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Centre for Ocular Research & Education

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# Protocol

## TO EVALUATE THE PERFORMANCE OF TWO MONTHLY REPLACEMENT SILICONE HYDROGEL LENSES AFTER 1 MONTH OF WEAR

### (STUDY CODENAME: STINGRAY)

**Sponsor:** CooperVision, Inc.

**Sponsor study number:** EX-MKTG-132

**CORE protocol number:** P/799/21/CVI

**Protocol author:** Marc Schulze

**Principal investigator(s):** Lyndon Jones



[redacted]

## DOCUMENT CHANGE HISTORY

| Version date | Author | Description of change(s) |
|---|---|---|
| 09dec2021 | Jason Chau | Original protocol |
| 14dec2021 | Jill Woods | Revised CooperVision signature on front page; |
| 03feb2022 | Marc Schulze | Several minor edits, including:<br>• Added At-Home questionnaire to sections 4.1.1, 4.4.3, 4.5, 4.5.2 & 4.5.3<br>• Updated section on randomization (4.1.2)<br>• Added/clarified eligibility criteria (section 4.2.3)<br>• Modified lens storage section (4.3.6) for clarity<br>• Modified order of procedures for the screening visit (section 4.5.1)<br>• Clarification regarding scales/scale steps used for lens fit assessments (sections 4.5.2 and 4.5.3)<br>• Added additional in-office questionnaire item and removed duplicate item (4.5.3)<br>• Correction of grammatical errors and typos |
| 28mar2022 | Marc Schulze | • Updated protocol author to Marc Schulze as Jason Chau has left CORE as of 22Mar2022<br>• OptiFree Puremoist solution has been reclassified from “drug” to “medical device” on the Health Canada website. Table 2 (section 4.3.2) was updated accordingly to now reflect the MDALL number.<br>• Clarification regarding number of study days (3) and number of study visits (5 including exit); this applies to sections (4.1.1, 4.1.2, 4.4, 4.4.2)<br>• Corrected randomization time-point in 4.1.2 (should be at V2 not V1) |

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**Disclaimer**

This study will be conducted for research purposes only.

# 1 INTRODUCTION

As new lenses come to market it is of interest to compare the performance of the new product to the performance of established products. This study will evaluate the performance of two monthly replacement silicone hydrogel lenses after one month of bilateral wear, in habitual frequent replacement (FRP) soft contact lens (CL) wearers. The established product is CooperVision's Biofinity Sphere (Lens A) and the new product to market is the recently launched Total 30 (lens B) manufactured by Alcon Inc..

# 2 OBJECTIVES

To evaluate the performance of two monthly replacement silicone hydrogel contact lenses in habitual FRP CL wearers when worn for 1-month.

The primary outcome variables for this study are:

- Lens handling on removal (0-10 scale, 0.5 steps) at 1-month visit

[redacted]

# 3 HYPOTHESIS

The null hypothesis is that there will be no difference between Lens A and Lens B for the primary outcome variable of lens handling on removal (0-10 scale, 0.5 steps) collected after 1-month of wear.

# 4 MATERIALS AND METHODS

## 4.1 STUDY DESIGN

### 4.1.1 OVERALL DESIGN

This study will be a prospective, randomized, double-masked, single-site, 1-month cross-over design involving bilateral eye daily wear of two different monthly replacement CL types. Each lens will be worn bilaterally for approximately one month.

There are 5 scheduled study visits that take place on 3 different days, including the screening and exit visits:

**Visit 1**: Screening/eligibility, baseline assessments and fitting of both study lenses

**Visit 2**: Subject randomization and Dispense of study lens Pair #1 (this will be combined with Visit 1 if participant meets all eligibility criteria at V1 )

**Visit 3**: 1-month follow up of study Pair #1, dispense of study Pair #2

- [redacted]1

**Visit 4**: 1-month follow up of study Pair #2, and study exit

- [redacted]

**EXIT**: Anticipated to follow immediately after Visit 4 unless participant discontinues early

[redacted]

### 4.1.2 RANDOMIZATION

A randomization schedule will determine the order of wear of lens A and lens B for the first and second month, for each participant. Participants will be randomized at the beginning of Visit 2 after eligibility has been confirmed during V1.

A randomization schedule will be generated by CORE's data management team and provided to the unmasked research assistant(s) for the study. It will be included in the final report. Study investigators will remain masked to the randomization schedule until the study is completed and the database is locked.

### 4.1.3 MASKING

Participants will be masked to the lens assignment. Lenses dispensed to participants may have the foil label completely removed or have all or part of the label obscured. Investigators will be masked as much as possible however it may not be possible to fully mask the investigators, because identifying lens markings may be visible during the biomicroscopy examination.

## 4.2 STUDY POPULATION

### 4.2.1 SAMPLE SIZE CALCULATION

The sample size was calculated using data of 'lens handling at removal' ratings collected in a previous study using a 0-10 rating scale. This data showed a standard deviation of paired differences of 1.02. With an alpha level of 0.05 in a paired difference test, and power of 84%, a minimum sample size of 20 participants is recommended in order to determine a statistically significant difference of 0.71 between study lenses , Figure 1.

To account for dropout, up to 25 participants may be randomized and dispensed with study product in total, with the target of at least 20 completing the study.

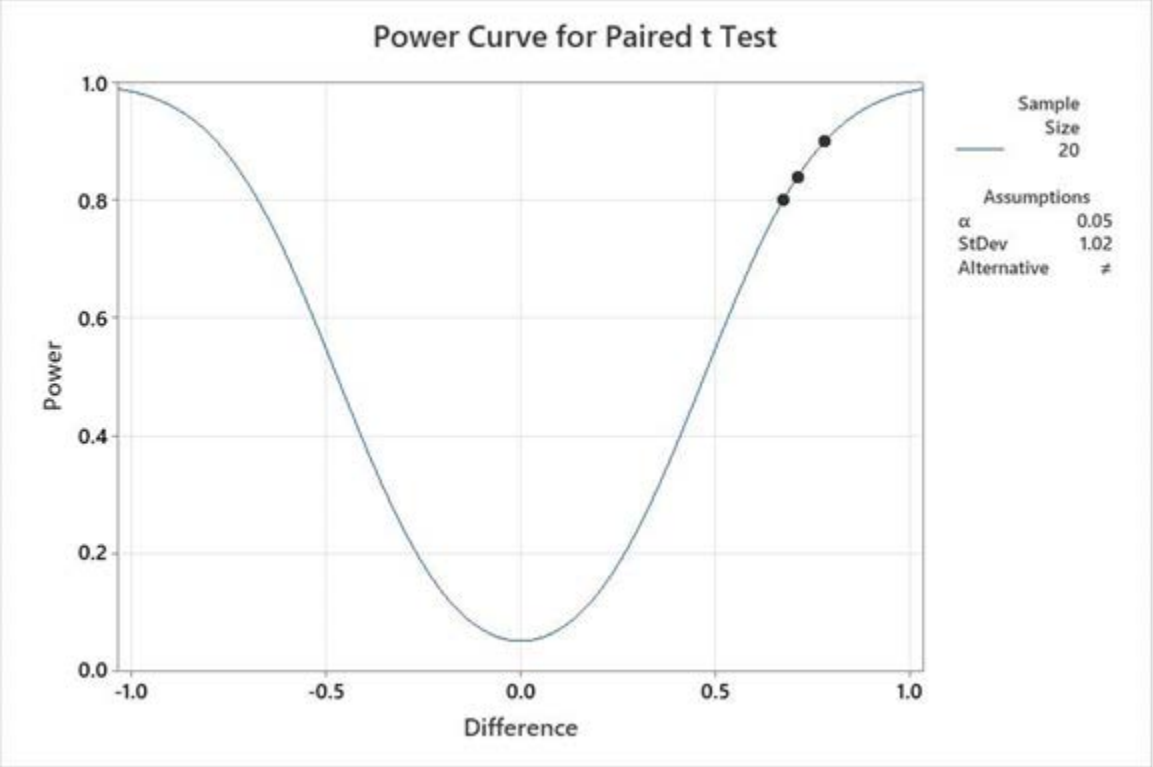


**Figure 1: Sample size calculation graph**

### 4.2.2 NUMBER OF PARTICIPANTS

Participants will be recruited using CORE records and advertising approved by the UW Office of Research Ethics. Approximately 25 eligible participants may be dispensed with study products,

with a target of at least 20 completing the study. Informed consent will be obtained for all participants prior to their enrolment in the study and prior to any study data collection.

### 4.2.3 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. Self-reports having had a full eye examination within the previous 2 years;
3. Has read and signed an information consent letter;
4. Is willing and able to follow instructions and maintain the appointment schedule;
5. Is a habitual wearer of frequent replacement contact lenses;
6. Anticipates no difficulty wearing the contact lenses for 6 days/week and 8 hours/day during the study;
7. Has refractive astigmatism no higher than -0.75DC in each eye;
8. Can be successfully fit with both study lens types;
9. Achieves at least 0.4 logMAR VA monocularly and at least 0.2 logMAR VA binocularly with each study lens type.

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

1. Is participating in any concurrent clinical research study;
2. Has any known active* ocular disease and/or infection;
3. Has an unstable systemic condition that in the opinion of the investigator may affect vision or contact lens comfort across the 2-month study duration;
4. Is using any systemic or topical medications in an irregular routine that in the opinion of the investigator may affect vision or contact lens comfort across the 2-month study duration;
5. Has known sensitivity to the diagnostic sodium fluorescein to be used in the study;
6. Is an employee of the Centre for Ocular Research & Education.

* 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 mild 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.

## 4.3 STUDY MATERIALS

### 4.3.1 LENSES

All study lenses are approved by Health Canada. They will be worn bilaterally and on a daily wear basis. The study lenses are monthly replacement lenses and therefore they will be removed at the end of each day and stored/cared for with OptiFree PureMoist (Alcon).

Table 1: Lens specifications

| Lens | Lens A: Biofinity (Coopervision) | Lens B: Total 30 (Alcon) |
|---|---|---|
| Material | comfilcon A | lehfilcon A |
| Device class | 3 | 2 |
| HC licence # | 70149 | 106376 |
| Dk/t (barrer/cm) | 160.0 | 154.0 |
| Sphere power (D) | -0.25 to -6.00 (0.25 steps)<br>-6.50 to -12.00 (0.50 steps)<br>+0.25 to +6.00 (0.25 steps)<br>+6.50 to +8.00 (0.50 steps) | -0.25 to -8.00 (0.25 steps)<br>-8.50 to -12.00 (0.50 steps)<br>+0.25 to +6.00 (0.25 steps)<br>+6.50 to +8.00 (0.50 steps) |
| Base curve (mm) | 8.6 | 8.4 |
| Diameter | 14.0 | 14.2 |

### 4.3.2 LENS CARE SYSTEM

The lens care system to be used by all participants is OptiFree PureMoist. Participants will be provided with sufficient product for the study duration. They will be provided with the package insert and instructed on the (rub and rinse) care procedure as well as on the storage of their study contact lenses.

Table 2: Lens care systems

| | OptiFree PureMoist |
|---|---|
| Manufacturer | Alcon Inc |
| Health Canada, MDALL | 102753 |

### 4.3.3 DRUGS

Fluorescein will be used to assess ocular health of the anterior ocular surface.

### 4.3.4 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 each visit.

### 4.3.5 ORDERING CONSUMABLES

All study lenses will be provided by CooperVision or sourced from local commercial channels.

[redacted]

### 4.3.7 CONTACT LENS DISPOSAL

Participants will be instructed to wear the lenses daily and remove at the end of the day to clean/store them in the OptiFree PureMoist provided. All contact lenses worn to each 1-month follow up visit will be collected and stored as per the instructions in section 4.3.6 above. These worn lenses will later be shipped to CooperVision for deposition and surface analysis and subsequent disposal. No genetic materials will be analysed. Unworn lenses may be transferred

to another study or destroyed, according to instructions from CooperVision at the end of the study.

### 4.3.8 PRODUCT ACCOUNTABILITY

Accountability logs will be kept to include the number of lenses and lens care system bottles received, dispensed, unused and disposed of. All products dispensed to participants will be recorded in the study binder. A manifest will be created for the worn lenses collected, stored and shipped.

## 4.4 SCHEDULED AND UNSCHEDULED VISITS

This study has a total of 5 study visits, including the screening and exit visits. They are as follows:

- Visit 1: Includes screening, baseline assessments, randomization and fitting of both study lenses
- Visit 2: Randomization & Dispense of study lens Pair #1 (this will be combined with Visit 1 if all eligibility criteria met at V1)
- Visit 3: 1-month follow up of study Pair #1, dispense of study Pair #2
- Visit 4: 1-month follow up of study Pair #2
- EXIT: Typically occurring immediately after Visit 4 unless participant discontinues early

The scheduled follow-up visits 3 and 4 may only take place when the participant attends wearing the study lenses for a minimum of 6 hours. If this is not the case, and the participant is not experiencing any problems with the lenses, the appointment will be rescheduled, ideally within the visit window.

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

### 4.4.1 SCREENING

The investigator will determine participant eligibility at Visit 1 using the inclusion and exclusion criteria. Participants will be assigned a study ID number after they sign the consent documentation process, i.e. before their eligibility for the study has been confirmed. Ineligible participants will be discontinued from the study.

### 4.4.2 REPEATED SCREENING

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

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

Two repeat screenings are allowed, i.e. the maximum number of screenings permitted will be 3.

### 4.4.3 SCHEDULED STUDY VISITS

Table 3 below summarises the scheduled visits, including their visit code number, estimated duration and the day count or visit window.

**Table 3: Summary of visits**

| Visit code | Visits | Duration (hours) | Day/Visit window |
|---|---|---|---|
| V1 | Screening and fitting | 1.0 | 0 |
| V1/R1 | 1st repeat of V1 if needed | As needed | 0 |
| V1/R2 | 2nd repeat of V1 if needed | As needed | 0 |
| V2 | Dispensing & masking 1st study lens, same day as V1 (or V1/R1 or V1/R2) | 0.75 | 0 |
| [redacted] | | | |
| V3 | 1-month follow up for 1st study lens, dispensing & masking 2nd study lens | 1.25 | Day 28, 29, 30 or 31 from V2 (where Visit 2 = Day 0). Pair 2 dispense = Day 0 |
| [redacted] | | | |
| V4 | 1-month follow up for 2nd study lens | 0.75 | Day 28, 29, 30 or 31 from V3 (where Visit 3 = Day 0). |
| EXIT | Anticipated to follow immediately after V4 unless participant discontinues early | 0.25 | n/a |
| US-1 | 1st Unscheduled visit | As needed | n/a |

### 4.4.4 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.

## 4.5 STUDY PROCEDURES

A summary of the study procedures to be conducted at scheduled visits is listed in Table 4. More procedure details are included for each visit in the following sections.

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

| | V1<br>Screen<br>Fit of study CL | V2<br>Dispense first study lens | V3<br>1-month follow-up first study lens, dispense second study lens | V4<br>1-month follow-up second study lens | Exit |
|---|---|---|---|---|---|
| Consent process | X | | | | |
| Subject age & sex | X | | | | |
| CL history (brand & power)^ and lens wear schedule | X | | X | X | |
| Health & medication | X | X | X | X | |
| Review any problems with eyes/study lenses | | X | X | X | |
| [redacted] | X | | | | X<br>(OR SUBJ. REFRACTION) |
| [redacted] | X | | | | |
| [redacted] | X | | | | |
| Randomization | | X | | | |
| [redacted] | X | | | | |
| Dispense study CLs | | X | X | | |
| [redacted] | X | X | X | X | |
| [redacted] | X | X | X | X | |
| [redacted] | X | | | | |
| [redacted] | | X | X | X | |
| [redacted] | | | X | X | |
| [redacted] | | X | X | | |
| [redacted] | | | X | X | |
| [redacted] | X | X* | X | X | X* |
| Study CL collection | | | X | X | |
| Study completion and Exit | | | | | X |

[redacted]

### 4.5.1 VISIT 1 SCREENING AND FIT VISIT

Informed consent shall be obtained in writing from the participant and the process shall be documented before any procedure specific to the clinical investigation is carried out. Participants will be assigned a study ID after they sign the consent documentation, i.e. before their eligibility for the study has been confirmed.

The investigator will determine participant eligibility using the inclusion and exclusion criteria. Ineligible participants will be discontinued from the study.

The study procedures to be conducted at this visit are detailed below:

1. The participant is expected to attend the screening / baseline visit wearing either their habitual contact lenses or spectacles.
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).
5. [redacted]
6. The participant removes their habitual contact lenses (if applicable).
7. [redacted]

c. [redacted]

[redacted]

12. Trial fitting of both study lenses. For logistical purposes to ensure the appropriate fitting for each lens type, the study investigator will not be masked during the trial fitting of the lenses.

    a. [redacted].

    b. The contact lenses will be provided to participants in a manner that does not unmask the participant as described in Section 4.1.3.

    c. The participant will insert the lenses.

    d. [redacted]

13. The investigator will confirm that the participant meets the eligibility specifications set out in the inclusion criteria and exclusion criteria and is eligible to continue in the study.

14. [redacted]

### 4.5.2 VISIT 2 DISPENSE PAIR # 1

This visit may or may not be immediately subsequent to the screening visit, depending on lens availability but will occur no later than 30 days after Visit 1.

The study procedures are outlined below:

1. If this visit does not immediately follow V1, then confirm health and adverse event status.
2. [redacted]
3. The participant will be assigned a randomization number (Randomization ID#) by the unmasked research assistant.
4. The first pair (lens pair #1) of study contact lenses (either Lens A or Lens B) will be selected by the unmasked research assistant according to the randomization table.
5. Lens pair #1 will be provided to participants in a manner which does not unmask the participant or investigator, as described in Section 4.1.3.
6. The participant will insert the lenses.
7. The contact lenses will be allowed to settle for 5 minutes.
8. [redacted]

c) [redacted]

[redacted]

11. The participant will be asked to wear the study lenses for at least 8 hours per day and 6 days per week.
12. [redacted]
13. The participant will be provided with instructions for the safe wear & care of the contact lenses as well as sufficient care product supply.
14. [redacted]

### 4.5.3 VISIT 3 1-MONTH FOLLOW-UP PAIR #1 & DISPENSE PAIR #2

Participants will be asked to attend this visit after wearing Lens Pair #1 for at least 6 hours. This visit will occur 28-31 days (inclusive) after visit 2.

The study procedures are outlined below:

1. Review changes to medical history and medications.
2. The participant will be asked to score their subjective responses and rate their typical wearing schedule and reflect on their overall satisfaction [redacted] during the month for the lens performance items listed below:

   a) [redacted]

   d) Overall satisfaction with handling for lens removal (0 – 10 scale, 0.5 steps);

   e) [redacted]

g) [redacted]

3. [redacted]

6. [redacted]
7. Study lens collection at 1-month: following the instructions listed in section 4.3.6, lenses will be removed from participant's eyes and stored.
8. [redacted]
9. 5-minute wash-out period following the lens removal.
10. The participant will be assigned the second pair (lens pair #2) of contact lenses (either Lens A or Lens B), which will be selected according to the randomization table.
11. Lens pair #2 will be provided to participants in a manner, which does not unmask the participant or investigator, as described in Section 4.1.3.
12. The same procedures will be followed to dispense study lens #2 as described in Section 4.5.2 DISPENSING LENS PAIR #1 (VISIT 2), points 6 to 13.
13. [redacted] Additional lens case and care products will be provided as needed.

### 4.5.4 VISIT 4 1-MONTH FOLLOW-UP PAIR #2

Participants will be asked to attend this visit after wearing Lens Pair #2 for at least 6 hours. This visit will occur 28-31 days (inclusive) after visit 3.

The study procedures are outlined below:

1. The same procedures will be carried out for study lens #2 as described in Section 4.5.3 1-MONTH FOLLOW-UP OF LENS TYPE #1 (VISIT 3), points 1 to 8.
2. [redacted]

### 4.5.5 EXIT VISIT

The study exit form will be completed when a participant exits the study. This form will be completed either at study completion, or if the participant is discontinued from the study at another time. A study exit form must be completed for all participants who have taken a study ID number. If in the opinion of the investigator post-study follow-up visits are required, the exit form will be completed after the last follow-up visit.

[redacted].

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

## 5 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 CORE. Deviations from the study plan as described in the protocol will be reported in the study report. As described in Section 13.4.3, major protocol deviations will be reported to the Sponsor and the University of Waterloo's Office of Research Ethics (ORE) within 7 days of becoming aware of them (as per ORE's guidelines).

## 6 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

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

Contact lenses in this study will be worn according to their approved use ie. worn daily on a monthly replacement schedule, and participants will be asked to wear them for a minimum of 6 days a week, 8 hours a day. Adverse events and/ or complications in daily 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. Participants in this study will be instructed to remove and clean the lenses at the end of each day, using the products and lens case provided.

Additionally, it is possible that participants may experience temporary discomfort associated with the study procedures and contact lens wear including: burning and stinging, blurred vision, sandiness or grittiness, light sensitivity, dryness, itching, crusty eyes and foreign body sensation.

Parts or all of this study will be conducted during the COVID-19 pandemic. Therefore, risks of infection with COVID-19 exist through participation. 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, 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. 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

See CORE SOP012 AE Reporting for a description of the reporting of adverse events, including management and reporting. An ‘adverse event’ refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not. Adverse events (AE) may be classified as ‘unanticipated adverse device effects’, ‘serious adverse events’, ‘significant adverse

events', or 'non-significant adverse events' as defined below in Table 5: Classification of types of adverse event.

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 5: Classification of types of adverse event

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

AE classification, coding (for reporting to the sponsor) and reporting details, plus examples, are provided in Table 6.

Table 6: 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:<br><br>Notify sponsor as soon as possible, **within 24 hours;**<br><br>ORE reporting will be **within 24 hours** as per requirements |
| 02 | Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA) | |
| 03 | Corneal injury that results in permanent opacification within central cornea (6mm) | |
| 04 | Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B) | |
| 05 | Endophthalmitis | |
| 06 | Hyphema | |

| | | |
|---|---|---|
| 07 | Hypopyon | |
| 08 | Neovascularization within the central 6mm of cornea | |
| 00 | Other serious event | |
| Significant Adverse Events | | |
| 11 | Peripheral (outside central 6mm), non-progressive, non-infectious ulcer | Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements |
| 12 | Symptomatic corneal infiltrative event | |
| 13 | Superior epithelial arcuate lesions (SEALs) involving epithelial split | |
| 14 | Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3) | |
| 15 | Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline | |
| 16 | Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks | |
| 17 | Any sign and/or symptom for which participant is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks | |
| 10 | Other significant event | |
| Non-significant Adverse Events | | |
| 21 | Conjunctivitis (bacterial, viral or allergic) | Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements |
| 22 | Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline | |
| 23 | Asymptomatic corneal infiltrative events | |
| 24 | Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified) | |
| 20 | Other sign and/or symptom warranting classification as a non-significant adverse event | |

# 8 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 active involvement in the study (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 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, 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 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. The participants will also be provided with a letter of appreciation. This letter provides information on how to seek the study results when the study is completed.

After signing the completion forms, participant remuneration will be provided in the form of a cheque and documentation will be signed to confirm receipt. Remuneration will be calculated at a rate of $20 per visit hour (including the initial screening visit). Full details are given in the information consent letter.

# 10 STATISTICAL ANALYSIS AND DATA MANAGEMENT

## 10.1 STATISTICAL ANALYSIS

Primary comparisons will be between study lenses (e.g. in-office subjective ratings of lens handling collected after 1 month).

All data will be analyzed by CORE at the University of Waterloo. Unmasked data analysis will be conducted using Statistica, SPSS or other appropriate software. Descriptive statistics will be provided on information regarding baseline variables (age, gender, refractive error distribution, etc.).

[redacted]

Table 7 lists the primary outcome variables and anticipated statistical procedures.

**Table 7: Statistical procedures**

| Variable | Analysis | Statistical test |
|---|---|---|
| *Subjective ratings* | Descriptive and other statistics | Mean, Median*, Standard Deviation, Minimum, Maximum, Frequency count |
| | Effect of treatment on outcome variable within subjects (comparison between study days) | Wilcoxon matched pairs test |
| [redacted] | [redacted] | Mean, Median*, Standard Deviation, Minimum, Maximum, Frequency count |
| | | Wilcoxon matched pairs test |

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

All participants who were evaluated will be included in the analysis, unless their removal is agreed by the sponsor due to protocol deviations and/or adverse events. In the event of missing data, individual data points will not extrapolated from the collected data.

## 10.2 DATA MANAGEMENT

Data from this study will be retained by CORE for a minimum of 25 years on a password-protected server. After 25 years, data will be disposed of in accordance with the guidelines laid out by the University of Waterloo. More details regarding storage procedures are provided in CORE SOP014 Clinical data management.

CORE will provide a copy of the anonymized 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 during the transfer.

## 10.3 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.

# 11 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.

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

Study monitoring will be conducted by CORE personnel. 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. All serious adverse events and major protocol deviations will be reviewed by the Principal Investigator.

# 13 STUDY MANAGEMENT

## 13.1 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/

## 13.2 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.

## 13.3 CLINICAL TRIAL REGISTRATION

The sponsor will register this study with clinicaltrials.gov in accordance with section 801 of the Food and Drug Administration (FDA) Act which mandates the registration of certain clinical trials of drugs and medical devices.

## 13.4 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.

### 13.4.1 MAJOR PROTOCOL DEVIATIONS

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

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

- Changes in procedures initiated to eliminate immediate risks/hazards to participants;
- Enrollment of participants outside the protocol inclusion/exclusion criteria whether agreed to or not by the sponsor;
- Medication / device / intervention errors (i.e. incorrect drug or dosage of drug / incorrect contact lens(es) dispensed / incorrect care system dispensed);
- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design;
- Information consent documentation violations: no documentation of informed consent; incorrect version of, or incomplete, informed consent documentation used.

### 13.4.2 MINOR PROTOCOL DEVIATIONS

Protocol deviations caused by or which originate with research participants are considered minor, and normally are not reported to the ORE unless these result in increased risk to the participant(s). The following are examples of protocol deviations that are considered minor and do not require reporting to the ORE:

- Logistical or administrative aspects of the study (e.g., study participant missed appointment, change in appointment date);
- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would not impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

### 13.4.3 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 protocol deviations (major and minor) occurring during the study will be documented, reported to the sponsor and included in the final report.

## 13.5 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.

## 13.6 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.

## 13.7 RETENTION OF STUDY RECORDS AND DATA

Records and data from this study will be retained for a minimum of 25 years. Details regarding storage procedures are given in CORE SOP014 Clinical data management.

## 14 REPORT

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