CORE
Centre for Ocular Research & Education

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
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Protocol

EVALUATING THE SUCCESS OF REFITTING LENS WEARERS WITH MYDAY MULTIFOCAL, WHO ARE ALREADY ADAPTED TO CLARITI 1DAY MULTIFOCAL 2-ADD DESIGN (STUDY CODENAME: GALAXY)

Sponsor Company:	**CooperVision Inc.**
Sponsor study number:	**EX-MKTG-140**
CORE protocol number:	**P/818/22/CVI**
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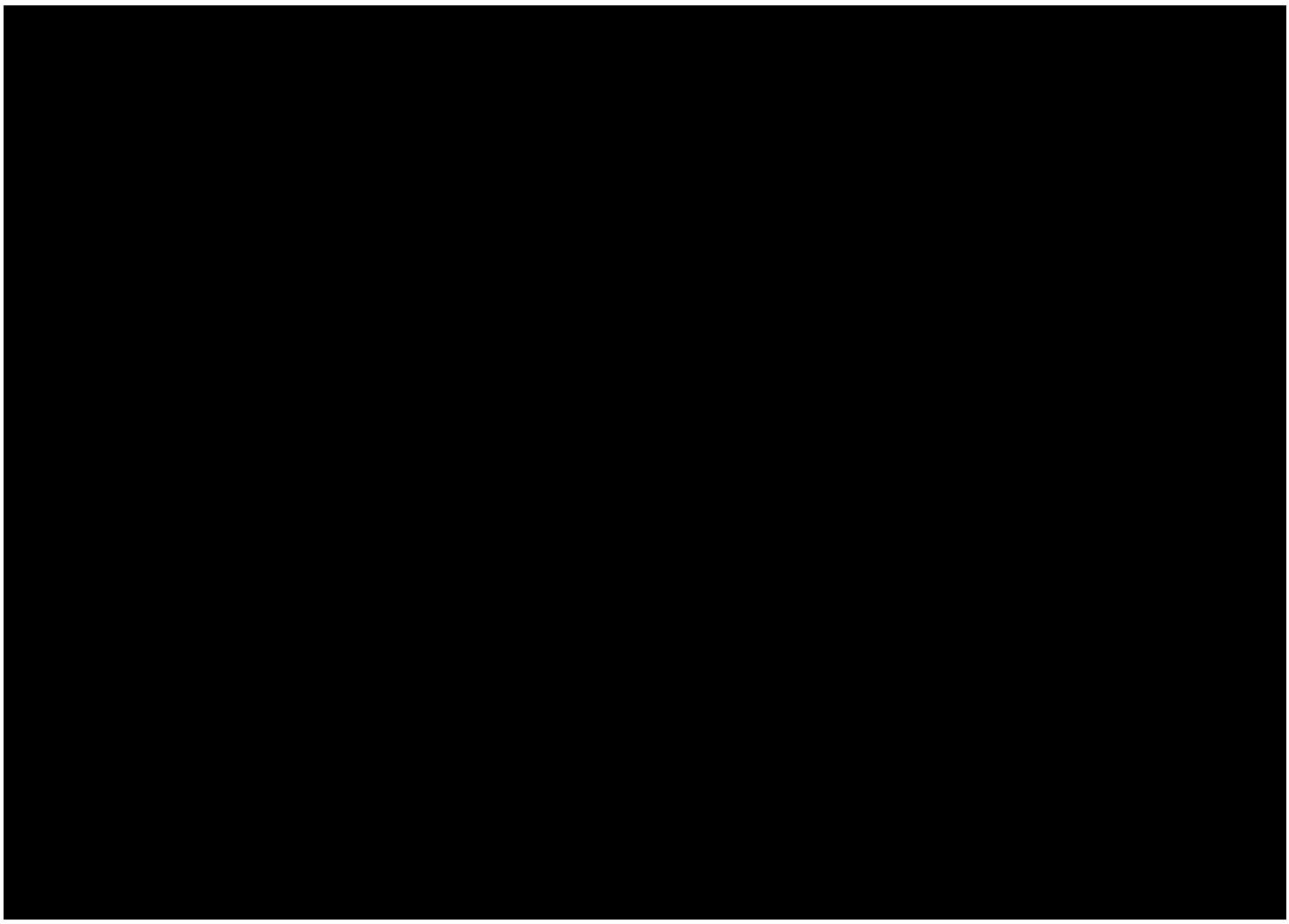
[redacted]



Study locations

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

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

2. **Clinical research conducted at several in-practice study sites in the United States.**
   Details of sites and PIs will be listed in the final report.

1 DOCUMENT CHANGE HISTORY

Version number	Version date	Author	Description of change(s)
1.0	03Aug2022	Doerte Luensmann	Original draft protocol
1.1	08Aug2022	Doerte Luensmann	Details added in sections 3, 4, and 5.3.3

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Confidentiality

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Disclaimer

This study will be conducted for research purposes only.

2 INTRODUCTION

Multifocal contact lenses (MF) 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 two of their own multifocal disposable contact lenses, clariti 1day multifocal 2-ADD design (CONTROL lens) and MyDay 3-ADD design multifocal (TEST lens). Achieving acceptable vision and comfort when transitioning from one lens to another is important for successful multifocal lens wear and will be the focus of this study.

3 OBJECTIVES

The objective of the study is to adapt existing multifocal soft lens wearers to a CONTROL lens (clariti 1day MF 2-ADD design) for at least 2 weeks and then evaluate the success of switching them to the TEST lens (MyDay MF 3-ADD design), with a review after 2 weeks. Particular attention will be paid to explaining the advanced features of MyDay MF and assessing the performance with respect to comfort, vision and overall performance using ratings, agreement questions and preferences.

The primary outcome variable for this study is:

- After 2 weeks of study lens wear (in office):
    - 0-10 ratings for comfort just after lens insertion

4 HYPOTHESIS

The null hypothesis is that there will be no difference between lens types for lens comfort at insertion after 2 weeks of wear.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

This is a prospective, bilateral eye, open label, daily wear switch study involving daily disposable multifocal lenses. There will be no randomisation, subjects will wear CONTROL for the first period of 2 weeks (14-21 days) and TEST for the second period of 2 weeks (14-21 days).

Both CLs will be fit according to fit guides, and the prescriptions will be optimized after an initial wear period of 3-7 days, prior to the 2-week study assessment period. During each 2-week wear period, participants will record their subjective lens-wear experience remotely on three different days (days 1, 6 and 13), using paper diaries.

5.1.2 RANDOMIZATION

There will be no randomization, participants will wear CONTROL for the first wear period and TEST for the second period.

5.1.3 MASKING

The participants and investigators will not be masked in this study. The dispensed contact lenses will not be over-labeled, instead the brand name will be visible.

5.2 INVESTIGATIONAL SITES

5.2.1 NUMBER OF SITES

This study will be conducted at several optometry practice sites in the United States. The site details will be included in the study report.

5.2.2 INVESTIGATOR RECRUITMENT

The principal investigator at each site 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 for prompt lens ordering and timely data review, query and entry.

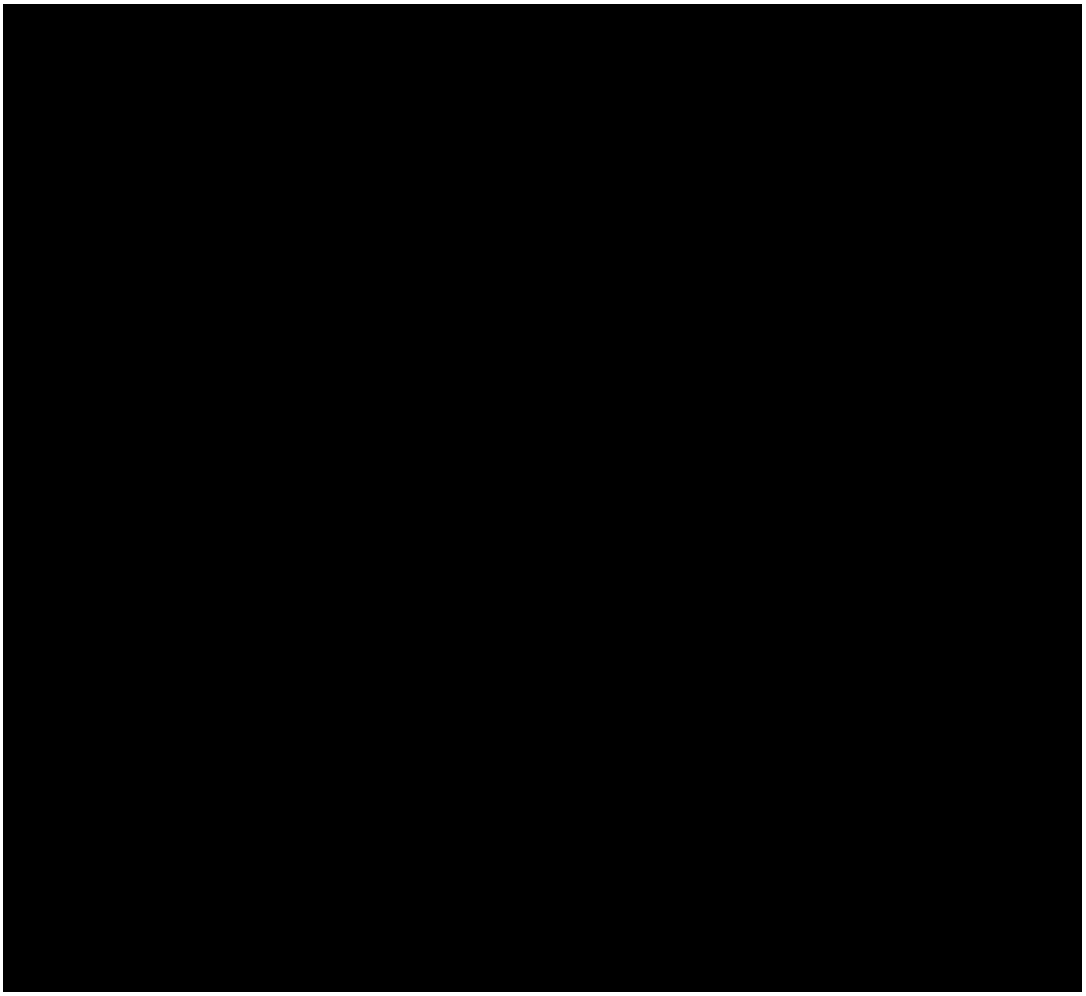
5.3 STUDY POPULATION

5.3.1 SAMPLE SIZE CALCULATION

The sample size was calculated using data of 'lens comfort at insertion' collected in a previous study involving clariti 1day (CooperVision, data on file). In that study a 0-100 scale was used, not the 0-10 used in this study. A difference of 7 on that 0-100 scale was targeted, which would be 0.7 on the 0-10 scale. However, in this study, a 0-10 scale will be used with 0.5 steps, and analysis is anticipated to be non-parametric, which relies on medians not means, thus a difference between medians can only be as low as 0.5.

Using the 0-100 scale data described above for 'lens comfort at insertion', the data showed a standard deviation of paired differences of 16.5. With an alpha 0.05 in a paired difference test, and power of 84%, a minimum sample size of 51 participants is recommended in order to detect a statistical difference between study lenses.

To account for dropout, up to 60 participants may be randomized and dispensed with study product in total, with the target of at least 51 completing the study.



5.3.2 NUMBER OF PARTICIPANTS

Approximately 60 participants will be recruited and dispensed with study contact lenses with the goal to complete at least 51 participants.

The sites will primarily use site records and databases where consent for contact about research has been provided. Recruitment efforts will use an email script and there will also be general advertising materials (e.g., posters, social media posts). All recruitment materials will be approved by the ethics review board. All initial individual-targeted recruitment activities, such as any direct mailing of recruitment scripts, will be conducted by practice staff that are not directly involved in conducting the research. This separation will reduce any undue influence of the optometrist-patient relationship. This process will also eliminate opportunity for the investigator to access personal health information before any consent for disclosure is provided by the potential participant.

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; (NOTE: the habitual contact lens type is restricted such that no more than one third are to be the Clariti 1 day multifocal and no more than one third are to be MyDay multifocal (this includes their equivalent private label brand name);
7. Has refractive astigmatism no higher than -0.75DC in each eye;
8. Is presbyopic and requires a reading addition of at least +0.75D and no more than +2.50D in each eye;
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 (powers +4.00 to -6.00DS) (see Table 1).

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

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

* 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 criterion 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

CooperVision will provide each site with an inventory of both the CONTROL and TEST lenses to allow participants to be fit with the lens powers available for this study ie. sphere +4.00D to -6.00D, in 0.25D steps, in all ADD powers.

The sites will use these inventories to both fit and dispense the CONTROL and the TEST lenses. If additional inventory or participant lenses are required, this will be managed by the sites by ordering through CORE who will arrange for CooperVision to ship the required lenses.

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 CONTROL and TEST lenses are cleared by the by the United States Food and Drug Administration (FDA) and are commercially available in the U.S. The lenses will be worn as daily wear and daily disposable, as per their approvals.

The table below lists the contact lens details for CONTROL lens and TEST lens including the lens parameters available for this study.

Table 1: Lens characteristics & parameter to be used

Lens	CONTROL lens (CONTROL)	TEST lens (TEST)
Manufacturer	CooperVision	CooperVision
Material	somofilcon A	stenfilcon 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, Low	High, Medium, Low
Base curve (mm)	8.6	8.4
Diameter (mm)	14.1	14.2

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 be advised to either return unused products to CooperVision, or to dispose of them according to local regulations. All shipping costs will be covered. 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 9 scheduled study visits, including the screening visit, though it is anticipated there will only be 5 visits to the office because some visits are expected to 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 2 summarizes the scheduled study visits and study codes.

Table 2: Summary of visits

Visit	Assessments	Duration	Visit window
VISIT 0 Screening and fit CONTROL	Consent, screening & eligibility, habitual & baseline, fit CONTROL.	1.5hr	Day 0
VISIT 1 Initial dispense of CONTROL	Assessments & dispense CONTROL.	0.5hr	Ideally concurrent with Visit 0
VISIT 2 Optimization visit CONTROL	Optimization of CONTROL. [redacted]	0.5hr	3-7 days after V1
VISIT 3 Dispense optimized CONTROL	Dispense of optimized CONTROL. [redacted]	0.5hr	Ideally concurrent with Visit 2
VISIT 4 2wk Follow-up CONTROL & fit TEST	[redacted]	1.5hr	14-21 days after V3 (target is 14 days)
VISIT 5 Initial dispense of TEST	Assessments & dispense TEST.	0.5hr	Ideally concurrent with Visit 4
VISIT 6 Optimization visit TEST	Optimization of TEST. [redacted]	0.5hr	3-7 days after V5
VISIT 7 Dispense optimized TEST	Dispense of optimized TEST. [redacted]	0.5hr	Ideally concurrent with Visit 6
VISIT 8 2wk Follow-up TEST	[redacted]	0.75hr	14-21 days after V7 (target is 14 days)
EXIT	Exit [redacted] exit paperwork completed, remuneration processed.	0.25hr	Concurrent with Visit 8, unless early exit

[redacted]

[redacted]

5.5.1 VISIT 0, SCREENING & FITTING VISIT

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

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

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.
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. Determine ocular dominance according to the instructions described in the respective fitting guides.

11. [redacted]

12. After a minimum 5-minute washout time after fluorescein insertion, the participant will be fit with the CONTROL study lenses following to the manufacturer's fitting guidelines.

    Trial fitting of CONTROL study lenses:

    a. The contact lens power will be chosen based on the vertex-corrected spectacle refraction.

    b. The participant will insert the lenses, allow to settle for at least 10 minutes.

    c. [redacted].

    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.

If sufficient CONTROL lenses are available then continue to Visit 1 concurrently (ie. Dispense CONTROL), otherwise schedule Visit 1 (or Repeat Screening) when CONTROL lenses are anticipated to be available.

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

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

5.5.3 VISIT 1 DISPENSE CONTROL

This visit is concurrent with Visit 0 if the required CONTROL lenses are available on-site or occurs later once lenses are available on site.

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 CONTROL multifocal lenses.
4. While the lenses settle for 10 minutes, provide and explain the CONTROL lens features document.
5. After lenses have settled for at least 10 minutes continue with assessments to determine the final lens order.
6. [redacted]
7. [redacted]

8. [redacted]
9. [redacted]
10. The participant will be scheduled to return for Visit 2.

5.5.4 VISIT 2 OPTIMIZE CONTROL

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 1.

1. Confirm participant's health and medications are unchanged.
2. Ask participant about lens performance for acceptability of contact lens comfort and vision at distance and near.
3. [redacted]
7. Allow settling time of 10 minutes before evaluation of vision and over-refraction to assess the final lens power needed.
8. [redacted]
9. Remove lenses
10. [redacted]
11. If sufficient supply of optimized lenses are available on site continue with Visit 3, otherwise order the lenses and schedule Visit 3. If new lenses need to be ordered, participants will be allowed to wear habitual MF lenses in the meantime.

5.5.5 VISIT 3 DISPENSE (OPTIMIZED) CONTROL

This visit may be conducted immediately following Visit 2 if the required CONTROL lenses are available on-site. Otherwise, this visit occurs when lenses are available on site.

Procedures as follows:

1. Confirm participant's health and medications are unchanged.
2. Slit lamp biomicroscopy assessments as described in Visit 0 (not applicable if Visit 3 occurs on the same day as Visit 2)
3. After a minimum 5-minute washout time after fluorescein insertion *(not applicable if on the same day as previous visit)*, participant to insert new pair of optimized CONTROL lenses.
4. After lenses have settled for at least 10 minutes continue with assessments
5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]
9. 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.
10. The participant will be scheduled to return for Visit 4.

5.5.6 VISIT 4, 2-WEEK FOLLOW-UP CONTROL AND FIT TEST

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

This visit will occur 14-21 days (inclusive) after Visit 3.

Assessments of CONTROL lens will be conducted as described below:

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

2. [redacted]
3. [redacted]
4. [redacted]
5. [redacted]
   a) [redacted]
   c) [redacted]
6. [redacted]
7. [redacted]
8. The participant will remove the lenses.
9. [redacted]

After completing the 2-week follow-up procedures for the CONTROL lens participants will be fit with the TEST lens. Same procedures as for fitting CONTROL will be followed as described in Visit 0.

If sufficient TEST lenses are available on site, then continue to Visit 5 concurrently (ie. Dispense TEST), otherwise schedule Visit 5 (or repeat fitting Visit 4-R Fit) when TEST lenses are anticipated to be available.

5.5.7 VISIT 5, DISPENSE TEST

This visit is concurrent with Visit 4 if required lenses are available on-site.

Assessments of TEST lens will be conducted as described for Visit 1, however this time during the 10-minute lens settling time provide and explain the TEST lens features document.

5.5.8 VISIT 6, OPTIMIZE TEST

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 5.

Assessments of TEST lenses will be conducted as described above for Visit 2.

5.5.9 VISIT 7, DISPENSE (OPTIMIZED) TEST

This visit is concurrent with Visit 6 if required lenses are available on-site.

Assessments of TEST lenses will be conducted as described above for Visit 3.

5.5.10 VISIT 8, 2-WEEK FOLLOW-UP TEST

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

This visit will occur 14-21 days (inclusive) after visit 7.

Assessments of TEST lenses will be conducted as described above for Visit 4. [redacted]

5.5.11 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.

5.5.12 UNSCHEDULED VISITS

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

5.6 STUDY PROCEDURES

Table 3 summarizes the procedures conducted at each visit.

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

	0 Screen Fit of CONTROL	1 Disp. Initial CONTROL	2 Optimize CONTROL	3 Dispense optimal CONTROL	4 2-week follow-up CONTROL & fit TEST	5 Disp. Initial TEST	6 Optimize TEST	7 Dispense optimal TEST	8 2-week follow-up TEST	Exit
Consent process	x									
Subject age & sex	x									

	0 Screen Fit of CONTROL	1 Disp. Initial CONTROL	2 Optimize CONTROL	3 Dispense optimal CONTROL	4 2-week follow-up CONTROL & fit TEST	5 Disp. Initial TEST	6 Optimize TEST	7 Dispense optimal TEST	8 2-week follow-up TEST	Exit
CL history and/or lens wear schedule	x		x		x		x		x	
Health & medication	x	x	x	x	x	x	x	x	x	
Review any problems with eyes/study lenses		x	x	x	x	x	x	x	x	
[redacted]										
Dispense study CLs		x		x		x		x		
[redacted]										

	0 Screen Fit of CONTROL	1 Disp. Initial CONTROL	2 Optimize CONTROL	3 Dispense optimal CONTROL	4 2-week follow-up CONTROL & fit TEST	5 Disp. Initial TEST	6 Optimize TEST	7 Dispense optimal TEST	8 2-week follow-up TEST	Exit
Study completion and Exit										x

* [redacted]

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 CONTROL lens fit will not be applied to the TEST lens fit because it is of interest to determine how many lenses were needed to achieve the final lens prescription.

[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 will 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 at no cost to them. The contact lens material used in this study is commercially available for daily wear. This study will investigate participants wearing the lenses in a daily wear modality (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 contact lenses are used as intended in this study and (1) do not represent a potential for serious risk to the health, safety or welfare of the subject, (2) are not implants, (3) are not used to support or sustain human life, and (4) are not of substantial importance in diagnosing, curing, mitigating or treating disease or otherwise prevents impairment of human health.

The CONTROL and TEST 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 conducted. Patients will be monitored frequently until the end of the study to reduce the occurrence of adverse or potential adverse events. Patients will be given instructions from their investigator regarding early symptoms and signs of adverse events.

8 ADVERSE EVENTS

An ‘adverse event’ refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not. Adverse events (AE) may be classified as ‘unanticipated adverse device effects,’ ‘serious adverse events,’ ‘significant adverse events,’ or ‘non-significant adverse events,’ as defined below, Table 4.

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

Table 4: Classification of types of adverse event

Classification	Definition
Serious Adverse Event	Those events that are life-threatening, or result in permanent impairment of a body function, or permanent damage to a body structure or necessitate medical (therapeutic) or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
Significant Adverse Event	Those non-serious adverse events that occur with contact lens usage that are not sight-threatening but are usually symptomatic and may warrant therapeutic management and /or temporary or permanent discontinuation of contact lens wear.
Non-Significant Adverse Events	Those less severe non-serious adverse events that occur with contact lens usage that are not sight-threatening, may or may not be symptomatic and may warrant palliative management, such as ocular lubricants or temporary interruption of contact lens wear.
Unanticipated Adverse Device Effect	Adverse events in a study that were not previously identified in the protocol in terms of nature, severity, or degree of incidence. An Unanticipated Serious Adverse Device Effect is an unanticipated adverse event that is serious in nature and caused by or associated with the device and is considered reportable.

AE classification, coding (for reporting to the sponsor) and reporting details, plus examples, are provided in Table 5.

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

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	For all serious AEs: Notify sponsor as soon as possible, **within 24 hours;** ORE reporting will be **within 24 hours** as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		

11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 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.

Significant and Non-Significant Adverse Events will be reported to CORE's lead study coordinator and the sponsor as soon as possible, but no later than 5 working days after the occurrence. Each site's Principal Investigator will report the event to Sterling IRB as per their 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 US$25 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 US$200 for completing the study. This is calculated at $35 per in office scheduled visit (5) and $25 for completing of at home ratings. The in-office visits are in

total 7 hours per participant for scheduled visits, though if additional fitting time is required, this may increase. Additional payment $25 per hour will be remunerated to participants if additional visits are required.

12 STATISTICAL ANALYSIS AND DATA MANAGEMENT

12.1 STATISTICAL ANALYSIS

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

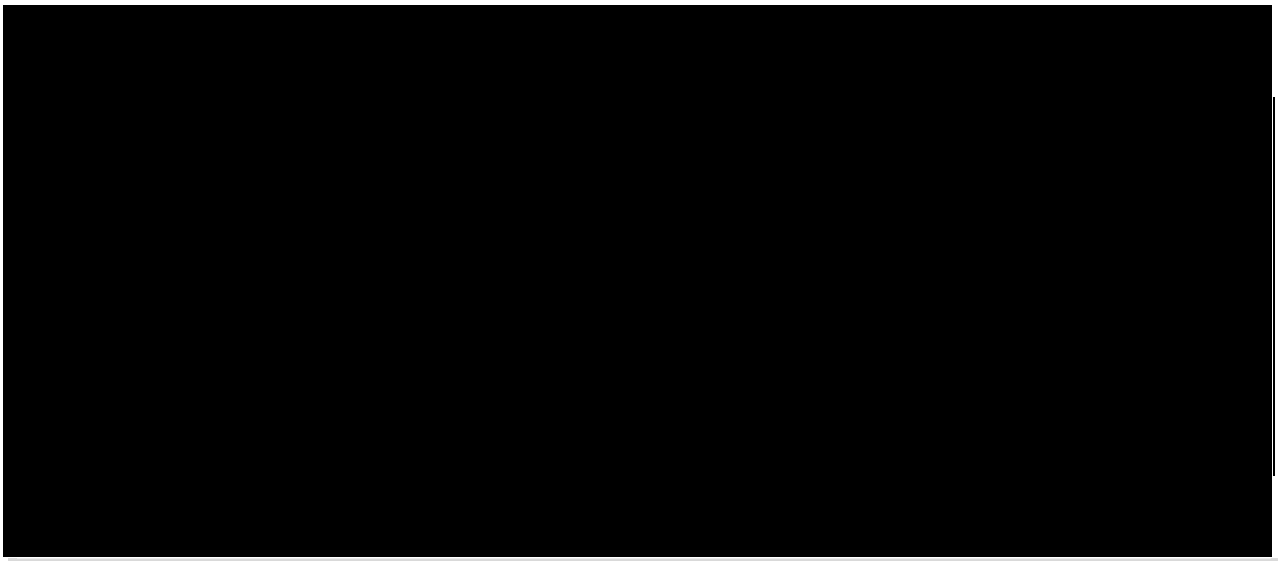
Visual acuity results will be converted to LogMAR for analysis purposes.

Comparisons will be made between the study lenses for the variables measured at the 2-week visits. Additionally the subjective ratings completed on days 1, 6 and 13 of each phase will be compared. A binomial test will be used to analyze the results for the count data of subjective preferences and experience responses. Where relevant, the number of “neither agree or disagree” responses will be evenly distributed to the two options on the basis they would be equally likely to choose either.

Any statistically significant differences of ratings will be judged as a clinically relevant difference if that difference is 0.7 or greater for parametric analyses (based on mean data), or 1.0 or greater for non-parametric analyses (based on median data). A p-value of 5% or lower, ($p \leq 0.05$), will be considered to be statistically significant.

Because of the phenomenon of binocular summation, binocular visual acuity will be analysed, not right eye data. For other variables, such as lens fit, the right eye data will be reported and compared.

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



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. Records of training will be kept at CORE. This will include training by CORE on the study protocol, study procedures, informed consent procedures, as well as training for Good Clinical Practice.

All site Principal Investigators and co-investigators will provide to CooperVision a scan of their curriculum vitae, license to practice optometry, training on Good Clinical practice, and evidence of professional indemnity insurance as part of CooperVision's investigator qualification procedure.

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 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 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.