CORE
Centre for Ocular Research & Education

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

Centre for Ocular Research & Education (CORE),

School of Optometry & Vision Science | University of Waterloo, 200 University Avenue West | Waterloo, ON, Canada N2L 3G1

+1 (519) 888-4742 | CORE.uwaterloo.ca

Protocol

CLARITI 1-DAY MULTIFOCAL STUDY – 'REAL WORLD' SUBJECTIVE ACCEPTANCE STUDY (HARP)

Sponsor Company	CooperVision, Inc.
Sponsor Study number:	EX-MKTG-81
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Document Type:	Study protocol
Core Clinical Site:	1) CORE, University of Waterloo
[redacted]	[redacted]

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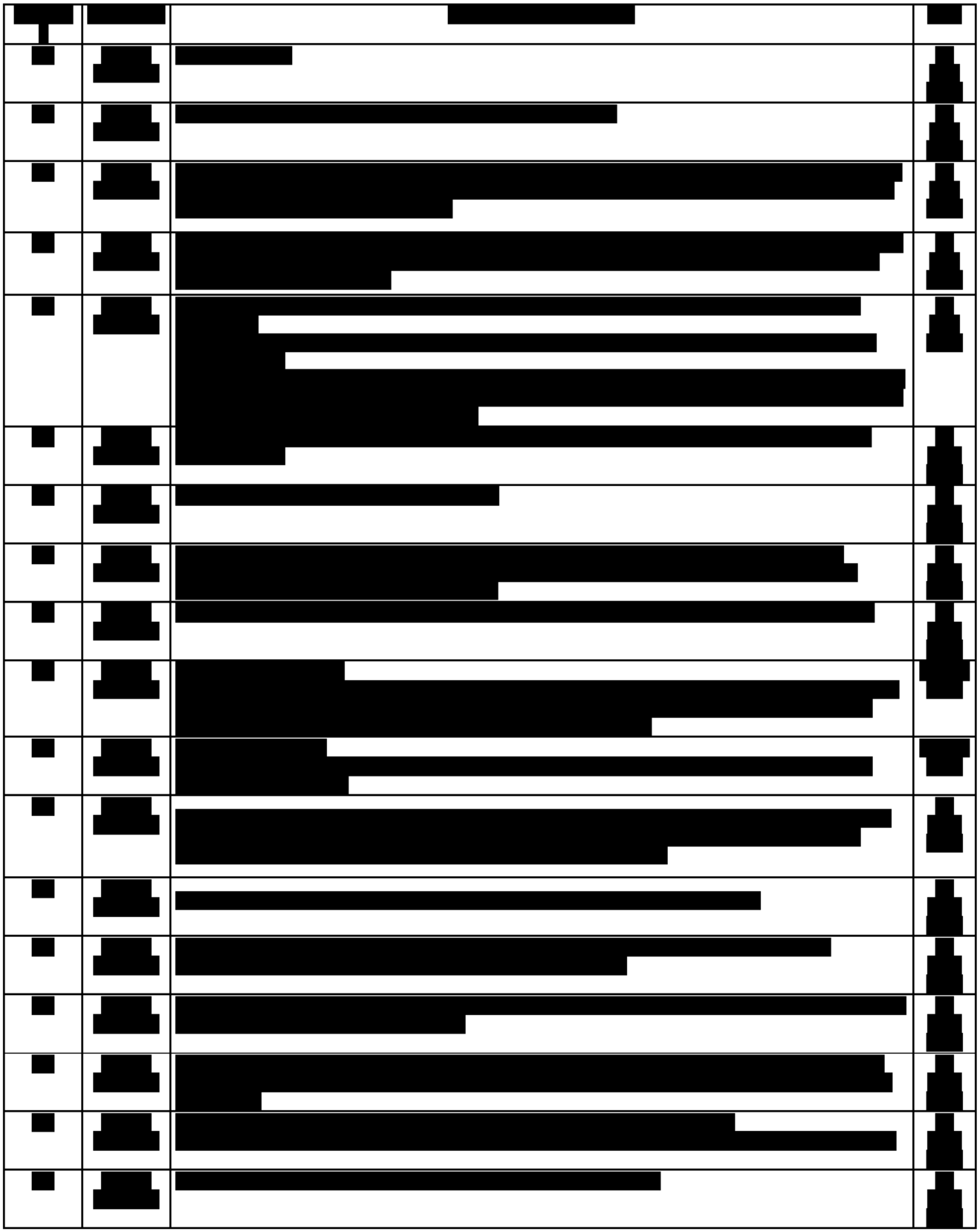

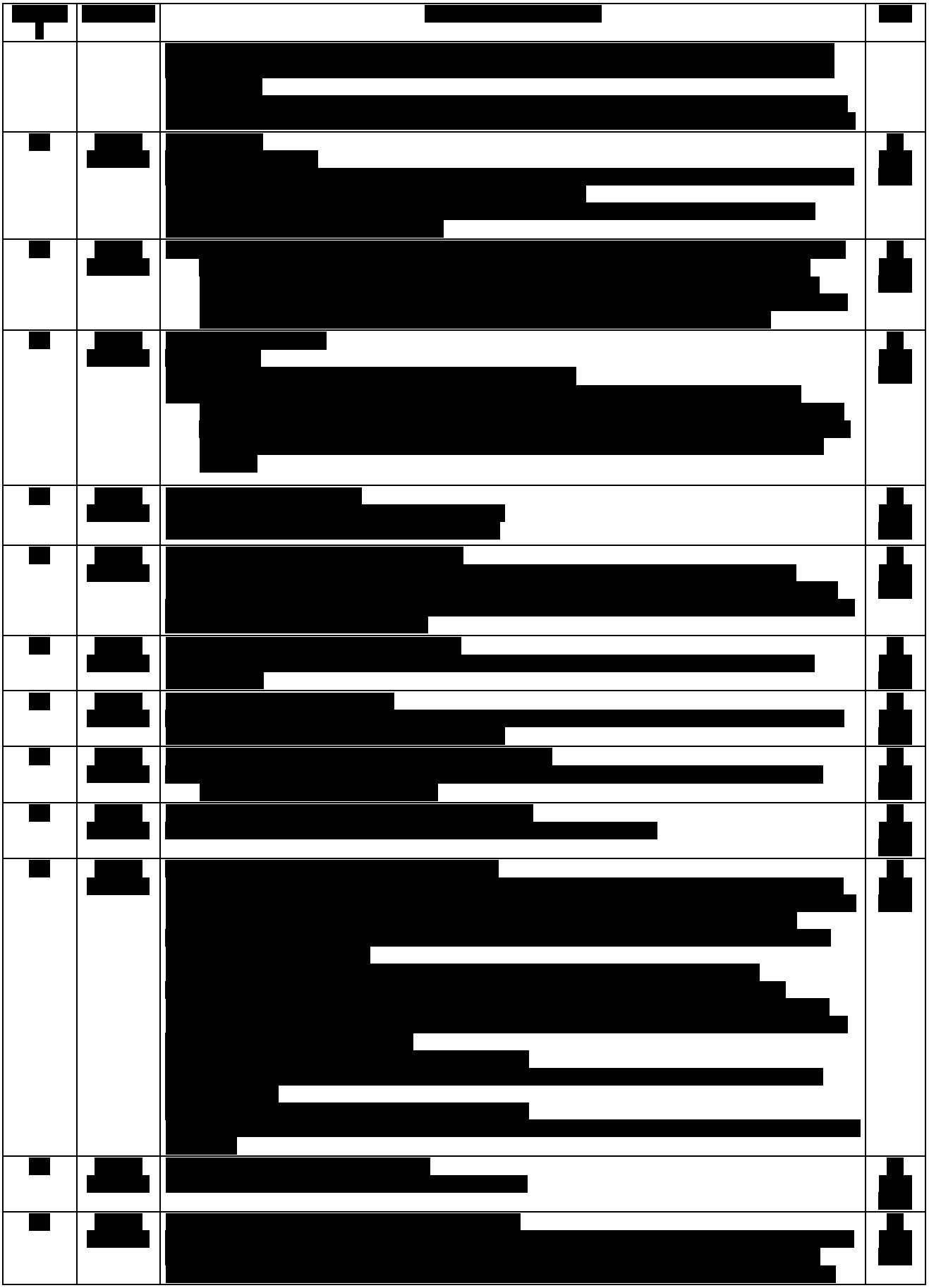

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Confidentiality

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Disclaimer

This study will be conducted for research purposes only and is not intended to be used to support safety in a regulatory submission.

1 INTRODUCTION

The average American spends approximately 87% of their time indoor (*Journal of Exposure Analysis and Environmental Epidemiology (2001*) 11, 231-252). As the use of digital devices increases in daily routine, both near and intermediate vision play an increasing role in our daily vision requirements.

CooperVision's, clariti 1 day multifocal has a design with a center near, surrounded by two staggered power intermediate zones and then a distance focus towards the lens periphery. The optical design that encompasses two staggered power intermediate zones is unique to clariti 1 day multifocal and is not shared by other one day multifocal lenses in the marketplace. A study to explore the acceptance of this lens design is of particular interest to gather data to support the changing vision requirements of today's lifestyle where majority of our time is spent indoor and in particular where near and intermediate vision quality plays an important role in people's satisfaction with their multifocal lenses.

2 OBJECTIVES

The objective of the study is to evaluate the performance of clariti 1 day multifocal when worn on a daily disposable wear modality over a period of up to 3 weeks.

Primary outcome variable: The primary outcome variable is Vision clarity during the day – distance vision.

The primary outcome variable, and other secondary outcome variables will be collected at the screening visit for habitual contact lenses, and at the final visit for the study contact lens i.e. clariti 1 day multifocal. The secondary outcome variables include:

- Vision clarity and vision satisfaction (subjective ratings) for the following tasks at various distances:
  - Driving at night – distance vision
  - TV viewing - distance vision
  - Desktop computer – long intermediate vision
  - Laptop/tablet –short intermediate vision
  - Reading on cell phone – near vision
  - Reading hand-held printed materials– near vision
- Comfort (subjective ratings)

[redacted]

- Visual acuity (logMAR)
- Lens centration and mobility
- Bulbar and conjunctival redness
- Corneal and conjunctival staining
- Satisfaction with lens package and lens handling (subjective ratings)
- Satisfaction with visual demand tasks with speed of changing focus.
- Subjective preference between study and habitual contact lenses for a range of requirements and tasks.
- Subjective preference between study and habitual contact lenses to lifestyle related questions.

3 HYPOTHESIS

The study hypothesis is that the clariti 1-day multifocal will perform as well or better clinically than the habitual multifocal lenses.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

4.1.1 OVERALL DESIGN AND STUDY VISITS

The study is a prospective bilateral wear, participant masked, dispensing study evaluating, among other things, vision clarity, vision satisfaction and comfort with clariti 1-day multifocal (i.e. test lens) for tasks performed indoors and outdoors, and for vision activities related to distance (≥3 m), long-intermediate (1-2 m approx), short-intermediate (0.5-1 m approx), and near vision (30 - 50 cms). Each participant who is a habitual multifocal lens wearer will be refit into the clariti 1-day multifocal lens. They will use subjective ratings to report their satisfaction with their habitual contact lenses and with clariti 1-day multifocal lens. It is anticipated that this study will involve up to 4 scheduled visits:

Visit 1 (1.5 hrs): Screening - includes consent, screening and evaluation of satisfaction with habitual contact lenses.

Visit 2 (1.5 hrs): Baseline - Fit and dispense test lens, assessments of test lens at dispense, and subjective ratings with test lens.

Visit 3 (1.5 hrs) Day 3 - 10 after visit 2:

- Part A: Review prescription of study lenses, and subjective ratings;

- Part B: if needed dispense revised lens powers, assessments, and subjective ratings.

Visit 4 (1.5 hrs): Follow-up visit of test lens, assessments of test lens at follow-up, evaluation of satisfaction with test lens, and study exit.

The study design is shown in Figure 1.

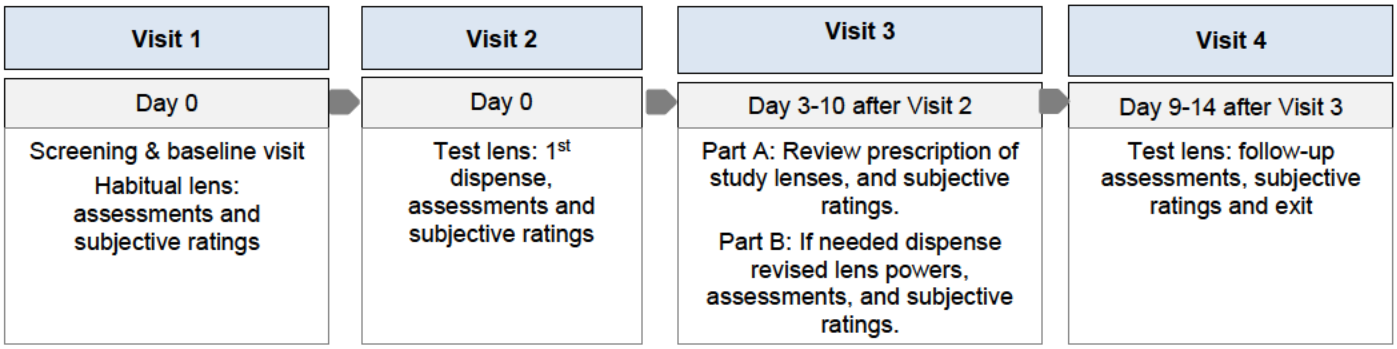

Figure 1: Study design

Participants will complete subjective ratings in real time using smartphones. There will be short subjective ratings to be completed the day after Visit 2 primarily aimed at vision performance. [redacted] For each rating day, participants will mention -hours of day spent on various indoor and outdoor tasks including, hours spent on desk-top computer, hours spent on laptop or tablet, and hours spent reading written material, and hours spent reading the smartphone. Participants will use a smartphone that is capable of [redacted] (requires Android 4.4.0 or higher, and iOS 8.0 or higher). They will download the app during visit 2, and respond to the first questionnaire to familiarize themselves with the set-up. Due to the usage of the [redacted] data collected for subjective ratings will not be entered on paper.

In the event data cannot be collected using the app, ratings will be entered by the participant on paper, and given to the investigator at the next scheduled visit.

Subjective ratings will be obtained for some or all of the tasks mentioned in Table 1, for distance [redacted] long intermediate vision [redacted] short intermediate vision [redacted] and near vision [redacted]

Table 1: Tasks used for subjective ratings

Task	Time of day	Indoors/ Outdoors	Distance vision	Long intermediate vision	Short intermediate vision	Near vision
Driving	Daytime After dark	Outdoor	√	(e.g. dashboard and GPS viewing)	-	-
TV viewing	Anytime	Indoor				
Desktop computer	Anytime	Indoor	-	√ (viewing monitor)	√ viewing keyboard	-
Laptop computer	Anytime	Indoor/ Outdoor			√	√
Shopping task	Anytime	Indoor	overhead aisle numbers		viewing price labels	-
Reading on cell phone	Anytime	Indoor/ Outdoor	-	-	-	√
Reading printed materials	Anytime	Indoor	-	-	-	√

4.1.2 MASKING

Participants will be masked as to lens type. Lenses dispensed to participants may be either over-labelled or have part of the label obscured, however the safety information on the outer package label of the contact lens, shall be clearly visible.

5 STUDY POPULATION

5.1.1 NUMBER OF PARTICIPANTS

Up to 50 participants will be dispensed with study products, with a target of 44 completing the study. Participants will be recruited using records from CORE and the external clinical site, using recruitment materials approved by the UW Office of Research Ethics (Appendices 18, 19, and 20). Each participant will be given a unique ID number. Additionally, all participants must meet the study inclusion and none of the exclusion criteria listed below. Informed consent will be obtained for all participants prior to their enrolment in the study (Appendix 1).

5.1.2 INCLUSION AND EXCLUSION CRITERIA

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

1. Is at least 17 years of age and has full legal capacity to volunteer;
2. Has read and signed an information consent letter;
3. Is willing and able to follow instructions and maintain the appointment schedule;
4. Has had a self-reported oculo-visual examination in the last two years.
5. Currently wears multifocal soft contact lenses, and have worn multifocal contact lenses for at least one month;
6. Presently wears lenses for minimum wear 4 days/week and 10 hours/day
7. Participant has an anticipated ability to wear test lenses for minimum 5 days/week and 10 hours/day.
8. Can be fit with the available test contact lens power range to achieve satisfactory vision i.e. 0.18 logMar (20/30) binocular distance acuity with the test lenses.
9. Current refraction indicates a reading addition of +1.50 or higher
10. Uses a digital device (computer/laptop/tablet etc.) for at least 5hrs/day
11. Spends 10hrs or more indoors at least 5 days/week
12. Possesses a smartphone and is willing to download the MetricWire app to receive and respond to surveys

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

1. Is presently wearing Clariti 1 day multifocal lenses
2. Has astigmatism greater than -0.75 DCyl as determined with subjective refraction
3. Is participating in any concurrent clinical or research study;
4. Has any known active* ocular disease and/or infection;
5. Has a systemic condition that in the opinion of the investigator may affect a study outcome variable;
6. Is using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable;
7. Has known sensitivity to fluorescein dye or products to be used in the study;
8. Is pregnant, lactating or planning a pregnancy at the time of enrolment (by verbal confirmation at the screening visit);
9. Is aphakic;
10. Has undergone refractive error surgery;
11. Is an employee of CORE or external clinical site.

* 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.

5.1.3 REPEATED SCREENINGS

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

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

The maximum total number of screenings permitted will be 3.

5.2 STUDY MATERIALS

5.2.1 LENSES

The clariti 1 day multifocal lens details are included in Table 2.

Table 2: Lens characteristics of clariti 1day multifocal

Specification	clariti 1day multifocal
Material	somofilcon A
HC licence #	81009
Dk/t (barrer/cm) @ -3.00DSph	86.0
Water content	56%
Sphere power (D)	• -6.00 to +5.00 (0.25 steps) with Low add up to 2.25; • -6.00 to +5.00 (0.25) with High add: +2.25 to +3.00 (0.25)
Base curve (mm)	8.6
Diameter	14.1

5.2.2 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. Rewetting drop use will be

recorded at the follow-up visit. In the event of an adverse event, rewetting drops may be given to participants.

5.2.3 CONTACT LENS DISPENSING

The lenses will be provided to the participant after being transferred, complete with blister pack solution, to a contact lens cup; this will maintain participant masking. The use of saline for rinsing the contact lens prior to insertion is permitted if necessary. Saline will not be dispensed during the study.

5.2.4 ORDERING CONSUMABLES

The clariti 1 day multifocal lenses will be supplied by the sponsor. If they have difficulty sourcing product in good time then lenses may instead be purchased by CORE through a commercial route. If necessary, the lenses may be shipped between sites.

The investigators/clinical sites must maintain an accurate accounting of the study product during the study. A detailed inventory must be completed for study supplies at each clinical site.

5.2.5 DISPOSING OF CONSUMABLES

This study provides consumables (lenses) to participants for use during the study. Participants will be instructed to dispose of worn lenses daily, but retain the foils of all used lens packs and return them together with any unworn lenses, at their next study visit. Lenses worn for the scheduled visits will be collected from the participants. Worn lenses and unworn lenses collected at the external clinical site will be returned to COREat the end of the study, where they will be disposed of according to UW guidelines. Worn lenses associated with adverse events may be retained either at CORE or returned to CooperVision. Typical analysis in these cases relates to inspection for damage and/ or bacterial contamination. Upon completion of the study, all worn lenses will be destroyed, unless otherwise directed by the study Sponsor.

5.2.6 PRODUCT ACCOUNTABILITY

Accountability logs will be kept to include the number of lenses and lens care system bottles received, dispensed, unused and returned to sponsor (where relevant). All products dispensed to participants will be recorded in the study binder.

5.3 SCHEDULED AND UNSCHEDULED VISITS

5.3.1 SCHEDULED VISITS

This study has a total of 4 scheduled visits, including:

Visit 1 (1.5 hrs): Screening - includes consent, screening and evaluation of satisfaction with habitual contact lenses.

Visit 2, Day 0 (1.5 hrs): Baseline - Fit and dispense of test lens, assessments of test lens at dispense, and subjective ratings with test lens. Visit 2 may be combined with Visit 1. [redacted]

Visit 3 (1.5 hrs) Day 3 - 10 after visit 2:

- Part A: Review prescription of study lenses, and subjective ratings;
- Part B: if needed dispense revised lens powers, assessments, and subjective ratings. Part A and B may be combined into one visit.

Visit 4, Day 9 - 14 after visit 3 (1.5 hrs): Follow-up visit of test lens, assessments of test lens at follow-up, evaluation of satisfaction with test lens, and study exit.

A scheduled follow-up visit may only take place when the participant attends wearing the study lenses. 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 will be assessed for its suitability to be included in the analysis population.

5.3.2 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 by the lead investigator.

5.3.3 STUDY VISIT CODES

The summary of visit codes is shown in Table 3

Table 3: Summary of visit codes

Study visit	Visit code	Visits
Visit 1	V1	Screening
	V1-R1, V1-R2	Re-screen visit
Visit 2	V2	Dispense, baseline assessments of test lens
Visit 3	V3-A	Part A: Review prescription of test lens and subjective ratings.
	V3-B	Part B: If needed dispense revised lens powers, assessment, and subjective ratings

Visit 4	V4	Follow-up assessment of test lens and Study exit

5.3.4 SCREENING & EVALUATION OF HABITUAL CONTACT LENSES, VISIT 1

All participants who sign the informed consent letter will be assigned a study ID number.The investigator will determine participant eligibility using the inclusion and exclusion criteria. Ineligible participants will be discontinued from the study. The procedures to be performed are outlined below:

- The participant is expected to attend the screening visit wearing their habitual contact lens products.
- 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 to be enrolled in to the study (and ID # is assigned).
- Participant demographics and medical history (age, sex, medical conditions, medications, allergies) obtained.
- Contact lens history (own lens information, and wear time)
- Use of digital devices and distance of device when in regular use (information request to be sent ahead of visit so that participant can measure)
- The participant will score their subjective responses (on 3-point Likert scale) for the habitual lens by reflecting on a typical day, and rate the following:
    - Subjective ratings of vision quality/clarity, for different everyday-life tasks performed at various distances such as:
        - Driving, at day & after sunset
        - TV viewing
        - Desk computer viewing
        - Laptop/tablet viewing
        - Reading on cell phone
        - Reading printed materials
    - Overall comfort, [redacted] with habitual lens (typical day experience)
    - Subjective satisfaction with lens handling (ease of insertion and removal) with habitual lens
    - Subjective satisfaction with changing focus speeds for in-office tasks with habitual lens
- Measure habitual reading distance for printed material and for smartphone
- Habitual lens high contrast visual acuity (logMAR) with high room illumination:

- distance; right eye, left eye & binocular
- distance (binocular) [redacted]
- near; right eye, left eye & binocular [redacted]

- Assessment of habitual lens fit.

  [redacted]

  - Lens centration (optimal; acceptable decentration; unacceptable decentration)
  - Corneal & Limbal coverage in primary gaze (Yes or No)
  - Post-blink lens movement in primary gaze (0-4, 1 steps)

  [redacted]

- The lenses will be removed
- Slit lamp biomicroscopy will be assessed according to the CVI approved study biomicroscopy CRF (Appendix 7).

[redacted]

- [redacted], monocular & binocular distance and near visual acuity (high contrast) (logMAR)
- Best corrected high contrast high illumination VA (distance and near)

[redacted]

- 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.

5.3.5 FIT AND DISPENSE, AND EVALUATION OF TEST LENS, VISIT 2

Lenses will be provided to participants in a manner which does not unmask the participant, as described in Section 5.2.3.

The test lens will be fit following the manufacturer's guidelines. The following procedures will be performed following:

- Baseline high contrast visual acuity (logMAR) with high room illumination:
  - distance; right eye, left eye & binocular
  - distance (binocular) [redacted]
  - near; right eye, left eye & binocular [redacted]
- Assessment of test lens fit.

  [redacted]

- Lens centration (optimal; acceptable decentration; unacceptable decentration)
- Corneal & Limbal coverage in primary gaze (Yes or No)
- Post-blink lens movement in primary gaze (0-4, 1 steps)

[redacted]

- The participant will download the [redacted] on their phone for completing subjective questionnaires starting the morning after the dispensing visit, to reflect their lens wear experience at the time of rating (in real-time). Participants will be given careful explanation of how and when to complete them.

- Subjective ratings [redacted] are completed on next day [redacted] and just before lens removal. [redacted] The time of lens insertion will be recorded. Subjective ratings include:
  - Comfort

    [redacted]
  - Visual clarity
  - Overall satisfaction

- Vision clarity/quality for the following tasks at various distances:
  - Driving, at day & after sunset
  - TV viewing
  - Desk computer viewing
  - Laptop/tablet viewing
  - Reading on cell phone
  - Reading printed materials
  - Subjective satisfaction with changing focus distance

- On day 1 after V2 (i.e. day after the dispensing visit) the participant will be asked to complete various subjective ratings (Appendix 6) [redacted] The time of lens insertion and removal will be recorded. The participant will also submit the following through the [redacted]
  - Hours spent on desktop computer [redacted]
  - Hours spent on laptop or tablet computer [redacted]
  - Hours spent reading smart phone [redacted]
  - Hours spent reading written material [redacted]
  - Any unusual symptoms with the contact lenses (No, Yes; if yes details)

The participant will be asked to wear the study lenses for at least 10 hours per day and 5 days per week.

Participant will be provided with sufficient contact lens supply.

The participant will be discharged and reminded to return for Visit 3 (Follow-up visit of test lens) and to bring back all lens package foils.

5.3.6 REVIEW OF LENS POWERS & DISPENSE REVISED LENS POWERS IF NEEDED, VISIT 3

The review assessment of the lens power dispensed at visit 2, will occur between day 3 and day 10. The following variables will be measured with the first test lens power (Appendix 3B).

5.3.6.1 VISIT 3 – PART A

The participant will score their subjective responses (on 3-point Likert scale) for the test lens by reflecting on a typical day during the previous days of lens wear, and rate the following (Appendix 4):

- Subjective ratings of vision clarity, for different everyday-life tasks performed at various distances such as:
    - Driving, at day & after sunset
    - TV viewing
    - Desk computer viewing
    - Laptop/tablet viewing
    - Reading on cell phone
    - Reading printed materials
- Overall comfort [redacted] with test lens (typical day experience)
- Subjective satisfaction with lens handling (ease of insertion and removal) with test lens
- Subjective satisfaction with changing focus speeds for in-office tasks with test lens
- Wearing time on visit day will be recorded
- Baseline high contrast visual acuity (logMAR) with high room illumination:
    - distance; right eye, left eye & binocular
    - distance (binocular) [redacted]
    - near; right eye, left eye & binocular [redacted]

If visual acuity is optimal, a lens change is not necessary.

- The participant will be asked to wear the study lenses for at least 10 hours per day and 5 days per week.
- Participant will be provided with sufficient contact lens supply.
- The participant will be discharged and reminded to return for Visit 4 (Follow-up visit of test lens) and to bring back all worn lens package foils and any remaining unworn lenses.

5.3.6.2 VISIT 3 – PART B

If lens change is deemed necessary during Visit 3- Part A, then the new power lenses will be dispensed. If the revised power lenses are to be ordered, this visit will be scheduled on a different date.

The following will be recorded after allowing the lens to settle:

- Subjective ratings on lens insertion (Appendix 5).
- Baseline high contrast visual acuity (logMAR) with high room illumination (Appendix 3):
  - distance; right eye, left eye & binocular
  - distance (binocular) [redacted]
  - near; right eye, left eye & binocular [redacted]
- Assessment of test lens fit (Appendix 3b):
  [redacted]
  - Lens centration (optimal; acceptable decentration; unacceptable decentration)
  - Corneal & Limbal coverage in primary gaze (Yes or No)
  - Post-blink lens movement in primary gaze [redacted]
- [redacted] The time of lens insertion and removal will be recorded. Participant will be provided with sufficient contact lens supply.
- The participant will be discharged and reminded to return for Visit 4 (Follow-up visit of test lens) and to bring back all lens package foils.

5.3.7 FOLLOW-UP ASSESSMENT OF TEST LENS, VISIT 4

The follow-up visit of test lens will occur between day 9-14 after Visit 3. The following procedures will be performed:

The participant will score their subjective responses (on 3-point Likert scale) for the test lens by reflecting on a typical day during the previous 9 - 14 days of lens wear, and rate the following:

- Subjective ratings of vision clarity, for different everyday-life tasks performed at various distances such as:
    - Driving, at day & after sunset
    - TV viewing
    - Desk computer viewing
    - Laptop/tablet viewing
    - Reading on cell phone
    - Reading printed materials
- Overall comfort, [redacted] with test lens (typical day experience)
- Subjective satisfaction with lens handling (ease of insertion and removal) with test lens
- Subjective satisfaction with changing focus speeds for in-office tasks with test lens
- Subjective preference between study and habitual CLs for a range of requirements and tasks. These include:
    - Overall comfort preference
    - Visual clarity preference
    - Overall lens preference
- Life-style related questions will be completed by the participants.

Other variables collected include:

- Wearing time on visit day
- Baseline high contrast visual acuity (logMAR) with high room illumination:
    - distance; right eye, left eye & binocular
    - distance (binocular) [redacted]
    - near; right eye, left eye & binocular [redacted]
- Assessment of test lens fit.
    - [redacted]
    - Lens centration (optimal; acceptable decentration; unacceptable decentration)
    - Corneal & Limbal coverage in primary gaze (Yes or No)

- Post-blink lens movement in primary gaze [redacted]

- The lenses will be removed
- Slit lamp biomicroscopy will be assessed according to the CVI approved study biomicroscopy CRF (Appendix 7).
- Exit visual acuity will be performed.
- Participants will be expected to uninstall the MetricWire app from their phone at the final exit visit.
- The study exit form will be completed when a participant exits the study. This will occur 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.
    - The participant will be discharged and will sign the study completion forms and receive remuneration for participating in the study.

5.3.8 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 by the lead investigator.

5.4 SUMMARY OF STUDY PROCEDURES

Table 4 summarizes the visits and procedures for the study.

Table 4: Summary of procedures to be conducted at scheduled visits

	Visit 1 Screening & evaluation of habitual contact lenses	**Visit 2** Fitting & evaluation of test lens	**Visit 3a** Review assessment of test lens power and **Visit 3b** dispense of revised lens powers if needed	**Visit 4** Follow-up visit of test lens
Informed consent (screening)	√			
Confirmation of inclusion/exclusion criteria	√			
Ocular & medical history	√			

	Visit 1 Screening & evaluation of habitual contact lenses	**Visit 2** Fitting & evaluation of test lens	**Visit 3a** Review assessment of test lens power and **Visit 3b** dispense of revised lens powers if needed	**Visit 4** Follow-up visit of test lens
Demographics	√			
VA with study lenses / and refraction	√	√	√	
Auto-refraction & keratometry	√			
Sphero-cylindrical refraction	√		√	
Best corrected (sphero-cyl) VA monocular and binocular (distance and near)	√			
Biomicroscopy	√	√	√	√
Trial fitting of study lenses (if applicable)		√	√	
Wearing time on visit day and rating day			√	√
Symptoms & problems enquiry	√	√	√	√
Dispense new lenses (if applicable)		√	√	
Participant ratings completed	√	√	√	√
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lens fit assessments	√	√	√	√
[redacted]		[redacted]	[redacted]	
VA with contact lenses	√	√	√	√
Assessment of adverse events (if applicable)	√	√	√	√
[redacted]		[redacted]	[redacted]	
Return questionnaires (if applicable)				√
Exit Study				√

5.5 RECORDING FINDINGS OF INTEREST

The following variables may be recorded using a digital slit lamp system (video and still images):

- Lens fits not considered to be clinically acceptable or associated with symptoms

- Relevant corneal and conjunctival staining
- [redacted]Abnormalities of lens performance (e.g. poor fit) [redacted]
- Additional videos (e.g. [redacted] lens movement, etc.) may also be recorded in order to better understand on-eye lens performance and to help communicate this information to the sponsor.

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 internally by the investigators. Deviations from the windows described in the protocol will be reported in the weekly progress reports and the final study report.

7 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

This is a minimal risk study because of the use of marketed products and standard optometric assessments.

Contact lenses in this study will be worn on a daily disposable wear basis. Adverse events and/ or complications in daily disposable wear of soft contact lenses can occur (eg: inflammation and infection). 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.

The most common adverse events to contact lens wear are infiltrates (small lesions in the cornea -- or the clear portion of the front of the eye, resulting from inflammation). Over a period of one year, infiltrates occur in one to two people per population of 100 who wear soft contact lenses on a daily basis, and in four to eight people per population of 100 who wear soft contact lenses on an extended wear basis. Participants may also experience an allergic reaction to the sodium fluorescein dye used to evaluate the ocular surface.

In rare instances more serious complications may occur, including corneal ulcers (a sight threatening eye infection) which can result in corneal scarring, temporarily or permanently decreased vision and in some cases blindness. Infections relating to contact lens wear occur in approximately four people in a population of 10,000 who wear soft lenses on a daily wear basis and in approximately two people in a population of 1,000 who wear soft contact lenses on an extended wear basis. All risk values listed in the above paragraph relate to annual risk.

Additionally, it is possible that participants may experience temporary discomfort associated with the study procedures (e.g. wearing of contact lens) including: mild transient discomfort, burning and stinging, hyperemia, blurred vision, sandiness or grittiness, light sensitivity, dryness, itching, crusty eyes and foreign body sensation.

Standard optometric assessments including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and contact lens fitting will be used.

Participants may not benefit directly from taking part in this study. Information from this study may help researchers come up with new soft contact lens designs to help others in the future. In addition, participants 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.

This study may help the study sponsor to better understand the performance of the products being used in this study.

8 ADVERSE EVENTS

See SOP012_v01 for a description of adverse events, including management and reporting (Appendix 10).

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

Adverse events are classified as detailed below:

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 clinical trial 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 examples are provided in the following table of Contact Lens Adverse Event Classification and Reporting table:

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	Notify sponsor as soon as possible, **within 24 hours;** ORE reporting 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)	

22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements
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 transient symptoms and symptoms of temporary discomfort associated with the study procedures (mentioned in Section 7) 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 referred to an appropriate health care professional 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 (Appendix 18) 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 the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Investigator will report Serious Adverse Events to the ORE within 24 hours of the investigator becoming aware of the event and as per

ORE requirements (by fax, mail/delivery, phone, or email). All fatal or life threatening events will be reported immediately to the ORE.

Significant and Non-Significant Adverse Events will be reported to the sponsor as soon as possible, but no later than 5 working days after the occurrence. The Investigator will report the event to the ORE as per ORE requirements (by fax, mail/delivery, phone, or email).

[redacted]

9 DISCONTINUATION FROM THE STUDY

Participants discontinued from a study will be reimbursed $20 per hour for their active involvement in the study (including the initial screening visit). Participants may be discontinued at the discretion of the investigator or sponsor in consideration of their safety or their compliance with study instructions, or by the participant themself. 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 5.1.2.
- 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 the Office of Research Ethics at the University of Waterloo.

A discontinuation form (Appendix 12) will be completed stating the reason for discontinuation, 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.

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 the Principal Investigator 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 the Sponsor as soon as possible (usually in weekly study updates to the Sponsor).

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 (Appendix 21) will be completed, which requires the signatures of both the participant and the investigator. The participants will also be provided with a letter of appreciation (Appendix 22).

Once their involvement in the study is complete, participants will be informed about receiving feedback following study completion in the Letter of Appreciation (Appendix 22).

[redacted] Full details are given in the information consent letter (Appendix 1).

12 STATISTICAL ANALYSIS AND DATA MANAGEMENT

12.1 SAMPLE SIZE CALCULATION

[redacted] the sample size for this study has been set to 50 to be dispensed with study product, to account for potential participant drop out.

12.2 STATISTICAL ANALYSIS

All data will be analyzed by CORE at the University of Waterloo. Unmasked data analysis will be conducted using Statistica/SPSS/SAS (depending on the variable being analysed). Descriptive statistics will be provided on information regarding baseline variables (age, gender, refractive error distribution, etc.).

Where relevant, analysis of variables will be conducted separately on each eye, and data will not be pooled. A Binomial test will be used to analyze the results for the count data of subjective preferences. The number of "no preference" will be evenly distributed to the two options on the basis they would be equally likely to choose either.

Table 5 lists the primary outcome variables and anticipated statistical procedures. All data will be tested for normality of distribution using Shapiro-Wilk tests.

Table 5: Statistical procedures

Variable	Analysis	Statistical test
Subjective ratings	Descriptive and other statistics	Mean, Median*, Mode, Standard Deviation, Minimum, Maximum, Frequency count
	Effect of treatment on outcome variable within subjects (comparison between study days) Effect of time on outcome variable *(comparison over time)*	Friedman Wilcoxon matched pairs test
Visual acuity, lens centration and mobility, bulbar and conjunctival	Descriptive statistics	Mean, Median*, Standard Deviation, Minimum, Maximum, Count

redness, corneal and conjunctival staining	Effect of treatment on outcome variable within subjects (comparison between study days)	RMANOVA Paired t-test

* For non-parametric data only

The critical alpha level for statistical significance will be set at $p \leq 0.05$, with no adjustments for multiple comparisons.

All participants who were evaluated will be used in the analysis. In the event of missing data, individual data points will be excluded in the analysis and not extrapolated from the collected data.

12.3 DATA MANAGEMENT

Data will be entered on paper CRFs or in MetricWire app. The clinical investigators will be responsible for data integrity and the completeness of data entry for each visit. Investigators at both sites will make an attempt to provide the CORE data team with the completed CRFs within ONE BUSINESS DAY of the visit date. For the external site the CRFs will be scanned and emailed [redacted]

CORE personnel will review all CRFs for integrity and completeness and communicate data queries back to the investigator as necessary. Investigators should make an attempt to answer all data queries within TWO business days of receipt.

After the study is closed, the external site will send the original CRFs and other study documents and products as requested to CORE.

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.

At the completion of the study CORE will provide a copy of the study data 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.

12.4 COMMENTS ON SOURCE DOCUMENTS

Data analysis will not be conducted on comments which have been recorded in the source documents. Only highlighted comments will be entered into the study database. Only relevant and applicable comments will be included in the final report as deemed necessary by the lead investigator.

13 PROTOCOL 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.

14 STUDY MONITORING

Status reports will be provided to the study sponsor by email on a regular basis.

Status reports will include:

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

Study monitoring visits may be conducted throughout the study and will be scheduled by the study sponsor in conjunction with the lead investigator. In addition study records may be inspected at CORE and the external site by the sponsor, the sponsor's designate, the Office of Research Ethics at the University of Waterloo, and by regulatory authorities in Canada and the United States, namely Health Canada and the United States Food and Drug Administration (FDA); however, no records containing identifiable/personal information will be permitted to leave the custody of CORE.

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/

15.2 ETHICS REVIEW

This protocol will be submitted to and reviewed through the Office of Research Ethics (ORE) at the University of Waterloo. Notification of ethics clearance of the application is required prior to the commencement of the study.

15.3 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.

15.3.1 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.

15.3.2 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).

15.3.3 REPORTING AND DOCUMENTING PROTCOL DEVIATIONS

Major protocol deviations must be reported to the ORE within 7 days of the deviation occurring (or its discovery) using the Protocol Deviation Report Form 107 (PDRF). Information from the PDRF is provided to the Clinical Research Ethics Committee (CREC) at the next monthly meeting.

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

15.4 PREMATURE TERMINATION OF THE STUDY

The sponsor, CORE or the Office of Research Ethics at the University of Waterloo may terminate the study at any time for any reason.

15.5 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 lead investigator that participant met eligibility criteria;
- Confirmation that participant received a signed and dated copy of informed consent;
- Exit date;
- Investigators signature confirming study exit.

15.6 RETENTION OF STUDY RECORDS AND DATA

Records and data from this study will be retained for a minimum of 25 years.

16 REPORT

A report will be sent to the sponsors according to terms described in the study contract.

17 APPENDICES

[redacted]