

# Protocol

## REFITTING FREQUENT REPLACEMENT LENS WEARERS INTO CLARITI 1 DAY AND 1-DAY ACUVUE MOIST DAILY DISPOSABLE SPHERICAL LENSES (BEAGLE2)

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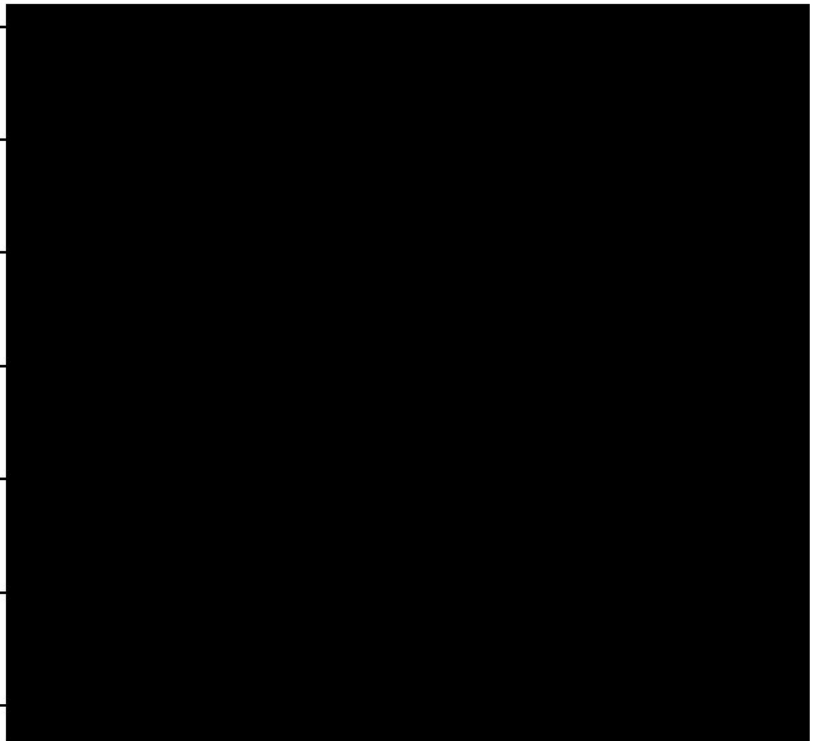
**Clinical Site:** CORE, University of Waterloo

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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 and efficacy in a regulatory submission.

## 1 INTRODUCTION

The 2018 International Contact Lens Prescribing report<sup>1</sup> describes 32% of soft lenses are prescribed on a daily disposable basis worldwide (27% in US), compared with 13% and 51% on a one-to-two week and monthly replacement schedule, respectively (30% and 41% in US). There has been an upward trend in prescribing daily disposables for several years.<sup>2</sup>

This study will evaluate the performance of CooperVision's clariti 1 day spherical lens to Johnson & Johnson Vision Care's 1-Day Acuvue Moist, in a group of participants who habitually wear frequent replacement (FRP) silicone hydrogel contact lenses. The lenses used in this study are both daily disposables widely used by patients.

## 2 OBJECTIVES

The objective of the study is to evaluate and compare the performance of clariti 1 day spherical lens (C1D) to 1-Day Acuvue Moist (1DAM) when worn on a daily disposable wear modality over a period of approximately one week.

The primary outcome variables for this study are:

- Lens handling for lens insertion (subjective rating; 0 - 10 integer scale) for C1D compared to 1DAM, ratings collected at the 1-week visit reflecting on a 'typical day' experience;
- Lens handling for lens removal (subjective rating; 0 - 10 integer scale) for C1D compared to 1DAM, ratings collected at the 1-week visit reflecting on a 'typical day' experience.

The secondary outcome variables are:

- Centration (optimal, slight decentration, moderate decentration but not encroaching limbus, excessive & occasionally encroaching limbus), collected at dispense & 1-week visit;
- Post-blink movement in primary gaze, mm, collected at dispense & 1-week visit;
- Push-up tightness in primary gaze (0-100), collected at dispense & 1-week visit.

The other variables include:

- [REDACTED]
- [REDACTED]
- [REDACTED]



- [REDACTED]
- [REDACTED]
- [REDACTED]
- Home diary for each lens type on Days 1, 3 and 5 to capture:
  - [REDACTED]
  - Comfort just after insertion, 0-10 integer scale;
  - [REDACTED]
  - [REDACTED]
- [REDACTED]

### 3 HYPOTHESIS

The study hypothesis is that the clariti 1 day lens will perform as well or better than the 1-Day Acuvue Moist for the ratings of lens handling for lens insertion and lens removal; each using a 0-10 integer scale, ratings collected at the 1-week visit reflecting on a 'typical day' experience.

### 4 MATERIALS AND METHODS

#### 4.1.1 STUDY DESIGN

#### 4.1.2 OVERALL DESIGN

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The study is a prospective, double masked (investigator and participant), bilateral, randomized cross-over dispensing study, which evaluates clariti 1 day spherical lens (test lens) and 1-Day Acuvue Moist spherical lens (control lens).

Each participant will be randomized to wear either the test or the control lens first. Both lenses will be worn in a daily disposable lens wear modality for one week (-1/+3 days). It is anticipated that this study will involve up to 5 scheduled visits. The study design is shown in Figure 1.

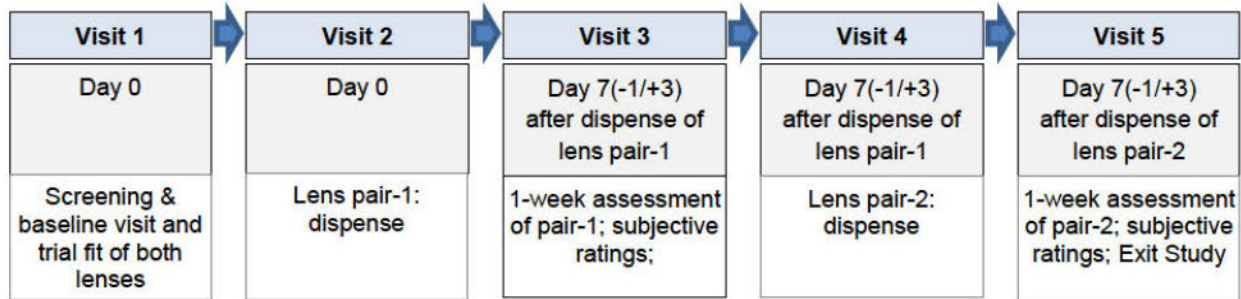


Figure 1: Study Design (visits 1 & 2 may be on a single day, also visits 3 & 4 may be on a single day)

Visit 1: Includes screening, baseline assessments, fitting of both study lenses.

Visit 2: Dispense lens pair #1 (either test or control lens).

Visit 3: 1-week follow-up assessment of lens pair #1

Visit 4: Dispense of lens pair #2 (either test or control lens)

Visit 5: 1-week follow-up assessment of lens pair #2 and study exit.

Participants will complete home subjective ratings on paper using a numeric rating scale (0 – 10). The subjective ratings will be completed on days 1 (i.e. day after visit 2), 3, and 5 for each lens type. These will be returned to the investigator at the next scheduled visit.

On Days 1 and 3, participants will complete the following at-home ratings:

- [REDACTED]
- Ease of insertion (0-10 integer scale);
- Comfort just after insertion (0-10 integer scale);
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

On Day 5, in addition to the at-home ratings of Days 1 and 3 (as above), comfort will also be rated at 4, 8 and 12 hours.

### 4.1.3 RANDOMIZATION

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A randomization schedule will be generated using a web-based program: (for example [www.randomization.com](http://www.randomization.com)) by CORE's Data management team, and provided to the research assistants for the study. Study investigators will remain masked to the randomization schedule until the study is completed and the database has been locked.

### 4.1.4 MASKING

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Participants will be masked to the lens assignment. Lenses dispensed to participants may be either over-labelled or have part of the label obscured, however the safety information shall be clearly visible. 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 [REDACTED] examination. At Visit 5, participants and investigators will be unmasked prior to the participant completing a final subjective rating and exit questionnaire.

## 5 STUDY POPULATION

### 5.1.1 NUMBER OF PARTICIPANTS

---

Participants will be screened using CORE records and advertising approved by the UW Office of Research Ethics. Approximately 40 participants will be dispensed with study products, with a target of 34 completing the study. To ensure an even representation of brands typically prescribed by eye care practitioners and to avoid bias, the target (n) for habitual contact lens brand distribution is as follows:

- Biofinity - target 10
- Air Optix Aqua - target 10
- Acuvue Oasys - target 10
- Acuvue Vita - target 2
- B&L Ultra - target 2
- Any other silicone hydrogel frequent replacement lens - target 6

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.

### 5.1.2 INCLUSION AND EXCLUSION CRITERIA

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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. Habitually wears silicone hydrogel frequent replacement soft contact lenses, for minimum of 6-months;
5. Is correctable to a visual acuity of 20/40 or better (in each eye) with the study lenses;
6. Can be fit with study contact lenses with a power between - 0.50 and -10.00 DS;
7. Demonstrates an acceptable fit with the study lenses;
8. Habitually wears contact lenses for at least 8 hours per day, and willing to wear contact lenses for at least 12 hours a day in the study.

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

1. Is participating in any concurrent clinical or research study;
2. Has any known active\* ocular disease and/or infection;
3. Has a systemic condition that in the opinion of the investigator may affect a study outcome variable;
4. Is using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable;
5. Has known sensitivity to the diagnostic pharmaceuticals to be used in the study;
6. Is pregnant, lactating or planning a pregnancy at the time of enrolment (verbal confirmation at the screening visit);
7. Is aphakic;
8. Has undergone refractive error surgery;
9. Is an employee of the Centre for Ocular Research & Education;
10. Has participated in the BEAGLE (EX-MKTG-104) 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.

### 5.1.3 REPEATED SCREENINGS

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In some circumstances, a repeated screening may need to be scheduled. The maximum total number of screenings permitted will be 3 (i.e. 2 re-screens). 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, 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. 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.).

## 5.2 STUDY MATERIALS

### 5.2.1 LENSES

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Both study lenses are commercially available in Canada. They will be worn bilaterally, and on a daily disposable basis, therefore no lens care solution is required.

Table 1: Details of contact lenses to be used in the study

	<b>Clariti 1-Day - Test (CooperVision, Inc.)</b>	<b>1-Day Acuvue® Moist® - Control (Johnson &amp; Johnson Vision Care, Inc.)</b>
<b>Material</b>	Somofilcon A	Etafilcon A
<b>HC licence #</b>	81009	2519
<b>Dk/t (barrer/cm)</b>	86	25.5
<b>Water content</b>	56%	58%
<b>Sphere power (D)</b>	-0.50 to -6.00 (0.25 steps) -6.50 to -10.00 (0.50 steps)	-0.50 to -6.00 (0.25 steps) -6.00 to -10.00 (0.50 steps)
<b>Base curve (mm)</b>	8.6	8.5
<b>Diameter</b>	14.1	14.2

### 5.2.2 REWETTING DROPS

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Participants who habitually use rewetting drops will be asked to refrain during the study, unless necessary for continued lens wear. Participants will keep track of rewetting drop usage, and this

will be recorded at each visit. Rewetting drops may be used in the event of any clinical observation and/or adverse event noted during the study.

### 5.2.3 ORDERING CONSUMABLES

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Clariti 1 day lenses will be provided by CooperVision. 1-Day Acuvue Moist lenses will be ordered by the site and costs invoiced outside the contract.

### 5.2.4 CONTACT LENS DISPENSING

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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 and aid investigator 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.

### 5.2.5 CONTACT LENS DISPOSAL

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Participants will be instructed to dispose of the worn lenses daily, but retain and return any unworn lenses at their next study visit. Lenses worn for the scheduled follow-up visits will be collected and disposed of immediately after completion of the follow-up visit, according to UW guidelines. Worn lenses associated with adverse events shall be retained at CORE and returned to CooperVision if requested to do so. Typical analysis in these cases relates to inspection for damage and/ or bacterial contamination. Upon completion of the study, all worn and unworn lenses will be destroyed, unless otherwise directed by the study Sponsor.

### 5.2.6 PRODUCT ACCOUNTABILITY

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Accountability logs will be kept to include the number of lenses 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

This study has 5 visits, including:

- **Visit 1:** Screening, baseline assessments, fitting of both study lenses.
- **Visit 2:** Dispense lens type #1 (normally combined with Visit 1)
- **Visit 3:** 1-week follow-up assessment of lens type #1 (6 to 10 days after Visit 2)
- **Visit 4:** Dispense of lens type #2 (normally combined with Visit 3)

- **Visit 5:** 1-week follow-up assessment of lens type #2 and study exit (6 to 10 days after Visit 4).

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

### 5.3.1 STUDY VISITS

The summary of visit codes is shown in Table 2.

Table 2: Summary of visit codes

Visit #	Day/s	Visit code	Visits	Duration (hours)
Visit 1	0	V1 (V1-R1,& V1-R2 for re-screening if required)	Screening, baseline & fit of both study lens	1.5
Visit 2	0	V2	Dispense lens type #1	0.5
Given to participant at Visit 2	Day 1 after V2	V2 -1 home	Subjective at-home ratings	0.5
	Day 3 after V2	V2 -3 home	Subjective at-home ratings	
	Day 5 after V2	V2 -5 home	Subjective at-home ratings	
Visit 3	7 (-1/+3) after V2	V3	1-week follow-up of type #1	0.75
Visit 4	7 (-1/+3) after V2	V4	Dispense lens type #2	0.75
Given to participant at Visit 4	Day 1 after V4	V4 -1 home	Subjective at-home ratings	0.5
	Day 3 after V4	V4 -3 home	Subjective at-home ratings	
	Day 5 after V4	V4 -5 home	Subjective at-home ratings	
Visit 5	7 (-1/+3) after V4	V5	1-week follow-up of type #2	0.75
Exit Visit	any	any	Study exit	0.25

### 5.3.2 SCREENING (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:

1. The participant is expected to attend the screening / baseline visit wearing their habitual contact lenses.
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. [REDACTED]
7. The participant removes their habitual contact lenses.
8. [REDACTED]
9. [REDACTED]
10. [REDACTED]
11. [REDACTED]
  - a. [REDACTED]
  - b. [REDACTED]
  - c. [REDACTED]
  - d. [REDACTED]
  - e. [REDACTED]
  - f. [REDACTED]
  - g. [REDACTED]
12. 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.



13. Trial fitting of both study 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 5.2.4.
- c. The participant will insert the lenses.
- d. [REDACTED]

5.3.3 DISPENSING LENS TYPE #1 (VISIT 2)

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The procedures to be performed are outlined below:

- 1. The participant will be assigned a randomization ID (by the research assistant) and the first pair (lens pair #1) of contact lenses (either test or control lens) will be selected according to the randomization table.
- 2. Lens pair #1 will be provided to participants in a manner which does not unmask the participant or investigator, as described in Section 5.2.4
- 3. The participant will insert the lenses.
- 4. The contact lenses will be allowed to settle for 10 minutes.
- 5. The participant will be asked to give subjective binocular ratings for:
  - a. Subjective comfort at insertion (0 – 10 integer scale);
  - b. [REDACTED]
- 6. [REDACTED]
- 7. Lens surface and fit will be assessed and graded according to the CVI grading scales for the following:
  - a. [REDACTED]
  - c. Lens push-up tightness in primary gaze (0 – 100 scale);

- d. Centration in primary gaze (scale: optimal, slight decentration, moderate decentration but not encroaching limbus, excessive & occasionally encroaching limbus);
  - e. Post-blink movement in primary gaze (mm);
  - f. [REDACTED]
8. Provide and explain to participant subjective at-home rating forms to be completed on Day 1, 3 and 5 after Visit 2 (i.e. Day 1 is the day after the dispensing visit). These forms will be completed just after lens insertion and just before lens removal. Ratings will include:
- a. Time of lens insertion;
  - b. Ease of lens handling for lens insertion (0 – 10 integer scale);
  - c. Comfort just after insertion (0 – 10 integer scale);
  - d. [REDACTED]
  - e. [REDACTED]
  - f. [REDACTED]
  - g. [REDACTED]
  - h. [REDACTED]
  - i. [REDACTED]

Additional information will be collected on Day 5 after V2:

- j. Comfort ratings just after lens insertion, 4, 8, and 12 hours (0 – 10 integer scale).
9. [REDACTED]
10. The participant will be provided with sufficient contact lens supply.
11. The participant will be reminded to return for Visit 3 (1-week follow-up visit of study lens #1) and instructed to return used lens foils plus all leftover unworn lenses.

#### 5.3.4 1-WEEK FOLLOW-UP OF LENS TYPE #1 (VISIT 3)

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Participants will be asked to wear lenses for at least 6 hours prior to the visit appointment. Participants who attend without lenses in-situ (wearing lenses) for at least six hours will be rescheduled (unless they report problems when wearing the lenses).

- 1. The at-home subjective ratings will be collected from participant.
- 2. The participant will be asked to score their subjective responses and rate their experience of a typical day during the past week, as follows on the subjective ratings form:
  - a) [REDACTED]
  - b) [REDACTED]

- c) Typical handling for lens insertion (0-10 scale);
- d) Typical handling for lens removal (0-10scale);
- e) Comfort just after lens insertion (0 – 10 scale);

- f) [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

3. [REDACTED]  
[REDACTED]

4. Lens [REDACTED] fit will then be assessed and graded according to the CVI grading scales for the following:

- a) [REDACTED]
- [REDACTED]
- [REDACTED]
- c) Lens push-up tightness in primary gaze (0 – 100 scale);
- d) Centration in primary gaze (scale: optimal, slight decentration, moderate decentration but not encroaching limbus, excessive & occasionally encroaching limbus);
- e) Post-blink movement in primary gaze (mm);
- f) [REDACTED]

5. The lenses will be removed. Lens disposal procedures are detailed in Section 5.2.5.

6. [REDACTED]  
■ [REDACTED]  
[REDACTED]

5.3.5 DISPENSING LENS TYPE #2 (VISIT 4)

1. The participant will be assigned the second pair (lens pair #2) of contact lenses (either test or control lens), which will be selected according to the randomization table.
2. Lens pair #2 will be provided to participants in a manner, which does not unmask the participant or investigator, as described in Section 5.2.4.

3. The participant will insert the lenses.
4. The contact lenses will be allowed to settle for 10 minutes.
5. The same procedures will be followed as described in Section 5.3.3 DISPENSING LENS PAIR #1 (VISIT 2), points 5 to 10. If this visit is concurrent with Visit 3 there is no need to repeat [REDACTED]
6. The participant will be reminded to return for Visit 5 (1-week follow-up visit of study lens #2) and instructed to return used lens foils plus all leftover unworn lenses.

### 5.3.6 1-WEEK FOLLOW-UP OF LENS TYPE #2 (VISIT 5)

---

Participants will be asked to wear lenses for at least 6 hours prior to the visit appointment. Participants who attend without wearing lenses for at least six hours will be rescheduled (unless they report problems when wearing the lenses).

1. The same procedures will be carried out as described in Section 5.3.4 1-WEEK FOLLOW-UP OF LENS TYPE #1 (VISIT 3), points 1 to 6.
2. [REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
  - [REDACTED]
3. [REDACTED]  
[REDACTED]  
[REDACTED]

- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]

### 5.3.7 STUDY EXIT

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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.

### 5.3.8 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 STUDY PROCEDURES

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

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

	V1 Screen & fit	V2 Disp lens#1	at-home ratings (days 1,3, 5) lens#1	V3 1-week progress lens#1	V4 Disp lens#2	at-home ratings (days 1,3, 5) lens#2	V5 1-week progress lens#2	V-Exit
Consent process	x							
CL history and/or lens wear schedule	x	x		x	x		x	
Health & medication	x	x		x	x		x	
Review any problems with eyes/study lenses				x			x	
██████████ ██████████	█							█ █ █
██████████ ██████████	█							
██████████ ██████████ ██████████	x							
Study lens fitting (both lens types)	x							
Dispense study CLs*		x			x			
██████████ ██████████ ██████████	x	x		x	x		x	
Trial lens fit	x							
Study CL fit assessment ██████████ ██████████	x	x		x	x		x	
██████████ ██████████		x		x	x		x	
██████████ ██████████							x	
Complete 'at-home' subjective ratings			x			x		
Collect 'at home' subjective ratings				x			x	
██████████	x	x**		x	x**		x	x**
Study completion and Exit								x

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

\*\* Not required if visit concurrent with previous one.

†High Contrast High Illumination

## 5.5 [REDACTED]

[REDACTED]

- [REDACTED]
- [REDACTED]
- [REDACTED]
- [REDACTED]  
[REDACTED]
- [REDACTED]  
[REDACTED]  
[REDACTED]

## 6 MONITORING PROTOCOL ADHERENCE

Adherence to study visit windows, lens wearing schedule, and time windows around other data collection points (i.e. subjective ratings) will be monitored internally by CORE. Deviations from the study plan as described in the protocol will be reported in the study report. As described in Section 15.4, 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).

## 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 wear (and daily disposable) basis. Adverse events and/ or complications in daily wear of soft contact lenses can occur (e.g. inflammation and infection). Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include 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 daily-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. Thirty five million Americans who currently wear contact lenses assume this risk.

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.

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

Participants may not benefit directly from taking part in this study. However, participation in a 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.

## 8 ADVERSE EVENTS

See CORE SOP012\_v02 for a description of all adverse events, including management and reporting. An 'adverse event' refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not. Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' as defined below, Table 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, <b>within 24 hours</b> ;  ORE reporting will be <b>within 24 hours</b> as per requirements
02	Permanent loss of $\geq 2$ 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, <b>within 5 working days</b> ; ORE reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining $\geq$ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization $\geq$ 1.0mm vessel penetration (e.g. $\geq$ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of $\geq$ 2 lines BSCVA for $\geq$ 2wks	
17	Any sign and/or symptom for which participant is administered therapeutic treatment or which necessitates discontinuation of lens wear for $\geq$ 2 weeks	
10	Other significant event	
Non-significant Adverse Events		
21	Conjunctivitis (bacterial, viral or allergic)	Notify sponsor as soon as possible, <b>within 5 working days</b> ; ORE reporting as per requirements
22	Papillary conjunctivitis if $\geq$ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	
23	Asymptomatic corneal infiltrative events	
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	

## 8.1 NORMAL OR ADAPTIVE SYMPTOMS

Transient symptoms such as end-of-day dryness, lens awareness, itching or burning or other discomfort may occur with contact lens wear and may occasionally reduce wearing time. These are not reported as adverse events unless in the investigator's opinion they are unexpected in nature, severe or have a high rate of occurrence.

## 8.2 PROCEDURES FOR ADVERSE EVENTS

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the participant may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the test device or a

result of other factors. An adverse event form will be completed for each adverse event. If both eyes are involved, a separate adverse event form will be completed *for each eye*. Whenever possible, the adverse event will be photo-documented.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The participant must be followed until resolution or no further change is anticipated and/or referred for further care with the appropriate health care professional and/or recorded as being under appropriate health care as per investigator's discretion. A written report will be completed indicating the subsequent treatment and resolution of the condition.

### 8.3 REPORTING ADVERSE EVENTS

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to participant's participation will be reported to 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.

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]

[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
	[REDACTED]

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

## 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 will be discontinued at the discretion of the investigator or sponsor in consideration of participant safety or protocol compliance, or at discretion of the participant. 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 5.1.3.
- 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.

## 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 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.

## 12 STATISTICAL ANALYSIS AND DATA MANAGEMENT

### 12.1 SAMPLE SIZE CALCULATION

The sample size was calculated using the lens handling data from the previous pilot study, BEAGLE [REDACTED]. The data from this study (BEAGLE2) will be pooled with data from the pilot [REDACTED] study, therefore anyone who participated in the pilot study will be excluded from participating in the BEAGLE2 study.

In order to detect a mean difference between lens handling for insertion of 0.7 units on the 0 to 10 scale, using a standard deviation of 1.8 with 80% power and alpha 0.05 in a two-tailed t-test, a total sample size of 54 participants is recommended. To account for dropout, 60 participants will be enrolled in total. Given that 20 participants completed [REDACTED] in this study (BEAGLE2, EX-MKTG-112), approximately 40 participants will be dispensed with study products with the target of 34 participants completing the study.

## 12.2 STATISTICAL ANALYSIS

Primary comparisons will be between study lenses, however there are some variables collected over time with the same lens and this time comparison will be analysed (e.g. 'at-home ratings on Days 1, 3 and 5).

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.). Table 6 lists the main outcome variables and anticipated statistical procedures. All data will be tested for normality of distribution using Shapiro-Wilk tests.

Data from 'at-home' ratings Day 5 will be analysed to determine the mean 'cumulative comfort score', as described by Keir et al.<sup>3</sup>

The number of "neither agree or disagree" responses will be evenly distributed to the two options on the basis they would be equally likely to choose either.

Table 6: Statistical analysis to be conducted

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) Effect of time on ratings ( <i>comparison over time</i> )	Friedman Wilcoxon matched pairs test
[REDACTED]	Descriptive statistics	Mean, Median*, Standard Deviation, Minimum, Maximum, Count
	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 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 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. All 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 until they are downloaded by the sponsor.

### 12.4 COMMENTS ON SOURCE DOCUMENTS

Data analysis will not be conducted on comments which have been recorded in the source documents, however all 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.

## 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 any protocol deviations.
- Details of any adverse events.
- 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 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, 2<sup>nd</sup> 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 CLINICAL TRIAL REGISTRATION

This study will be registered with ClinicalTrials.gov by the study sponsor.

### 15.4 PROTOCOL DEVIATIONS

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

#### 15.4.1 MAJOR PROTOCOL DEVIATIONS

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

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

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

#### 15.4.2 MINOR PROTOCOL DEVIATIONS

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

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

#### 15.4.3 REPORTING AND DOCUMENTING PROTOCOL DEVIATIONS

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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.

## 15.5 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.

## 15.6 STUDY PARTICIPANT RECORDS

Study participant records will be completed to comply with GCP guidelines. Records will contain:

- Unique study acronym and/or code;
- Participant ID;
- Date enrolled;
- Confirmation by investigator that participant met eligibility criteria;
- Confirmation that participant received a signed and dated copy of informed consent;
- Exit date;
- Investigator's signature confirming study exit.

## 15.7 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\_v01\_Clinical data management.

## 16 REPORT

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

## 17 REFERENCES

- [REDACTED]
- [REDACTED]
- [REDACTED]