[redacted]

Protocol

COMPARING CLARITI ELITE VERSUS PROCLEAR 1 DAY [redacted]

Sponsor: CooperVision

Sponsor study number: [redacted]

CORE protocol numbe [redacted]

Protocol author: [redacted]

Principal investigator(s): [redacted]

Role & printed name	Reviewed and approved (sign)	Date DD/MMM/YYYY
[redacted]		

Study Personnel

[redacted]

Clinical site address : [redacted]

DOCUMENT CHANGE HISTORY

Version date	Author	Description of change(s)
[redacted]		

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1 INTRODUCTION

CooperVision, Inc. (CVI) is aiming to compare subjective ratings of lens handling at insertion of two CooperVision lenses: clariti elite versus Proclear 1 day in habitual soft lens wearers. The clariti elite lens will be considered an investigational lens in this study (as this frequent replacement monthly lens is not yet commercially available in Canada), the Proclear 1 day is commercially available in Canada.

Most soft contact lenses are worn on a daily wear basis, requiring that lenses are inserted at the beginning of the wear day and removed at night. A large variety of contact lenses are currently available on the market, each with different lens properties. These properties are influenced by the lens material composition and other factors, such as whether the lens is a re-usable contact lens or daily disposable contact lens. Differences between lenses include the stiffness of the material, a handling tint, indicators for telling the user whether the lens is inside-out, and whether the lens retains its shape on the finger during placement on eye. These varying properties can largely affect the ease of handling at insertion and removal, contributing to lens success or failure.

The clariti elite lens is a monthly replacement, silicone hydrogel lens without a handling tint. The Proclear 1 Day lens is a daily disposable, hydrogel lens with a handling tint. Both lenses have unique material characteristics.

CooperVision, Inc. is interested in comparing subjective handling acceptance, specifically lens handling at insertion between these two lenses of different materials to gain insight into the differences between these lenses from this aspect.

2 OBJECTIVES

The objective of this investigation is to evaluate subjective ratings of lens handling at insertion, specifically subjective rating of the ease of lens application to eye by participants for two CooperVision lenses, clariti elite versus Proclear 1 day, in habitual soft lens wearers.

<u>The primary outcome variable for this study is:</u>

- Subjective rating of ease of lens application to eye (0-100, integer steps)

<u>The other outcome variable for this study is:</u>

- [redacted]

3 HYPOTHESIS

The study null hypothesis is that the subjective rating of ease of lens application to eye for clariti elite will not be different from Proclear 1 Day lenses.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

4.1.1 OVERALL DESIGN

Participants will attend a screening visit to determine their eligibility for the study (Visit 1). Eligible participants continue in the study visits right after the screening visit on the same day and wear the study lenses bilaterally in randomized order.

Participants will complete subjective ratings using a numeric rating scale (0-100) at each visit and a Likert scale for handling related to lens insertion and overall handling experience at the end of the study. The subjective ratings will be reviewed by the investigator at the respective visits.

4.1.2 STUDY DURATION

All visits will be conducted on the same day, in sequential order. Estimated duration of involvement for each participant is 4hrs.The duration of this study from start of enrolment to the end of final appointment is expected to be approximately 5 weeks, with the enrolment period lasting approximately 4 weeks.

4.1.3 RANDOMIZATION

Considering the bilateral cross-over study design, participants will either wear Proclear 1 day or clariti elite lenses in both eyes first and then switch over to the alternate lens type. The order of lenses will be determined using a randomization schedule.

A randomization schedule will be generated for the study by CORE's data management team and provided to the research assistants. Study investigators will remain masked to the randomization schedule until the study is completed and the database is locked.

4.1.4 MASKING

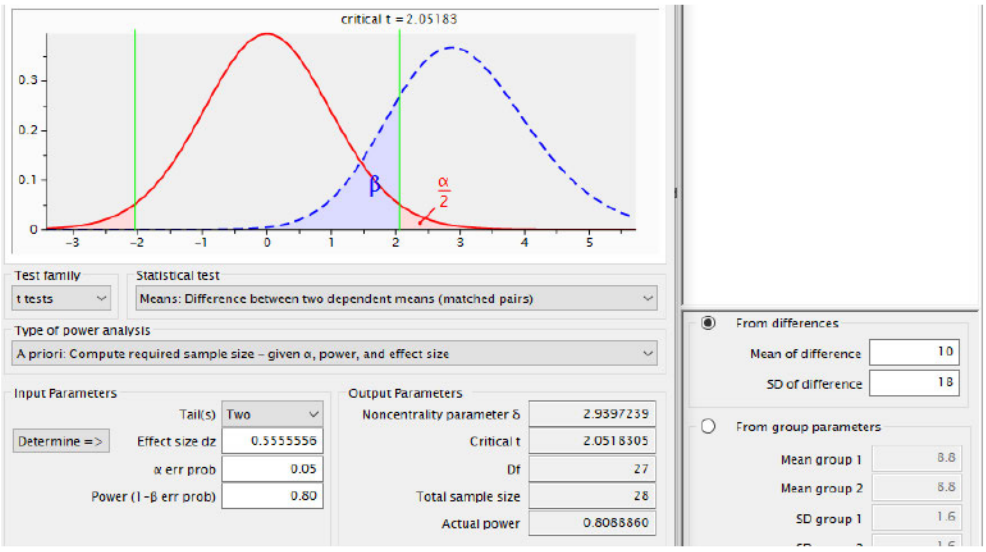
This is a double-masked study. Both participants and investigators will be masked to the lens assignment.

4.2 STUDY POPULATION

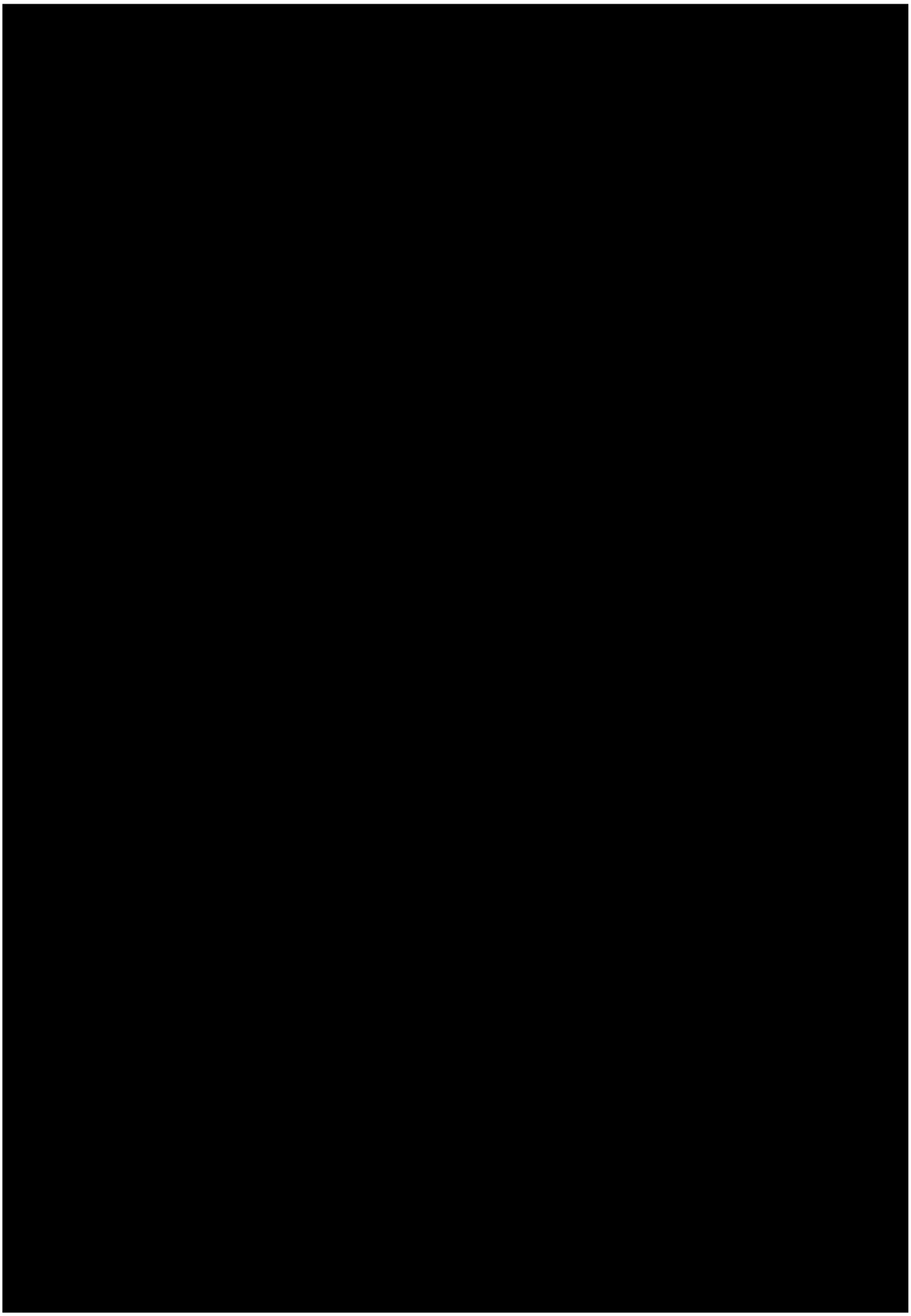
4.2.1 SAMPLE SIZE CALCULATION

Sample size: The target sample size for this study is 30 participants to be randomized and to wear both lens types. This target was determined based on the sample size calculation below:

Based on previous data for "lens handling for removal" which showed a standard deviation of the difference between means of 18 points (0-100 scale), a minimum sample size of 28 is required to detect a paired difference between groups of 10 units on a 0-100 scale with 80% power and alpha 0.05 in a two-tailed t-test.



Therefore, in this study, a maximum of 30 participants to be randomized and wear both lens types.



11. Have undergone refractive error surgery or intraocular surgery;
12. Are a member of CORE directly involved in the study.

* 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.

* Any potential exclusion will be reviewed with the Lead Investigator or Principal Investigator prior to final decision making.

4.2.4 REPEATED SCREENINGS

In some circumstances a repeated screening may need to be scheduled. The maximum total number of screenings permitted will be 2, i.e. 1 re-screen. Examples of reasons include, but are not limited to:

1. Incomplete information available at time of screening to determine eligibility (e.g. current lens brands worn, current mediation, etc.);
2. Study procedures unable to be completed in time scheduled for visit;
3. Study products not available at the time of the screening visit;
4. The short-term use of medications (e.g. antibiotics, antihistamines etc.);
5. Reassessment of baseline ocular conditions (e.g. corneal and/or conjunctival staining, scars etc.).

4.3 STUDY MATERIALS

4.3.1 LENSES

If deemed eligible after screening, participants will wear two different contact lenses bilaterally on the same day, in a randomized sequential order: clariti elite and Proclear 1 day.

The control lens is the commercially available, daily disposable Proclear 1 day, manufactured by CooperVision, Inc. The test lens is the frequent replacement (monthly) clariti elite, manufactured by CooperVision, Inc.

The test lenses are not approved for sale in Canada and therefore and ITA (Investigational Testing Authority) will be sought from Health Canada prior to them being used in the study. The control lens, Proclear 1 day, is commercially available in Canada.

Lenses will be worn for a period of approximately 90 minutes each during the study visit only.

Table 1: Study lens specifications

	Test	Control
Lens name	**clariti elite**	**Proclear 1 day**
Manufacturer	CooperVision	CooperVision
HC licence #	N/A- investigational	106827
Material	somofilcon A	omafilcon A
EWC (%)	56%	60%
Dk/t (-3.00)	86	28
Base Curve (mm)	8.6	8.7
Diameter (mm)	14.2	14.2
Sphere Power (D)	-1.00 to -6.00 (0.25 steps)	-1.00 to -6.00 (0.25 steps)
Replacement schedule	Monthly replacement	Daily disposable

4.3.2 DRUGS

Sodium fluorescein strips (Example: Diofluor, Dioptic Pharmaceuticals Inc; DIN:02160773) will be used to evaluate the ocular surface.

4.3.3 REWETTING DROPS

Participants who habitually use rewetting drops will be asked to refrain from using their drops on the study day. Rewetting drops may be used in the event of any clinical observation and/ or adverse event noted during the study.

4.3.4 ORDERING CONSUMABLES

The clariti elite lenses will be provided by CooperVision, Inc. The Proclear 1 day lenses will either be provided by CooperVision, Inc. or they will be ordered by the site and these costs will be invoiced to CooperVision as pass through costs outside the contract.

4.3.5 CONTACT LENS DISPENSING - MASKED

For the purpose of masking of participants and investigators, lenses will be over-labelled prior to dispense (based on the randomization assignment) by the study research assistant/unmasked personnel.

At study visits, lenses will be provided to participants in over-labelled blister packs to facilitate masking of participants and investigators. The use of saline for rinsing the contact lens prior to insertion is permitted if necessary. Saline will not be dispensed during the study.

4.3.6 CONTACT LENS DISPOSAL

Contact lenses worn during study visits will be immediately discarded after use.

Worn lenses associated with adverse events, product observations, product defects, or product quality complaints shall be retained at CORE and returned to CooperVision, Inc. if requested. Typical analysis in these cases relates to inspection for damage and/ or bacterial contamination. Upon completion of the study, all unworn lenses will be destroyed, unless otherwise directed by the study sponsor.

4.3.7 PRODUCT ACCOUNTABILITY

Accountability logs will be kept to record the number of lenses received, dispensed, unused and disposed of or returned to sponsor (where relevant). All products dispensed to participants will be recorded in individual participant logs.

4.4 SCHEDULED AND UNSCHEDULED VISITS

4.4.1 STUDY VISITS

All visits will be conducted subsequent to each other, on the same day. Estimated on-site visit time and duration of involvement for each participant is 4hrs. A summary of the visit codes and duration are listed in Table 2 below.

Table 2: Summary of visits

Visit number	Visits	Visit length
1	Screening	1.0 hrs
2	CL Pair 1 wearing period	1.25 hr
3	CL Pair 2 wearing period	1.5 hr
4	End of study visit and Study Exit	0.25 hr
Total		**4 hrs**

4.4.2 SCREENING (V1)

A documented informed consent process will be conducted with all participants prior to their enrolment in the study and prior to any data collection or measurements.

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.

Visit procedures:

1. The participant is expected to attend the screening visit with their habitual glasses NOT having worn their habitual contact lenses and/or used any rewetting/tear drops on the study day.
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.
3. Participant demographics and medical history (age, sex, medical conditions, medications, allergies).
4. Contact lens history (habitual lens information and wearing habits).

14. Slit lamp biomicroscopy including FI staining to assess ocular health.
15. 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.

4.4.3 LENS 1 WEAR PERIOD (V2)

The Screening Visit (V1) will be immediately followed by Lens 1 Wear Period (V2) on the same day.

Visit procedures:

1. Participant will be assigned a randomization ID (by the study research assistant/unmasked staff)
2. Lens pair #1 will be provided to participants in a manner, which does not unmask the participant or investigator, as described in Section 4.3.5.
3. Participant to open blister packs and apply the Lens pair 1 OU – [redacted]
4. The participant will be asked to provide binocular subjective ratings at insertion for the following (0-100, integer steps):
    i) Ease of blister pack opening
    ii) CL stability on fingertip
    iii) Ease of CL application to eye
5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]
9. [redacted]
10. [redacted]
11. [redacted]
12. [redacted]
13. The participant will remove the lenses.

4.4.4 LENS 2 WEAR PERIOD (V3)

The Lens 1 Wear Period (V2) will be immediately followed by Lens 2 Wear Period (V3) on the same day. This visit will involve the alternate lens type, i.e. the study lens type not yet worn.

Visit procedures:

1. The participant will be assigned the second pair (lens pair #2) of study contact lenses, which will be selected according to the randomization table by unmasked study personnel.
2. The crossover lens pair #2 will be provided to participants in a manner, which does not unmask the participant or investigator, as described in Section 4.3.5.
3. Repeat steps 3-13 from V2 (section 4.4.3).
4. Subjective preference 5-point Likert between lenses for handling related to lens insertion/ removal and overall handling experience (binocular preference).

4.4.5 STUDY EXIT (V4)

Exit visual acuity (HIHC) will be recorded with refraction (OD & OS & OU (logMAR)). An exit biomicroscopy assessment will be conducted including FI staining, if participant was randomised.

After the exit assessments have been completed, the participant and investigator will complete the study exit and remuneration forms. At this time, the participant will be considered as having exited the study.

When a participant exits the study, the study exit form will be completed. Therefore, this form will be completed either at completion of the study, 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-follow-up visits are required, the exit form will be completed after the last follow-up visit.

4.4.6 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. Relevant and applicable unscheduled visit information will be included in the final report as deemed necessary by the lead investigator. Unscheduled visit information pertaining to adverse events, product quality complaints and protocol deviations will be included in the final report. This will include the details, causality and outcome.

4.5 STUDY PROCEDURES

A summary of the study procedures to be conducted at the different scheduled visits is listed in Table 3.

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

	Screening V1	Lens pair 1 V2	Lens pair 2 V3	Exit V4
Informed Consent	√			
Demographics, concomitant medications and medical history	√			
Contact lens history and wear habits,	√			
[redacted]				
Participant ratings for i) ease of blister pack opening, ii) CL stability on fingertip, and iii) ease of application to eye (0-100, integer steps)		√	√	
[redacted]				
Subj preference 5-point Likert between lenses for handling related to lens insertion/removal and overall handling experience			√	
Study Exit				√

4.6 DETAILS OF PROCEDURES

4.6.1 INFORMED CONSENT

A documented informed consent process will be conducted with each participant prior to their enrolment in the study and prior to any data collection or measurements.

Before entry into the study, the prospective participant will be informed by the investigator about all pertinent aspects of the research (i.e. all essential elements as described in the information and consent letter), including any additional REB/IEC-approved written information, in non-technical language, easily understandable for the participant. The prospective participant will be informed that their participation is voluntary, and they may withdraw consent to participate at any time.

The prospective participant will be given ample time to read the information and consent letter and the opportunity to ask questions. After ascertaining the prospective participant's willingness to take part in the study and prior to entry into the study, the prospective participant's consent will be recorded by means of the participant's dated signature on the Information and Consent Letter. The Information and Consent Letter that is used must be approved by the sponsor and by the Office of Research Ethics (ORE). After having obtained the consent, the participant must be provided with a signed copy of the information and consent letter.

4.6.2 CASE HISTORY

Demographics:

Demographic information from the participant will be obtained, including age and sex.

Medical History:

At screening, information will be obtained from the participant about the current medication, allergies, and any medical conditions.

Contact Lens History:

Information will be obtained from the participant about the current contact lens type (lens name, brand, lens power), replacement frequency, typical number of lens wear days per week, typical wear time per day, years of lens wear.

4.6.3 AUTOREFRACTION

[redacted]

[redacted]

[redacted]

4.6.9 SLIT LAMP BIOMICROSCOPY

A slit lamp biomicroscopy examination will be conducted to assess anterior segment ocular health. The participant will be seated behind a slit lamp and the ocular findings will be graded using Efron grading scale (0-4, 0.1 steps – unless otherwise stated).

Bulbar, Limbal Hypereamia

The redness of each quadrant of the bulbar and limbal conjunctiva of both eyes will be assessed.

Corneal, conjunctival staining

A sodium fluorescein strip, wetted with a few drops of saline, will be applied to the lower lid margin of both eyes. Staining of all five zones of the cornea and four zones of the conjunctiva will be graded while viewing with cobalt blue light through a Wratten no. 12 barrier filter.

Palpebral conjunctival hyperemia and roughness

The redness and roughness of the upper and lower eyelids (tarsal plate zone 2) will be assessed.

[redacted]

4.6.12 QUESTIONNAIRES AND SUBJECTIVE RATINGS

Subjective ratings:

After lens insertion at visits 2 and 3, participants will be asked to complete questionnaires for binocular subjective ratings (0-100, integer steps) related to:

i) Ease of blister pack opening,
ii) Lens stability on fingertip
iii) Ease of lens application to eye (key outcome)

[redacted]

At the end of visit 3 after removing lens pair 2, participant will be asked to complete a 5-point Likert preference questionnaire (to select one of the following answers for each question: prefer Lens pair #1 strongly, prefer Lens pair #1 slightly, No preference, prefer Lens pair #2 slightly, prefer Lens pair #1 strongly) binocularly related to:

i) Overall lens handling at insertion
ii) Overall lens handling at removal
iii) Overall lens handling experience

[redacted]

5 MONITORING PROTOCOL ADHERENCE

All personnel involved in this study will be listed on a delegation log and their training will be documented. Consent documentation will be reviewed by personnel not involved in the consent process. All adverse events and protocol deviations will be reviewed by the Lead Investigator. Serious adverse events and major protocol deviations will be reviewed by the Principal Investigator.

6 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

Due to the short-term, daily wear nature of the study, this study is considered a non-significant risk study based on International Standards Organization (ISO) guidelines. This is a higher than minimal risk study according to Health Canada because of the use of non-marketed products. The study assessments are all non-invasive, standard optometric assessments.

The investigational contact lenses used in this study are silicone hydrogel lenses, worn on a daily wear basis, with a monthly replacement frequency. Whilst this lens is not marketed in Canada, it is essentially the same as the clariti 1 day lens, which is marketed in Canada. It is also commercially available in the United Kingdom.

Each of the 2 lens types will be worn for approximately 90 minutes during the day, closely monitored by the investigator.

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 of daily wear of soft contact lenses can occur (e.g. inflammation and infection). Complications that may occur during contact lens wear include discomfort, dryness, burning, excessive tearing, aching or itching eyes, discharge, hyperemia and variable, cloudy or blurred vision. Other non-serious contact lens related complications include peripheral ulcers, papillary conjunctivitis, superior epithelial arcuate lesions, etc. More serious risks may include 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 3.5 million Canadians, 35 million Americans and more than 140 million people worldwide who wear contact lenses.

Fluorescein is used in this study to assess the ocular surface. Although rare, it is possible that participants may have an allergic reaction to the dye. They will be advised of the fluorescein use

in the consent document and will be instructed to advise the investigator if they have a known allergy to fluorescein.

It is possible that participants may experience temporary discomfort associated with the study procedures /products including: light sensitivity, dryness, and foreign body sensation.

Parts or all of this study will be conducted during the ongoing COVID-19 pandemic. Therefore, risks of infection with COVID-19 through participation remain. These risks arise due to possible exposure during commute to and from the study visit as well as during the study visit, particularly due to the closeness of the investigator and participant (within 2m for some assessments). The potential effects of COVID-19 are not yet fully known and may include long-term health consequences. In a small percentage, infection with COVID-19 can lead to serious illness, hospitalization, and in rare cases to complications leading to death. Individuals aged 60 and above and those with underlying medical conditions are considered at a greater risk for severe illness from the COVID-19 virus.

In consideration of risks associated with COVID-19, CORE has implemented a series of on-site safety procedures which have been reviewed and approved by the University of Waterloo. These include, but are not limited to, self-screening of investigators and participants prior to entering the building, maintaining physical distancing as much as possible, frequent handwashing, wearing of face masks by the investigator and participant as per University recommendation/ guidelines, and frequent room and equipment hygiene and decontamination. In addition, members of CORE and participants follow the University policies regarding Covid-19 vaccination.

Participants will not benefit directly from taking part in this study. However, participation in this study may contribute to scientific research information that may be used in the development of new contact lens products. In addition, participants will have the opportunity to try a different type of soft contact lenses at no cost to them.

Information from this study may help researchers come up with new soft contact lens designs to help others in the future. This study may help the study sponsor to better understand the performance of the products being used in this study.

7 ADVERSE EVENTS

[redacted]

Any observations taking place prior to determining that a participant meets all inclusion/ exclusion criteria for the study and which are not related to the performed study procedures are not considered an AE. An AE can be any unfavourable and unintended sign, symptom, or disease temporarily associated with a study procedure, whether there is a causal relationship 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	

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

Code	Condition	Reporting
07	Hypopyon	Report to Health Canada within 72 hours of discovery as applicable
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	

7.1 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.

7.2 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 adverse event will be managed within CORE or may be referred to an eye care practitioner external to CORE. 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. 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.

7.3 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 the event to the IRB as per IRB requirements (by fax, mail/delivery, phone, or email). All fatal or life-threatening events will be reported immediately to the IRB.

All serious adverse events that (1) are related to a failure of the device or a deterioration in its effectiveness, or any inadequacy in its labelling or in its direction for use, AND (2) have led to the death or serious deterioration in the state of health of a participant, user or other person, or could do so were they to recur, must be reported to Health Canada and the sponsor within 72 hours. Preliminary and final reports must be submitted as per Health Canada requirements.

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).

Sponsor contact details are:

[redacted]

Details of all adverse events will be included in the study report.

8 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 $20 per hour for their in-office visits (including the initial screening visit). 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 4.2.3.
- Unacceptable performance with products to be used in study: Participants may be discontinued if they are unable to achieve acceptable fit, 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.
- 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.
- 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, 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.

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

9 DEVICE DEFICIENCY REPORTING

9.1 INVESTIGATOR RESPONSIBILITY

Product Defect is the terminology typically used in contact lens products for an unexpected observation related to the identity, quality, durability, reliability, or usability of the product under investigation. 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 but no later than 5 working days are occurrence.

Note: Observations on study products that are anticipated as a part of the device development process are not considered to be Product Defects or Device Deficiencies.

If the Product Defect is associated with an adverse event, the investigator shall report the Product defect via the CooperVision Adverse Event Notification Form. If the Product Defect is not associated with an adverse event, the investigator shall report the Product Defect via the Clinical Product Defect Notification Case Report Form. Sponsor contact details **for Product Defect Notifications** are:

[redacted]

9.2 SPONSOR RESPONSIBILITY

Device Deficiency is defined as the inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance.

The Sponsor will review the Product Defect Notification Case Report Form, gather additional information if needed from the Investigator/CRO and determine whether the notification represents a Device Deficiency. Device Deficiencies will be reported as per Internal CVI procedures.

A summary of Device Deficiencies will be documented in the clinical study report. If no Device Deficiencies are observed in a study, then a statement stating as such will be included in the clinical study report.

10 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. 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 $20 per scheduled protocol visit hour (including the initial screening visit). Full details are given in the information consent letter.

11 STATISTICAL ANALYSIS AND DATA MANAGEMENT

11.1 STATISTICAL ANALYSIS

All study data will be analyzed by CORE at the University of Waterloo. Summary statistics will be produced (e.g. mean, standard deviation). Data analysis will be conducted using Statistica and / or SPSS, or other appropriate software. Descriptive statistics will be provided on information regarding baseline demographic variables (age, sex, refractive error distribution, etc.). Table 6 lists the primary outcome and other variables and anticipated statistical procedures. All data will be tested for normality of distribution using Shapiro-Wilk tests.

A binomial test will be used to nalyze the results for the count data of subjective preferences. The number of “no preference” responses will be evenly distributed to the two options on the basis they would be equally likely to choose either.

The critical alpha level for statistical significance will be set at 0.05.

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

All participants who completed the study will be used in the analysis, unless exclusion agreed with the sponsor based on protocol deviation or adverse event information. In the event of missing data, individual data points will not be extrapolated from the collected data.

Table 6: Outcome variables and anticipated statistical procedures

Variable	Analysis	Statistical test
Subjective ratings, Primary outcome: binocular subjective rating of the ease of lens application to eye	Descriptive and other statistics	Mean, Median, Standard Deviation, Minimum, Maximum, Frequency count
	Effect of study treatment (comparison between study lenses)	Paired t-test Wilcoxon matched pairs test Friedman

[redacted]

11.2 DATA MANAGEMENT

[redacted]

11.3 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 the lead investigator.

12 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.

13 STUDY MONITORING

The Sponsor will ensure site qualification of the investigative site has been completed prior to conducting the clinical study in order to ensure that the site facility is adequate, personnel are qualified and resources are satisfactory.

CORE will provide status reports 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.

Consent documentation will be reviewed by a person not involved in the consent process. 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.

All adverse events and protocol deviations will be reviewed by the Lead Investigator and reported to the sponsor. Documentation of any serious adverse events and major protocol deviations will be reviewed by the Head of Clinical Research and the PI.

14 STUDY MANAGEMENT

14.1 STATEMENT OF COMPLIANCE

This clinical study was developed in accordance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for Good Clinical Practice (GCP) (ICH E6 R2), with ISO 14155:2020 Clinical Investigation of Medical Devices for Human Subjects, 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 (2022)
- https://uwaterloo.ca/research/office-research-ethics/research-human-participants

[redacted]

14.3 CLINICAL TRIAL REGISTRATION

This study will be registered on clinicaltrials.gov.

14.4 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.

14.4.1 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;
- Device / intervention errors (i.e. incorrect contact lens(es) 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.

14.4.2 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;
- 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).

14.4.3 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 deviations shall be reported to the study sponsor within two working days.

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

[redacted]

14.6 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.

[redacted]

15 REPORT

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