CORE
Centre for Ocular Research & Education

UNIVERSITY OF WATERLOO
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Protocol

COMPARING BIOFINITY TORIC MULTIFOCAL TO ULTRA MULTIFOCAL FOR ASTIGMATISM

(STUDY CODENAME: DINGO)

Sponsor Company:	**CooperVision Inc.**
Sponsor study number:	**EX-MKTG-110**
CORE protocol number:	**P/711/19/CVI**
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Study Personnel

1 DOCUMENT CHANGE HISTORY

Version number	Version date	Author	Description of change(s)
1.0	22dec2019	Jill Woods	Original protocol
1.1	02jan2020	Jill Woods	Changes to Inclusion Criteria, section 5.2.3: changed minimum age to 42 yrs; added minimum refractive astigmatism of -0.75DC. Expanded section 5.4 to provide more detail regarding assessments to be conducted at each study visit. Other minor edits following sponsor review.
1.2	10feb2020	Doerte Luensmann	Administrative changes
1.3	11mar2020	Jill Woods	Added Health Canada DIN for Biofinity Toric Multifocal (Table 1) and clarified objectives and visit windows (Table 3).
1.4	16apr2020	Jill Woods	Several minor corrections to improve consistency and aid clarifications throughout plus, specifically: corrected address for site A.; removed site F who are now unable to participate; updated and clarified Section 5.3.5; corrected procedure for determining ocular dominance, Section 5.4.1.
1.5	19may2020	Jill Woods	Removed the note under Table 1 "* *Study will not commence until the Health Canada license has been assigned to Biofinity Toric Multifocal."* because the HC license has now been approved.
1.6	14sep2020	Doerte Luensmann	Minor text updates throughout to reflect the change that CORE will be the only research site that seeks ethics approval through the Office of Research Ethics (ORE) at the University of Waterloo, for all other sites this study will be reviewed by either the Sterling Institutional Review Board (IRB) or the Health Research Ethics Board of Alberta – Clinical Trials Committee (HREBA-CTC).

1.7	21dec2020	Doerte Luensmann	Two new clinical sites were added (Dr. Foster and Dr. Cymbor) and one clinical site which was never initiated was removed (Dr. Nelson) Other administrative changes

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Confidentiality

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Disclaimer

This study will be conducted for research purposes only.

2 INTRODUCTION

Multifocal contact lenses provide correction for vision at near as well as in the distance. This segment of the contact lens market has been slowly growing as more products become available. In the past year, two monthly replacement, multifocal contact lenses have come to market that also correct the astigmatism component of a prescription.

CooperVision are interested in comparing their contact lens (Biofinity Toric Multifocal) with a competitor lens (Ultra Multifocal for Astigmatism, Bausch & Lomb). Of particular interest is the comparison of handling the lens to insert onto the eye. A previous study sponsored by CooperVision compared the non-multifocal lenses of these lens brand families, and showed that the Biofinity Toric lens was easier to insert than the Ultra for Astigmatism lens. Ease of handling a lens for insertion is arguably more critical in a presbyopic population who require specific prescription for seeing well up close.

3 OBJECTIVES

The objective of the study is to compare the handling and performance of Biofinity Toric Multifocal to Ultra Multifocal for Astigmatism.

The primary outcome variable for this study is:

1. Subjective at-home ratings of 'Lens handling for insertion', using a 0-10 scale, collected on Day 28.

4 HYPOTHESIS

The null hypothesis is that there will be no difference between the subjective at-home ratings of 'Lens handling for insertion', collected on day 28 for each lens type.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

This is a prospective, randomized, participant masked, crossover, bilateral dispensing study conducted at CORE and seven other clinical practice sites in Canada and the USA. Each lens type will be worn for approximately one month. The lens prescription of each lens type will be optimized after 3-7 days before the one month wear period.

5.1.2 RANDOMIZATION

A randomization schedule will be generated using a web-based program: (www.randomization.com). The final study randomization schedule will be generated by CORE's Database Administrator and provided to the research assistants at each site for the study.

5.1.3 MASKING

Participants will be masked to the lens type they are wearing during the study. Foils will not be visible to participants when the lenses are removed from the blister packs and information specifying which lens is being worn will not be shared with the participant.

It is not possible for the study investigators to be masked because of the need to follow the specific lens fitting guide during the lens prescription optimization visit (visits 1-1 and 2-1).

5.2 STUDY POPULATION

5.2.1 SAMPLE SIZE CALCULATION

The sample size was calculated using the end of month subjective ratings for 'lens handling for insertion' from a previous study.

In order to detect a mean difference of 0.7 units on the 0 to 10 scale for the end of month ratings of 'lens handling for insertion', using a standard deviation of 1.7 with 80% power and alpha 0.05 in a two-tailed t-test, a minimum sample size of 49 participants is recommended. To account for dropout, up to 60 participants may be randomized and dispensed with study product in total, with the target of at least 49 completing the study.

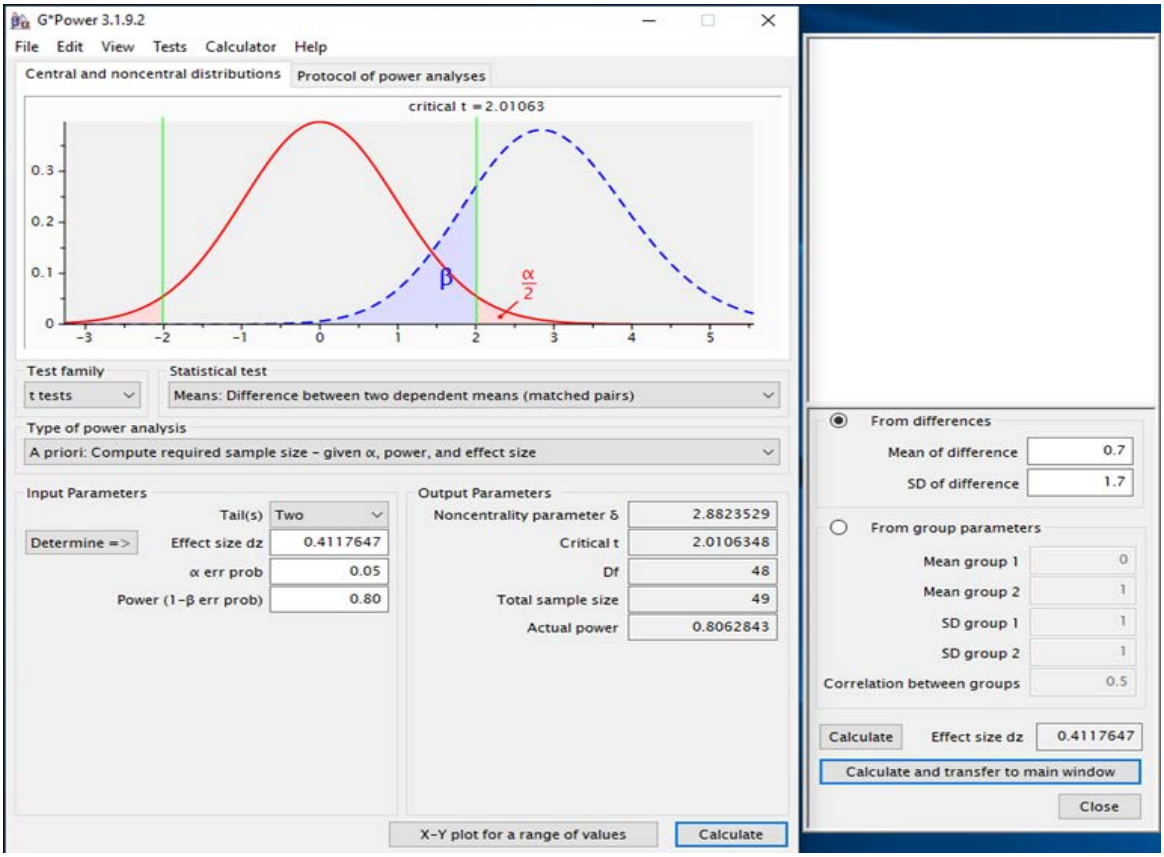

Figure 1: Sample size calculation graph

5.2.2 NUMBER OF PARTICIPANTS

Participants will be recruited using site records, databases and advertising materials (eg. posters, email scripts) approved by the relevant research ethics review board. All initial individual-targeted recruitment activities, such as any direct mailing of recruitment scripts, will be conducted by practice staff that are not directly involved in conducting the research. This separation will reduce any undue influence of the optometrist-patient relationship. This process will also eliminate opportunity for the investigator to access personal health information before any consent for disclosure is provided by the potential participant.

It is anticipated that up to 80 potential participants may attend a Screening visit and up to 60 participants may be randomized and dispensed with study products, with a target of 49 completing the study. Informed consent will be obtained for all participants prior to their enrolment in the study (Appendix 1).

5.2.3 INCLUSION AND EXCLUSION CRITERIA

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

1. Is at least 42 years of age and has full legal capacity to volunteer;
2. Has read and signed an information consent letter;
3. Self reports having a full eye examination in the previous two years;
4. Anticipates being able to wear the study lenses for at least 8 hours a day, 5 days a week;
5. Is willing and able to follow instructions and maintain the appointment schedule;
6. Habitually wears soft contact lens for the past 3 months minimum;
7. Has refractive astigmatism of at least -0.75DC;
8. Is presbyopic and requires a reading addition of at least +0.75D;
9. Can be fit and achieve binocular distance vision of at least 20/30 Snellen (or +0.20 logMAR) which participants also deem to be 'acceptable', with the available study lens parameters (sphere +4 to -6; cylinder -0.75 to -1.75DC; near addition +0.75 to +2.50).

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

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

* For the purposes of this study, active ocular disease is defined as infection or inflammation which requires therapeutic treatment. Mild (i.e. not considered clinically relevant) lid abnormalities (blepharitis, meibomian gland dysfunction, papillae), corneal and conjunctival staining and dry eye are not considered active ocular disease. Neovascularization and corneal scars are the result of previous hypoxia, infection or inflammation and are therefore not active.

Age ≥42 years is an inclusion criteria because presbyopia is unlikely in persons aged <42 years and, if present, may not be due solely to presbyopic changes representative of the wider population.

Pregnant and lactating women are not being excluded from the study due to safety concerns but due to fluctuations in refractive error, accommodation and/ or visual acuity that occur secondary to systemic hormonal changes. It has further been shown that pregnancy could impact tear production, which could impact dry eye symptoms. Such fluctuations could affect data, thereby negatively affecting study data integrity.

5.3 STUDY MATERIALS

CORE's Research Assistants will coordinate with all sites (including CORE) to provide them with the study paperwork and study products, as required. This will include participant informed consent letters and study forms, contact lenses and lens care product.

[redacted]

5.3.1 LENSES

The table below lists the contact lens details and the available lens parameters.

Table 1: Lens characteristics & parameter to be used

Lens	Biofinity Toric Multifocal	Ultra Multifocal for Astigmatism
Manufacturer	CooperVision	Bausch & Lomb
Material	comfilcon A	samfilcon A
HC licence #	70149	101686
Sphere power (D)	+4.00 to -6.00 (0.25 steps)	+4.00 to -6.00 (0.25 steps)
Cylinder power (DC)	-0.75, -1.25, -1.75	-0.75, -1.25, -1.75
Axis (degrees)	5 to 180 (5 steps)	10 to 180 (10 steps)
ADD power (D)	+1.00, +1.50, +2.00, +2.50	Low (+0.75 to +1.50), High (+1.75 to +2.50)
Base curve (mm)	8.7	8.6
Diameter (mm)	14.5	14.5

5.3.2 LENS CARE SYSTEM

The lens care system to be used by all participants is OptiFree PureMoist. Participants will be provided the package insert as an instruction guide for the (rub and rinse) care and storage of their study contact lenses.

Table 2: Lens care system

	OptiFree PureMoist
Manufacturer	Alcon
Health Canada, DIN	02420619

5.3.3 OTHER PRODUCTS

Sodium fluorescein will be used to assess corneal and conjunctival staining.

5.3.4 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.

5.3.5 ORDERING STUDY PRODUCTS

Study lenses: CORE will provide sites with a small trial fitting sets for Biofinity Toric Multifocal and for Ultra Multifocal for Astigmatism. Lenses from these sets will be used at the screening visit to determine overall lens centration acceptability and axis orientation. Based on these initial trials, sites will provide CORE with their lens needs for the lens fitting visit and lens dispense using the study specific product ordering form (CRF 1). CORE will order these lenses directly from CooperVision or Bausch & Lomb and then distribute these to the sites.

OptiFree PureMoist: CORE will order this lens care product directly and ship to the other sites.

CORE will reconcile and invoice the cost of all study products and shipping to CooperVision at the end of the study.

Reimbursement to practice sites for any study product expenses directly will be provided by CooperVision at the end of the study, after CORE has reconciled the invoices and the product accountability and dispensing logs.

5.3.6 DISPOSING OF STUDY PRODUCTS

At the end of the study, all sites will return all unused products to CORE, unless otherwise directed. Worn lenses will be disposed of at the sites according to local regulations.

5.3.7 PRODUCT ACCOUNTABILITY

Accountability logs must be kept by each site to include the number of contact lenses and lens care system bottles received, dispensed and returned. (where relevant). All products dispensed to participants must also be recorded in participant dispensing logs. All logs should be sent to CORE on request.

5.4 SCHEDULED AND UNSCHEDULED VISITS

This study has a minimum of 9 scheduled study visits, including the screening visit, though some visits may be scheduled concurrently on the same day. There is an option for repeated screening and lens fitting visits as needed.

A scheduled follow-up visit may only take place when the participant attends wearing the study lenses for at least two hours. If this is not the case and the participant is not experiencing any problems with the lenses, the appointment will be rescheduled, ideally within the visit window.

Visits that fall outside of the specified visit windows will be designated as protocol deviations and at the end of the study, the data collected during protocol deviations will be assessed for their suitability to be included in the analysis population. Table 3 summarizes the scheduled study visits and study codes.

Table 3: Summary of visits

Visit code	Approximate Duration	Visits
0	1.5 hr	Screening & option for fitting both
0/R1, 0/R2	As needed	Repeat Screening if needed
0-1	1.5 hr	Fitting of both lens types
0-1/R1 , 0-1/R2 . 0-1/R3	As needed	Repeat Fitting if needed
Phase 1		
1-0	0.5 hr	Dispense Pair #1 (day 0)
1-1, 1-1/R1, 1-1/R2	0.5 hr	Optimize Pair #1 & dispense new Pair #1 (day 3-7 from V1-0)
1-2	1.0 hr	1 month follow-up (day 29-31 from V1-1)
Phase 2		
2-0	0.5 hr	Dispense Pair #2 (day 0)
2-1, 2-1/R1, 2-1/R2	0.5 hr	Optimize Pair #2 & dispense new Pair #2 (day 3-7 from V2-0)
2-2	0.75 hr	1 month follow-up (day 29-31 from V2-1)
EXIT	0.25 hr	Exit VA, exit forms & remuneration

Participants will complete subjective ratings 'at-home' on days 7, 14 and 28 following visits 1-1 and 2-1; anticipated to take a total of 30 minutes per phase. These ratings will be returned and reviewed at visits 1-2 and 2-2 respectively.

5.4.1 VISIT 0, SCREENING VISIT

Participants will be assigned a unique alpha-numeric study ID after they sign the consent documentation process i.e. before their eligibility for the study has been confirmed. Each site will use a different letter preceding the participant ID number. For example, participant 01 at site A will be A01, and participant 01 at site B will be B01. Ineligible participants will be discontinued from the study.

The investigator will determine participant eligibility using the inclusion and exclusion criteria. The study procedures are outlined below:

1. The participant is expected to attend 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 and will be assigned a study ID.
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.
7. [redacted]

[redacted]

9. [redacted]
10. [redacted]

11. 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.
12. From both fitting sets, the investigator will chose lenses that are close to the required prescription to determine the axis rotation of the lenses on each eye. The investigator will complete their lens order sheet after giving consideration to the axis rotation of this initial fitting lens.
13. Schedule Visit 0-1 in approximately 4-6 weeks time or schedule once lenses are available on site.

5.4.2 REPEATED SCREENING VISITS

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.)

The maximum total number of screenings permitted will be 3, the initial and two repeat screening visits.

5.4.3 VISIT 0-1, LENS FITTING

This visit may or may not be subsequent to the screening visit, depending on lens availability.

Participant to attend this visit wearing spectacles.

Procedures as follows:

1. Confirm participant's health and medications are unchanged.
2. [redacted]

3. Trial fitting of 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 5.1.3.
    c. The participant will insert the lenses.
    d. [redacted]
    e. [redacted]
    f. The final lens power to be dispensed will be recorded.
    g. [redacted]
    h. If lens prescriptions of both lens types are final today, place lenses in OptiFree PureMoist solution and continue with the dispense visit 1-0.
    i. If more lenses need to be ordered to complete the lens fitting process then complete a lens ordering form. Schedule a repeat visit in approximately 2-3 weeks time or wait until lenses arrive on site.

5.4.4 REPEATED LENS FITTING VISITS

Because it is not possible to provide each site with a complete fitting set of all available power combinations, multiple lens power combinations will be ordered to maximize the likelihood of a successful lens fit at visit 0-1. However if this initial lens fitting is unsuccessful and further lens powers are required, they will be ordered and a repeated visit, visit V0-1/R1, will be scheduled. There is no limit to the number of repeated visits allowed within the protocol. They will be numbered successively eg. V0-1/R1, then V0-1/R2, then V0-1/R3 etc.

5.4.5 VISIT 1-0, LENS DISPENSING PAIR #1

The procedures to be performed are outlined below:

1. Confirm participant's health and medications are unchanged.
2. [redacted]
3. [redacted]
7. [redacted]
9. Remind the participant to wear the study lenses for at least 8 hours per day and 5 days per week.
10. Provide the participant with OptiFree PureMoist and provided verbal and written instructions on how to store and care for the contact lenses.
11. The participant will be scheduled/reminded to return for Visit 1-1 to optimize the lens prescription, having worn their study contact lenses for at least 2-hours.

5.4.6 VISIT 1-1, LENS POWER OPTIMIZATION PAIR #1

This visit will occur 3-7 days after the lenses were dispensed at visit 1-0. Participants will be asked to insert lenses at least 2 hours prior to the visit.

The contact lens power optimization procedures to be performed are outlined below:

1. Confirm participant's health and medications are unchanged.
2. [redacted]
3. [redacted]
4. [redacted]
6. [redacted]
11. If final lenses were determined today and are available for dispense, provide and explain to participant the subjective at-home rating forms to be completed on Days 7, 14 and 28 (Note: Day 1 is the day after the dispensing visit). Fill in the days and dates on these forms. Explain the ratings will include:
    a. [redacted]
    c. Ease of lens handling for insertion onto eyes (0 – 10 integer scale);
    d. [redacted]

f. [redacted]

12. The participant will be scheduled/reminded to return for Visit 1-2 having worn their study contact lenses for at least 2-hours.

NOTE: If any power changes are required and the new power lenses are not available on site to assess, complete a lens order form (on CRF 5). When the lenses arrive on site, schedule an additional optimization visit to assess and dispense the new lens powers ordered. If new lenses need to be ordered, participants should wear their habitual lenses in the mean time and attend the nest optimization visit wearing spectacles.

5.4.7 VISIT 1-2, 1 MONTH FOLLOW-UP PAIR #1

This visit will occur on day 29-31 (inclusive) after the pair #1 lenses have been dispensed, following visit 1-1.

1. Confirm participant's health and medications are unchanged.
2. [redacted]
3. [redacted]
4. [redacted]
5. [redacted]

b. [redacted]

5.4.8 VISIT 2-0, LENS DISPENSING PAIR #2

Repeat steps 2-11 as listed for visit 1-0.

5.4.9 VISIT 2-1, LENS POWER OPTIMIZATION PAIR #2

This visit will occur 3-7 days after the lenses were dispensed at visit 2-0. Repeat steps 1-12 as listed for visit 1-1.

5.4.10 VISIT 2-2, 1 MONTH FOLLOW-UP PAIR #2

This visit will occur on day 29-31 (inclusive) after the pair #2 lenses have been dispensed following visit 2-1.

Repeat steps 1-9 as listed for visit 1-2.

Participants will also complete preference questionnaires to compare the two study lens pairs.

5.4.11 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.

5.4.12 UNSCHEDULED VISITS

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

5.5 STUDY PROCEDURES

Table 4 summarizes the procedures conducted at each visit.

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

	V0 Screen & Fit	V0-1 Fitting	V1-0 Dispense lens#1	V1-1 Optimize lens#1 powers & Dispense	V1-2 1-month progress lens#1	V2-0 Dispense lens#2	V2-1 Optimize lens#2 powers & Dispense	V2-2 1-month progress lens#2	V-Exit
Day #			0		29-31		0	29-31	
Consent process	x								
Participant age & sex	x								
CL history and/or lens wear schedule	x			x	x		x	x	
Health & medication	x	x	x	x	x	x	x	x	
Review any problems with eyes/study lenses		x	x	x	x	x	x	x	
[redacted]	x								X (or with ref'n)

	V0 Screen & Fit	V0-1 Fitting	V1-0 Dispense lens#1	V1-1 Optimize lens#1 powers & Dispense	V1-2 1-month progress lens#1	V2-0 Dispense lens#2	V2-1 Optimize lens#2 powers & Dispense	V2-2 1-month progress lens#2	V-Exit
Day #			0		29-31		0	29-31	
[redacted]	x								
[redacted]	x								
[redacted]	x								
[redacted]	x	x							
[redacted]				x			x		
Dispense study CLs*			x	x		x	x		
[redacted]		x	x	x	x	x	x	x	
[redacted]	x	x	x	x	x	x	x	x	
[redacted]					x			x	
[redacted]								x	
Issue 'at-home' subjective ratings				x			x		
[redacted]					[redacted]			[redacted]	
[redacted]	x	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.

[1] High Contrast High Illumination

5.5.1 STUDY LENS FITTING

Both lens types will be fit according to the manufacturers fitting guide, using the vertex-corrected spectacle refraction as a guide. Learnings from the first lens fit will not be applied to the second lens fit because it is of interest to determine how many lenses were needed to achieve the final lens prescription at V0-1 and at each optimization visit (V1-1 and V2-1).

For both lens types, the multifocal contact lenses may need to be ordered to conduct and complete the trial fitting. Lenses will be ordered through CORE, see section 5.3 for details. If necessary, the same brand of 'non-multifocal' toric lens (ie. Biofinity Toric or Ultra for Astigmatism) may be used to determine the orientation and possibly the sphere and cylinder powers required for the respective brand of multifocal contact lens. These toric lenses will not be recorded in lens accountability logs but their prescription, expiry date and Lot# details will be recorded on the study data collection forms.

This protocol allows for an unrestricted number of lens fitting visits and they will be numbered as follows:

- V0-1 (first fitting visit)
- V0-1/R1 (first repeated fitting visit)
- V0-1/R2 (second repeated fitting visit)
- V0-1/R3 (third repeated fitting visit)
- Etc.

No lenses will be dispensed until the final prescriptions for each lenses have been determined during a fitting visit.

[redacted]

2. [redacted]

6 MONITORING PROTOCOL ADHERENCE

Adherence to study visit windows, lens wearing schedule, and time windows around other data collection points (i.e. subjective ratings) will be monitored by CORE. Deviations from the study plan as described in the protocol will be reported in the study report. As described in Section 15.4.3, major protocol deviations will be reported to the Sponsor and the relevant research ethics review board within 7 days of the Principal Investigator becoming aware of them (or as per research ethics review board 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.

The two contact lens types in this study will be worn as per their approved use; on a daily wear basis, for up to 1 month each. Adverse events and/ or complications in daily wear of soft contact lenses can occur (eg: inflammation and infection). Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include 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.

A dye (fluorescein) normally used for eye examinations is being used in this study. Although rare, it is possible to have an allergic reaction to the dye. Participants will be asked if they have a known allergy or sensitivity to fluorescein.

Participants will be provided with OptiFree PureMoist to care for the study contact lenses. Participants will be asked if they have a known allergy or sensitivity to this product.

Participants may not benefit directly from taking part in this study. Information from this study may help practitioners understand more about the performance of the products used in this study. 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 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 5.

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: Notify sponsor as soon as possible, **within 24 hours;** IRB reporting will be **within 24 hours** or 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**; IRB 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**; IRB reporting as per requirements
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	
23	Asymptomatic corneal infiltrative events	
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	

20	Other sign and/or symptom warranting classification as a non-significant adverse event	

8.1 NORMAL OR ADAPTIVE SYMPTOMS

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

8.2 PROCEDURES FOR ADVERSE EVENTS

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the participant may be 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 site Principal Investigator and CORE's contact below within 24 hours of becoming aware of the event. Reporting to the IRB will be completed by the respective site Principal Investigator, overseen by CORE's contact, within 24 hours, via the IRB specified method (by fax, mail/ delivery, phone or email, unless otherwise specified by the IRB. CORE's contact will inform the sponsor immediately upon becoming aware of the event, at least within 24 hours. All fatal or life threatening events will be reported immediately to the IRB.

CORE sub-investigators and all sites will report all other Adverse Events to CORE's contact below who will report them to the sponsor as soon as possible, but no later than 5 working days after the

occurrence. CORE will ensure all adverse events are reported to all IRBs involved in this study approval, as per IRB requirements (by fax, mail/delivery, phone, or email).

[redacted]

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

9 DISCONTINUATION FROM THE STUDY

Participants may be discontinued at the discretion of the investigator or sponsor in consideration of participant safety or protocol compliance, or at discretion of the participant. Participants discontinued from a study will be reimbursed for their active involvement in the study (including the initial screening visit and all lens fitting visits). Upon discontinuing, a participant will be offered the option of their data being withdrawn from future statistical analysis. The following is a list of possible reasons for discontinuation from the study:

- Screening failure: Participants will be discontinued if they do not meet the inclusion and exclusion criteria outlined in section 5.2.3.
- Unacceptable performance with products to be used in study: Participants may be discontinued if they are unable to achieve acceptable comfort and /or vision with the study products.
- Positive slit lamp finding: Participants may be permanently discontinued from the study depending on the severity of the condition and on the judgement of the investigator.

- Adverse event: If a participant experiences an adverse event during the study they may be discontinued based on the clinical judgement of the investigator.
- Symptoms: If the participant has persistent symptoms they may be discontinued based on the clinical judgement of the investigator.
- Disinterest, relocation or illness: The participant may choose to discontinue due to reasons within or beyond their control.
- Violation of protocol or non-compliance: The participant will be discontinued if they are unable or unwilling to follow the protocol specified visit schedules and/or study procedures.
- Instillation of topical ocular medication: The participant will be discontinued if they elect to use a topical ocular medication during the study unless that topical ocular medication is prescribed for a limited duration (less than two weeks) to treat a transient condition; in this case the participant may remain an active participant (at the discretion of the investigator) after stopping topical ocular medication following resolution of the ocular condition).
- Lost to follow-up: The participant will be discontinued if they cannot be contacted and do not return for a final exit visit, and if the investigator has made a reasonable effort to contact the participant for a final study visit.
- Premature termination of the study by the sponsor, CORE or a research ethics review board.

A discontinuation form, stating the reason for discontinuation will be completed, which requires the signatures of both the participant and the investigator except where the participant is lost to follow-up in which case only the signature of the investigator is required.

When a participant choses to discontinue from the study they will be given the opportunity to withdraw their data from the statistical analysis. This choice will be captured on the discontinuation form.

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

10 DEVICE MALFUNCTIONS

A device malfunction means the failure of the device to meet its performance specification or otherwise perform as intended. Any defective lens that is *likely* to cause or contribute to a *Serious*

Adverse Event should be reported to CORE and the sponsor **within 24 hours** of the investigator becoming aware of the malfunction. The research ethics review board would also be notified within 24 hours of any device malfunction that may contribute to a *Serious Adverse Event.*

Other defective lenses should be reported to CORE as soon as possible (usually in weekly study updates).

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as complaints or device malfunctions.

11 STUDY COMPLETION AND REMUNERATION

At the last scheduled protocol visit a study completion form will be completed, which requires the signatures of both the participant and the investigator. Participants will also be provided with a letter of appreciation.

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

Participant remuneration will be provided at the end of their study involvement.

12 STATISTICAL ANALYSIS AND DATA MANAGEMENT

12.1 STATISTICAL ANALYSIS

All data will be analyzed by CORE at the University of Waterloo. Unmasked data analysis will be conducted using Statistica 10, Statsoft or other suitable software. Descriptive statistics will be provided on demographic data (age, gender, refractive error distribution, etc.). Table 7 lists the primary and other outcome variables and anticipated statistical procedures.

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

Comparisons will be made between the study lenses for the variables measured at the 1 month visits. Additionally the subjective ratings completed on days 7, 14 and 28 of each phase will be compared. A binomial test will be used to analyze the results for the count data of subjective preferences and experience responses. Where relevant, the number of “neither agree or disagree” responses will be evenly distributed to the two options on the basis they would be equally likely to choose either.

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

Where appropriate, such as for lens orientation, data may be presented as both mean and as counts by 'bucket' groups.

Table 7: Statistical procedures

Variable	Analysis	Statistical test
Ratings: Likert & Preference	Comparison between study days and/or between contact lenses per time point.	Freidman ANOVA Wilcoxon matched pairs test
Ratings: numerical ratings *Biomicroscopy*	Comparison between study days and/or between contact lenses per time point.	Freidman ANOVA Wilcoxon matched pairs test RMANOVA
Demographics *Lens fit variables*	Descriptive stats	One or more: mean, median*, mode, standard deviation, minimum, maximum, frequency count

* For non-parametric data only

12.2 DATA MANAGEMENT

Data will be collected and written on paper forms which will be provided to each site by CORE. Each external site will email scanned forms to a designated person at CORE who will file the forms into pre-assigned binders and pass these binders to the data entry team. Data will be entered into a REDCap database developed and tested specifically for this study and accessible only to trained, authorised users. A data management plan will be developed to describe the data handling in more detail, including the personnel involved.

Data from this study will be retained by CORE for a minimum of 25 years on a password-protected server. After 25 years, data will be disposed of in accordance with the guidelines laid out by the University of Waterloo. More details regarding storage procedures are provided in section 15.7 and also in CORE SOP014 Clinical data management.

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

12.3 COMMENTS ON SOURCE DOCUMENTS

Data analysis will not be conducted on comments which have been recorded in the source documents. Only relevant and applicable comments will be included in the final report as deemed necessary by CORE's Lead Investigator.

13 PROTOCOL & OTHER TRAINING

All study personnel will be required to complete training prior to their involvement in the study. Records of training will be kept at CORE. This will include training by CORE on the study protocol, study procedures, informed consent procedures, and on the randomization and participant masking procedures, as well as training for Good Clinical Practice.

All site Principal Investigators and co-investigators will provide a scan of their license to practice optometry and evidence of professional indemnity insurance.

14 STUDY MONITORING

Each site will provide regular status reports to CORE. Status reports will include:

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

CORE will collate the site updates and provide 2-weekly status reports to the study sponsor.

Study monitoring visits may be conducted by the sponsor, or sponsor's designate, throughout the study and will be scheduled in conjunction with the Principal Investigator at each site. In addition study records may be inspected by the sponsor, the sponsor's designate, the relevant research ethics review board, and by regulatory authorities in Canada and the United States, namely Health Canada and the United States Food and Drug Administration (FDA); however, they will not be permitted to take away any records containing identifiable personal information.

Study data review and data monitoring will be conducted by CORE personnel. To improve data integrity, data entry will be conducted by two people and the entries will be compared. Data

queries will be reported to the site within 5 working days of receipt of initial data. A response resolving the query will be expected from the site within 5 working days of receipt of the query.

All adverse events and protocol deviations will be reviewed by the site Principal Investigator and CORE. All serious adverse events and major protocol deviations will be reviewed by the site Principal Investigator and CORE's Head of Clinical Research and/ or CORE's Principal Investigator.

15 STUDY MANAGEMENT

15.1 STATEMENT OF COMPLIANCE

This clinical study is designed to be in compliance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for Good Clinical Practice (GCP), with the University of Waterloo's Guidelines for Research with Human Participants and with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, 2nd Edition.

- Declaration of Helsinki
- ICH E6 - International Conference on Harmonisation; Good Clinical Practice
- http://iris.uwaterloo.ca/ethics/human/guidelines/index.htm
- http://iris.uwaterloo.ca/ethics/human/ethicsReview/UWStatement.htm
- http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

15.2 ETHICS REVIEW

This protocol will be submitted to and reviewed through the Office of Research Ethics (ORE) at the University of Waterloo for study site H (CORE), the Health Research Ethics Board of Alberta – Clinical Trials Committee (HREBA-CTC) for study site G and the Sterling Institutional Review Board (IRB) for all other clinical study sites. Notification of ethics clearance of the application is required prior to the commencement of the study the respective provinces and sites.

15.3 CLINICAL TRIAL REGISTRATION

CooperVision will register this study with clinicaltrials.gov and maintain the information.

15.4 PROTOCOL DEVIATIONS

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

15.4.1 MAJOR PROTOCOL DEVIATIONS

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

The following are examples of major protocol deviations that require reporting to research ethics review boards::

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

15.4.2 MINOR PROTOCOL DEVIATIONS

Protocol deviations caused by or which originate with research participants are considered minor, and normally are not reported to the research ethics review board 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 research ethics review board::

- 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

Protocol deviations must be reported to the site Principal Investigator and CORE's contact below. CORE will inform the sponsor within 7 days of any major protocol deviations that occurred during the study. Major protocol deviations must be reported by the site Principal

Investigator, overseen by CORE's contact, to the research ethics review board via the IRB specified method (by fax, mail/ delivery, phone or email) within 7 days of the deviation occurring (or its discovery) unless otherwise specified by the IRB.

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

[redacted]

15.5 PREMATURE TERMINATION OF THE STUDY

The sponsor, CORE or the relevant research ethics review board may terminate the study at any time for any reason.

15.6 STUDY PARTICIPANT RECORDS

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

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

An enrolment log will be maintained which will list all participants who attended for a screening visit.

15.7 RETENTION OF STUDY RECORDS AND DATA

When the study has been completed, all sites will send the original study product accountability and dispensing logs, and the original consent documentation and enrolment logs to CORE. Each site should retain the original study data collection forms documentation for one year following the close of the database in case data queries arise during the analysis and report writing stages. CORE may request that these originals be sent to them for storage.

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

16 REPORT

A report will be sent to the sponsor by CORE according to terms described in the study contract.