This will consist of three separate assessments:

1. [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 7 days of becoming aware of them (as per Sterling Institutional Review Board guidelines).

7 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

There may be no direct benefits to the subjects in this study. Participation in a study may contribute to scientific research information that may be used in the development of new contact lens products. The subjects will receive an examination of the front part of their eyes and may have the

opportunity to try a different type of soft contact lenses and/or different lens care products at no cost to them. The contact lens materials used in this study are commercially available as daily wear. This study will investigate participants' wearing schedule intended for daily wear (NOT extended wear), similar to the average wearing time of 10-16 hours for daily wear lenses.

This study is considered to be a non-significant risk study based on United State Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines, because the study devices used as intended in this study (1) do not represent a potential for serious risk to the health, safety or welfare of the subject, and (2) are not implants, (3) are not used to support or sustain human life, (4) are not of substantial importance in diagnosing, curing, mitigating or treating disease or otherwise prevents impairment of human health.

The 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:
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)	Notify sponsor as soon as possible, within 24 hours ; ORE reporting will be within 24 hours as per requirements
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 \geq dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization \geq 1.0mm vessel penetration (e.g. \geq ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of \geq 2 lines BSCVA for \geq 2wks	
17	Any sign and/or symptom for which participant is administered therapeutic treatment or which necessitates discontinuation of lens wear for \geq 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 \geq 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	

[REDACTED]

Sponsor contact details for adverse events are:

[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 US\$20 per hour 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 for a final exit visit, and if the investigator has made a reasonable effort to contact the participant for a final study visit.
- Premature termination of the study by the sponsor, CORE or Sterling IRB.

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

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

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

10 DEVICE MALFUNCTIONS

A device malfunction means the failure of the device to meet its performance specification or otherwise perform as intended. Any defective lens that is *likely* to cause or contribute to a *Serious Adverse Event* should be reported to CORE and the sponsor **within 24 hours** of the investigator becoming aware of the malfunction. The ORE 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 approximately US\$165 for completing the study. This is calculated at \$20 per hour for the 1 hour of at home ratings questionnaires and 7.25 hours of predicted scheduled visits, though if additional fitting time is required, this may increase.

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.

[REDACTED]

Comparisons will be made between the study lenses for the variables measured at the 2-week visits. Additionally the subjective ratings completed on day [REDACTED] 13 of each phase will be compared. A binomial test will be used to analyze the results for the count data [REDACTED]. [REDACTED] Where relevant, the number of “neither agree or disagree” responses will be evenly distributed to the two options on the basis they would be equally likely to choose either.

[REDACTED]

[REDACTED]

[REDACTED]

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

Table 6: Statistical procedures

Variable	Analysis	Statistical test
<i>Ratings: Likert & Preference</i>	Comparison between study days and/or between contact lenses per time point.	Freidman ANOVA Wilcoxon matched pairs test
<i>Ratings: numerical ratings Biomicroscopy</i>	Comparison between study days and/or between contact lenses per time point.	Freidman ANOVA Wilcoxon matched pairs test RMANOVA
<i>Demographics Lens fit variables</i>	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 will email scanned forms to a designated person at CORE who will pass these scans to the data entry team. The site will endeavour to send the scanned forms to CORE on the same day as the study visit and at a maximum, two days after the study visit.

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_v01_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 a secure file share system operated by the University of Waterloo called Sendit which uses 128bit (or 256bit) SSL encryption. 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. They will also complete CORE's Conflict Disclosure Form.

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 two people and the entries will be compared. Data queries will be reported to the site within 5 working days of receipt of initial data. A response resolving the query will be expected from the site within 5 working days of receipt of the query.

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

15 STUDY MANAGEMENT

15.1 STATEMENT OF COMPLIANCE

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

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

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

15.2 ETHICS REVIEW

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

This study will be conducted in accordance with Institutional Review Board regulations (U.S. 21CFR Part 56.103) or applicable IEC regulations. Copies of all IRB/IEC correspondence with the investigator/sponsor will be kept on file. The study will commence upon approval from the following Institutional Review Board: Sterling Institutional Review Board; Telephone number: (888) 636-1062 and email address: info@sterlingirb.com.

15.3 CLINICAL TRIAL REGISTRATION

CooperVision will register this study with clinical trials.gov in accordance with section 801 of the Food and Drug Administration (FDA) Act which mandates the registration of certain clinical trials of drugs and medical devices. They will maintain the information on that site.

15.4 PROTOCOL DEVIATIONS

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

15.4.1 MAJOR PROTOCOL DEVIATIONS

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

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

- 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 the ORE 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 PROTOCOL 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 two 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.