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Protocol

PERFORMANCE OF CLARITI 1 DAY OVER ONE WEEK IN WEARERS ADAPTED TO PROCLEAR 1 DAY (OBOE)

Sponsor: CooperVision, Inc.
6150 Stoneridge Mall Road,
Suite 370, Pleasanton, CA 94588 USA

Sponsor study number: EX-MKTG-84
CCLR protocol number: P/597/17/CVI

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Study Personnel

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DOCUMENT CHANGE HISTORY

version #	Originator	Description of change(s)	Date
1.0	[redacted]	Original protocol	08 June 2017
1.1	[redacted]	Minor edits following review	15 June 2017
1.2	[redacted]	Minor edits following review by Office of Research Ethics: • Section 4.2.3 – “study measures” instead of “study outcome variables” • Added Health Canada license number for Proclear 1 Day • Addition of Appendix 29, Unscheduled visit form	04 July 2017

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Confidentiality

This is a private document and the property of the Centre for Contact Lens Research. It is therefore confidential to the recipient and must not be quoted from or distributed beyond the company to which it is sent without the express written permission of the Director (or her/his designate) of the Centre for Contact Lens Research. Release of information from this document is governed by the research agreement on file.

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

CooperVision's Proclear material (omafilcon A) has been longstanding, successful hydrogel lens material available in a daily disposable modality. The popularity of silicone hydrogels materials in a daily disposable modality has increased over time, offering superior oxygen delivery to the eye and the convenience of single-use lenses. One recent publication has found no clinically significant physiological differences in five retrospective studies where patients were refit from a range of hydrogel lenses to silicone hydrogel lenses.[1]

This aim of this study is to determine if habitual or adapted contact lens wearers of Proclear 1 Day (omafilcon A) can be confidently refit into Clariti 1 Day (somofilcon A) lenses and be successful after one week of daily wear. The primary target population for this study will ideally be habitual wearers of Proclear 1 Day. However, as a secondary target population, habitual wearers of other lens types will be recruited and will be adapted to Proclear 1 Day lenses for at least 7 days before being refit into Clariti 1 Day.

2 OBJECTIVES

The objective of the study is to determine if habitual or adapted contact lens wearers of Proclear 1 Day can be confidently refit into Clariti 1 Day (somofilcon A) lenses and be successful after one week of daily wear.

The primary outcome variables for this study are:

- Investigator responses to refit questions;
- Lens fit.

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3 HYPOTHESIS

The null hypothesis for this study is that there is no difference in lens fit performance between Proclear 1 Day (omafilcon A) and Clariti 1 Day (somofilcon A) lenses.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

4.1.1 OVERALL DESIGN

This is a prospective, single-site, dispensing, bilateral wear, open label, daily wear switch study, with the test lens (Clariti 1 Day) being worn for 7 (+5) days.

Participants will attend a screening visit (Visit 1), at which consent will be obtained and eligibility to participate will be confirmed. The number of visits is dependent the participant's habitual lens type (i.e. whether it is Proclear 1 Day, or another lens type) and whether the power of the habitual lens needs to be changed. All subjects will be fit with Clariti 1 Day at the screening visit to ensure they can successfully wear the product.

Habitual wearers of Proclear 1 Day lenses will be reviewed at Visit 1 to ensure optimal visual acuity is being achieved. If the visual acuity and power of the habitual Proclear 1 Day lens is optimal, participants will be fit with Clariti 1 Day and asked to return for evaluation after 7 days of lens wear.

If an amendment of the power of the habitual Proclear 1 Day is required, participants will be dispensed with the new power of the Proclear 1 Day lenses to be worn for at least 7 days. Participants will return after wearing the Proclear 1 Day lenses to collect baseline variables. The participant will then be dispensed with Clariti 1 Day and asked to return for evaluation after 7 days of lens wear.

In the instance where the participant habitually wears lenses which are not Proclear 1 Day, the participant will be fit and dispensed Proclear 1 Day lenses to be worn for at least 7 days. After experiencing Proclear 1 Day lenses for at least 7 days, the participant will return for baseline variables to be evaluated and will be then be dispensed with Clariti 1 Day. The participant will be asked to return for evaluation after 7 days of lens wear. Participants will exit the study following the final evaluation of Clariti 1 Day.

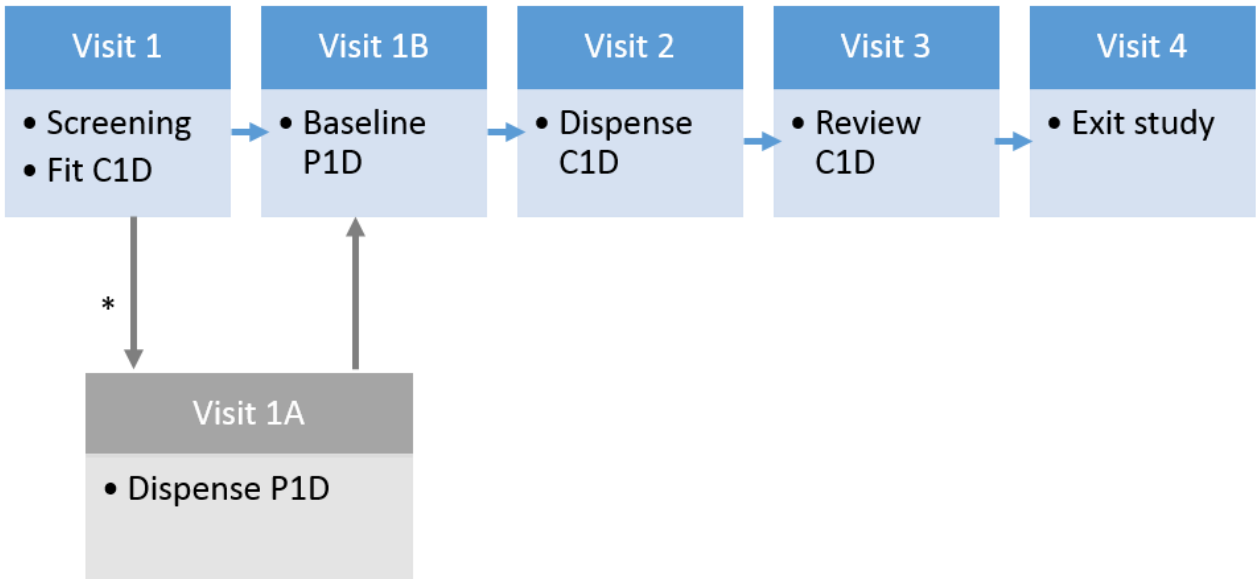

Figure 1 Study flow chart (C1D = Clariti 1 Day; P1D = Proclear 1D). * Visit 1A applicable only if habitual Proclear 1 Day wearers require a change in lens power OR if participant is a habitual lens wearer of other types (see Section 4.4 for further details)

4.1.2 RANDOMIZATION

There is no randomization in this study. All participants will be habitual (or adapted) Proclear 1 Day lens wearers that will be switched into Clariti 1 Day lenses.

4.1.3 MASKING

Due to the design of the study, there is no masking of participants or investigators.

4.2 STUDY POPULATION

4.2.1 SAMPLE SIZE CALCULATION

A sample size calculation was provided by CooperVision based on the combined data for comfort scores in the BEETHOVEN 2 study (CooperVision EX-MKTG-61, data on file). For an alpha level of 0.05 and power of 0.8, a sample size of 67 participants will detect a difference of 7 units on a 0-100 scale. Seven units is accepted as a minimum meaningful difference in comfort between lenses for this scale range.[2]

4.2.2 NUMBER OF PARTICIPANTS

Participants will be recruited using CCLR records and advertising approved by the UW Office of Research Ethics (Appendices 25, 26, 27). Up to 75 participants will be dispensed with study

products, with a target of 67 completing the study. Informed consent will be obtained for all participants prior to their enrolment in the study (Appendix 1).

4.2.3 INCLUSION AND EXCLUSION CRITERIA

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

1. Is at least 17 years of age and has full legal capacity to volunteer;
2. Has read and signed an information consent letter;
3. Is willing and able to follow instructions and maintain the appointment schedule;
4. Habitually wears soft spherical contact lenses with a power between +6.00 to -10.00D (inclusive) for a minimum 5 days per week, 10 hours per day **and** anticipates no difficulty wearing contact lenses for 7 days per week, 10 hours per day;
5. Habitually wears, or is able to be adequately refit into Proclear 1 Day lenses;
6. Demonstrates an acceptable fit with Proclear 1 Day and Clariti 1 Day contact lenses;
7. Is correctable to a visual acuity of 0.20 LogMAR (approximately 20/30) or better (in each eye) with the study lenses or habitual correction;
8. Manifest cylindrical spectacle refraction does not exceed -1.00DC in either eye.

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

1. Is participating in any concurrent clinical research study;
2. Has any known active* ocular disease and/or infection;
3. Has a systemic condition that in the opinion of the investigator may affect a study measure;
4. Is using any systemic or topical medications that in the opinion of the investigator may affect a study measure;
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 (by verbal communication);
7. Is aphakic;
8. Has undergone refractive error surgery;
9. Is an employee of the Centre for Contact Lens Research;
10. Has taken part in another clinical or (pharmaceutical) research study within the last 7 days.

* 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.

4.2.4 REPEATED SCREENINGS

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 (i.e. a maximum of two rescreen visits is permitted).

4.3 STUDY MATERIALS

4.3.1 LENSES

All participants will have worn, or be fit with an optimized prescription of Proclear 1 Day for at least 7 days prior to being fit and dispensed with Clariti 1 Day. Details of both lens types used in this study are listed in Table 1.

Table 1: Lens characteristics

Lens	**Clariti 1 Day (Coopervision, Inc.)**	**Proclear 1 Day (Coopervision, Inc.)**
Material	Somofilcon A	Omafilcon A
HC licence #	81009	60845
Water content (%)	56	60
Dk/t (barrer/cm)	86	36.6
Sphere power (D)	+6.00 to -10.00D	+8.00 to – 12.00
Base curve (mm)	8.6	8.7
Diameter	14.1	14.2

4.3.2 LENS CARE SYSTEM

No lens care systems are required as this study involves the use of daily disposable contact lenses.

4.3.3 REWETTING DROPS

Participants will not be encouraged to use rewetting drops; however, those who habitually used rewetting drops will be allowed to continue using their normal drops. Rewetting drop use will be recorded at the follow-up visit. In the event of an adverse event, rewetting drops may be given to participants.

4.3.4 ORDERING CONSUMABLES

Clariti 1 Day will be supplied by the sponsor. If they have difficulty sourcing product in good time then lenses may instead be purchased by the CCLR through a commercial route. Proclear 1 Day may be sourced from the sponsor or through a commercial route, depending on delivery times and urgency of need.

4.3.5 DISPOSING OF CONSUMABLES

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

4.3.6 PRODUCT ACCOUNTABILITY

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.

4.4 SCHEDULED AND UNSCHEDULED VISITS

4.4.1 STUDY VISITS

This study has 4 to 6 scheduled study visits (including the screening visit), depending on the participant's habitual lens type and lens power needs (Table 2). The total time commitment for scheduled visits is expected to be 2.75 to 3.75 hours.

[redacted]

Table 2: Summary of visits

Visit code	Visit schedule	Visit Description	Duration (hrs)
1		Screening and establish optimum power of Proclear 1 Day; fit Proclear 1 Day (if applicable) and Clariti 1 Day.	1 (1.25 if fitting both lenses)
1A*		Dispense new or modified power Proclear 1 Day**	0.5
1B***	≥7 days after V1A **or** concurrent to V1	Review Proclear 1 Day and baseline data collection	0.5
2		Dispense Clariti 1 Day****	0.5
3	7-12 days after V2	Review Clariti 1 Day	1
4		Study exit	0.25

**Note: Visit 1A is only necessary if a change in Proclear 1 Day lens power is required, or if a fit with Proclear 1 Day is required for adaptation*

***Note: Visit 1A can be concurrent to Visit 1*

****Note: Visit 1B can also be concurrent to Visit 1 if a habitual Proclear 1 Day wearer does not require a change in lens power*

*****Note: For habitual Proclear 1 Day wearers that do not require a change in lens power, Visit 2 can be concurrent to Visit 1*

4.4.1.1 VISIT 1: SCREENING AND ESTABLISH OPTIMIMUM POWER OF PROCLEAR 1 DAY

Participants will attend a screening visit during which informed consent will be obtained and the investigator will determine participant eligibility using the inclusion and exclusion criteria. Participants will be assigned a study ID number when they sign the informed consent document, and before their eligibility for the study has been confirmed. Ineligible participants will be discontinued from the study. Depending on the participant's habitual lens type, participants may follow the following procedures and visits outlined (illustrated in Figure 2).

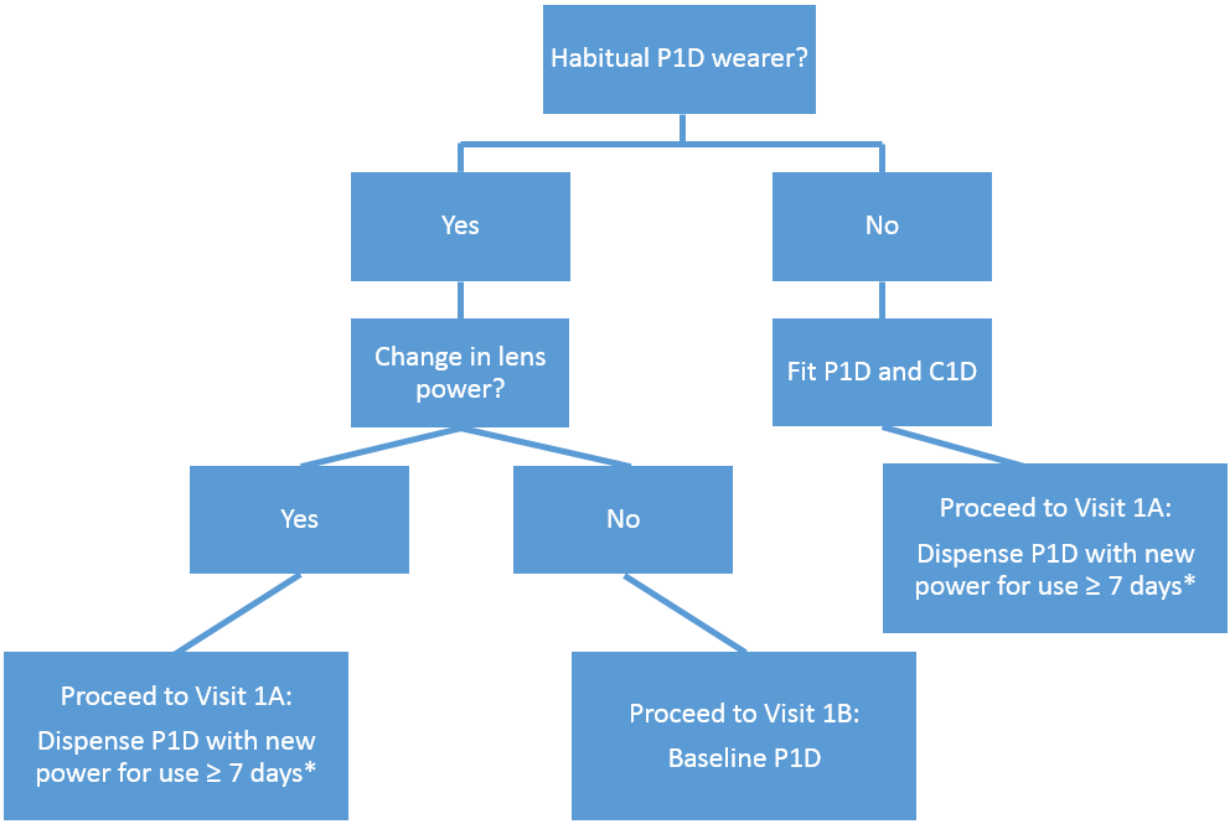

Figure 2: Flow chart for visits depending on habitual lens type (P1D = Proclear 1 Day; C1D = Clariti 1 Day). *Following Visit 1A, participant also completes Visit 1B before proceeding the Visit 2

Habitual Proclear 1 Day wearers:

Participants that habitually wear Proclear 1 Day lenses will attend Visit 1 wearing their own Proclear 1 Day lenses. Participant demographics, including their contact lens history, wear schedule, health and medication will be recorded. Monocular and binocular distance visual acuity (high contrast, high illumination) and an over-refraction will be conducted with the participant's habitual Proclear 1 Day lenses in situ. The lenses will be assessed for fit acceptance.

If the power of the participant's habitual Proclear 1 Day lenses is confirmed to be optimal, the following procedures will be conducted:

- Visit 1B will be completed immediately (specifically: fit assessment and collection of subjective ratings for Proclear 1 Day)
- Remove contact lenses
- Visual acuity with habitual spectacles (high contrast, high illumination)

- Automated refraction and keratometry
- Subjective sphero-cyclindrical and best-vision sphere refraction plus distance visual acuity (high contrast, high illumination), monocular and binocular
- Ocular health assessment
- The participant will be fit with Clariti 1 Day
- Investigator refit ratings
- Eligibility will be confirmed and the participant continues to Visit 2

If the power of the participant's habitual Proclear 1 Day lenses requires amendment, the following procedures will be conducted:

- Remove contact lenses
- Visual acuity with habitual spectacles (high contrast, high illumination)
- Automated refraction and keratometry
- Subjective sphero-cyclindrical and best-vision sphere refraction plus distance visual acuity (high contrast, high illumination), monocular and binocular
- An ocular health assessment will be conducted
- The participant will be fit with Clariti 1 Day
- Investigator refit ratings
- Eligibility will be confirmed and the participant continues to Visit 1A

Habitual wearers of other lenses:

Participants that habitually wear other soft lens types will be asked to attend Visit 1 wearing their glasses. Participant demographics, including their contact lens history, wear schedule, health and medication will be recorded. The following procedures will then be conducted:

- Visual acuity with habitual spectacles (high contrast, high illumination)
- Automated refraction and keratometry
- Subjective sphero-cyclindrical and best-vision sphere refraction plus distance visual acuity (high contrast, high illumination), monocular and binocular
- Ocular health assessment
- The participant will be fit with Clariti 1 Day
- Investigator refit ratings
- Eligibility will be confirmed and the participant continues to Visit 1A

4.4.1.2 VISIT 1A: DISPENSE PROCLEAR 1 DAY

Visit 1A only occurs for participants that: a) required an amendment to the power of their habitual Proclear 1 Day lenses or b) are habitual wearers of other lenses. This visit may be scheduled to be on the same day as Visit 1. The following procedures will be conducted during this visit:

- Changes to health or medication*
- Ocular health assessment*
- Dispense Proclear 1 Day
- Monocular and binocular distance visual acuity (high contrast, high illumination) with contact lenses
- Fit assessment of contact lenses
- Provide sufficient Proclear 1 Day to wear daily for at least 7 days
- Participant advised to return for Visit 1B wearing Proclear 1 Day

*These procedures are not required if Visit 1A is concurrent to Visit 1.

4.4.1.3 VISIT 1B: BASELINE PROCLEAR 1 DAY REVIEW

Visit 1B documents the baseline Proclear 1 Day performance. It may occur: a) during Visit 1 for participants where their habitual Proclear 1 Day lenses are of an optimal power, or b) after Visit 1A after the dispensed Proclear 1 Day lenses have been used for at least the past 7 days. The following procedures will be conducted during this visit:

- Changes to health or medication*
- Monocular and binocular distance visual acuity (high contrast, high illumination)
- Fit assessment of Proclear 1 Day
- [redacted]
- Remove contact lenses
- Ocular health assessment*
- Visual acuity with habitual spectacles (high contrast, high illumination)*
- Participant continues to Visit 2

*These procedures are not required if Visit 1B is concurrent to Visit 1.

4.4.1.4 VISIT 2: DISPENSE CLARITI 1 DAY

Visit 2 occurs after Baseline Proclear 1 Day data has been collected (Visit 1B). At this visit, Clariti 1 Day will be dispensed. The following procedures will be conducted during this visit:

- Changes to health or medication*
- Ocular health assessment*
- Insert Clariti 1 Day
- Monocular and binocular distance visual acuity (high contrast, high illumination) with contact lenses
- Fit assessment of contact lenses

[redacted]

- Provide sufficient Clariti 1 Day to wear daily for at least 7 days (maximum 12 days)

[redacted]

- Participant advised to return for Visit 3 wearing Clariti 1 Day

*These procedures are not required if Visit 2 is concurrent to Visit 1, or Visit 1B.

4.4.1.5 VISIT 3: REVIEW CLARITI 1 DAY

Visit 3 occurs after the participant has worn Clariti 1 Day for 7-12 days. Participants will attend this visit wearing Clariti 1 Day for at least 2 hours. The following procedures will be conducted at this visit:

- Changes to health or medication
- Collect at-home diaries
- Monocular and binocular distance visual acuity (high contrast, high illumination)
- Fit assessment of Clariti 1 Day lenses

[redacted]

- Remove contact lenses
- Ocular health assessment
- Participant continues to the Study Exit Visit

4.4.1.6 VISIT 4: STUDY EXIT

Visit 4 is completed when the participant exits the study. This may occur after study completion (i.e. after Visit 3), or if the participant discontinues from the study. The following procedures will be conducted at this visit:

- Remove study lenses
- Ocular health assessment*
- Visual acuity with habitual spectacles or refraction (high contrast, high illumination)
- Study completion or discontinuation form (as appropriate)
- Remuneration form

*These procedures are not required if Visit 4 is concurrent to a visit where an ocular health assessment has already been conducted.

4.4.2 UNSCHEDULED VISITS

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

4.5 STUDY PROCEDURES

Table 3 summarizes all the study procedures that are conducted in this study.

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

Procedure	1	1A	1B	2	3	4
Informed consent	X					
Demographics (including contact lens history, wear schedule, medical history)	X					
*Changes to health and medication		X	X	X	X	
LogMAR visual acuity (high illumination, high contrast)	X	X	X	X	X	X
Subjective refraction	X					
Auto-refraction and keratometry	X					
Study lens optimized fitting (Proclear 1 Day and Clariti 1 Day)	X					
*Dispense study lenses		X		X		
Spherical over-refraction with contact lenses	X					
Study lens fit assessment	X	X	X	X	X	
[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	
[redacted]				[redacted]		
[redacted]					[redacted]	
[redacted]					[redacted]	
[redacted]	[redacted]					
*Biomicroscopy	X	X	X	X	X	

*Procedure not required if visit immediately follows another visit

4.5.1 DEMOGRAPHICS

Demographic information will be obtained from the participant, including: age, gender, contact lens history, wear schedule, use of rewetting drops and relevant health and medical information. Medical history questions to determine any medical conditions, prior/concomitant medications and allergies will be asked and documented.

4.5.2 LOGMAR VISUAL ACUITY

Distance logMAR visual acuity will be measured using high contrast computer-generated acuity charts in high illumination room lighting. Participants will be asked to read letters with the study lenses, their glasses and their refraction that progressively decrease in size on a computer screen at a viewing distance of 6 metres.

4.5.3 AUTO-REFRACTION AND KERATOMETRY

Automated refraction and keratometry measurements will be taken to determine the participant's approximate spectacle refraction.

4.5.4 SUBJECTIVE REFRACTION

A subjective sphero-cylindrical distance refraction will be conducted with the participant viewing letters at the computer-generated logMAR visual acuity chart at a viewing distance of 6 metres.

4.5.5 STUDY LENS OPTIMIZED FITTING (PROCLEAR 1 DAY AND CLARITI 1 DAY)

The overall fit of Proclear 1 Day (habitual or new fitting) and Clariti 1 Day will be assessed for the following, after at least 2 minutes settling time:

- Lens wettability (0-4, 0.25 steps, where 0 = excellent, 4 = very poor)
- Lens deposition (0-4, 0.5 steps, where 0 = no deposits, 4 = deposits ≥ 0.5mm or film > 75% of surface)
- Decentration (optimum / decentration acceptable / decentration unacceptable)
- Corneal coverage in primary gaze (yes / no)
- Post-blink movement (0-4, 1 step, where 0 = insufficient, unacceptable movement, 2=optimal movement, 4=excessive, unacceptable movement)
- Tightness on push-up (0-100%, 5% steps, where 0% = falls from the cornea, 50% = optimum, 100% = no movement)
- Overall fit acceptance (0-4, 1 step, where 0 = should not be worn, 4 = perfect), providing a reason if Grade 2 or less

4.5.5.1 SPHERICAL OVER-REFRACTION WITH CONTACT LENSES

A spherical over-refraction will be conducted during the fitting of Proclear 1 Day and Clariti 1 Day for each eye to optimize the power of the lenses. Distance logMAR visual acuity will be recorded with the over-refraction. If the need to change lens power is found, a new lens with the appropriate power will be obtained. Distance logMAR visual acuity will be reassessed and a spherical over-refraction will be conducted.

4.5.6 STUDY LENS FIT ASSESSMENT

The study lenses will be assessed for the following during the lens fit assessment at Visit 1B and Visit 3:

- Lens wettability (0-4, 0.25 steps, where 0 = excellent, 4 = very poor)
- Lens deposition (0-4, 0.5 steps, where 0 = no deposits, 4 = deposits ≥ 0.5mm or film > 75% of surface)

- Decentration (optimum / decentration acceptable / decentration unacceptable)
- Corneal coverage in primary gaze (yes / no)
- Post-blink movement (0-4, 1 step, where 0 = insufficient, unacceptable movement, 2 = optimal movement, 4 = excessive, unacceptable movement)
- Tightness on push-up (0-100%, 1% steps, where 0% = falls from the cornea, 50% = optimum, 100% = no movement)
- Overall fit acceptance (0-4, 1 step, where 0 = should not be worn, 4 = perfect), providing a reason if Grade 2 or less

[redacted]

[redacted]

4.5.11 BIOMICROSCOPY

A slit lamp biomicroscopy examination will be conducted to assess anterior segment ocular health. Ocular findings will be graded using the BHVI grading scale (0-4, 0.25 steps – unless otherwise stated):

- External adnexa anomalies (absent / present & describe)
- Hyperemia:

    - Overall bulbar
    - Overall limbal
- Corneal examination:
    - Scars or other corneal observations (absent / present & describe)
    - Infiltrates (absent / present & number, size, depth)
    - Sectoral corneal staining with fluorescein (type and extent [using CCLR 0-100 scale, 1 step] and depth [0-4, 1 step])
- Overall conjunctival staining and indentation (0-4, 0.5 steps)
- Palpebral conjunctiva:
    - Hyperemia
    - Roughness

5 MONITORING PROTOCOL ADHERENCE

Adherence to study visit windows, lens wearing schedule and time windows around other data collection points (e.g. subjective ratings) will be monitored internally by the CCLR. Deviations from the windows described in the protocol will be reported in the final study report. Major protocol deviations will be reported to the Sponsor and the University of Waterloo's Office of Research Ethics (ORE) within 7 days of becoming aware of them (as per ORE's guidelines).

6 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

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

Contact lenses in this study will be worn on a daily wear basis. Adverse events and/ or complications in daily wear of soft contact lenses can occur (e.g. inflammation and infection). When contact lenses are worn on a daily wear basis there is a small risk of an adverse event compared to not wearing contact lenses. When contact lenses are worn on an extended wear basis, there is a significantly increased risk of an adverse reaction compared with wearing contact lenses on a daily wear basis.

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

A dye (fluorescein) normally used for eye exams will be used in this study. Although rare, it is possible that participants may have an allergic reaction to the dye. This could cause discomfort to

their eye. Participants are advised to inform the investigator of any sensitivities to any ophthalmic drops or study products.

Participants may not benefit directly from taking part in this study. Information from this study may help researchers come up with new soft contact lenses to help others in the future. In addition, participants will receive an examination of the anterior eye and may have the opportunity to try different types of soft contact lenses at no cost to them. This study may help the study sponsor to better understand the performance of the products being used in this study.

7 ADVERSE EVENTS

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.

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

See CCLR SOP012_v01 for a description of adverse events, including management and reporting (Appendix 24).

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

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	For all serious AEs: Notify sponsor as soon as possible, **within 24 hours;** ORE reporting will be **within 24 hours** as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		
11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	
17	Any sign and/or symptom for which participant is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	
10	Other significant event	
Non-significant Adverse Events		

21	Conjunctivitis (bacterial, viral or allergic)	Notify sponsor as soon as possible, **within 5 working days**; ORE reporting as per requirements
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	
23	Asymptomatic corneal infiltrative events	
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	

7.1 NORMAL OR ADAPTIVE SYMPTOMS

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

7.2 PROCEDURES FOR ADVERSE EVENTS

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the 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 (Appendix 20 and 21) 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.

7.3 REPORTING ADVERSE EVENTS

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to participant's participation will be reported to the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Investigator will report Serious Adverse

Events to the ORE within 24 hours of the investigator becoming aware of the event and as per ORE requirements (by fax, mail/delivery, phone, or email). All fatal or life threatening events will be reported immediately to the ORE.

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

Contact: Jose A. Vega, CooperVision
Email: JVega2@coopervision.com
Phone: (925) 621-3761 / Fax: (925) 621-2487
Address: 6150 Stoneridge Mall Rd, Suite 370,
Pleasanton, CA 94588

8 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, sponsor or participant. A participant's study participation may be discontinued at any time, if in the opinion of the sponsor or investigator it is in the best interest of the participant. All discontinuations will be fully documented on the appropriate study forms, including the Discontinuation Form (Appendix 18). The Discontinuation Form 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.

The following is a list of possible reasons for discontinuation from the study:

- Screening failure: Participants will be discontinued if they do not meet the inclusion and exclusion criteria outlined in section 4.2.3.
- Unacceptable performance with products to be used in study: Participants may be discontinued if they are unable to achieve acceptable comfort and /or vision with the study products.
- Positive slit lamp finding: Participants may be permanently discontinued from the study depending on the severity of the condition and on the judgement of the investigator.

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

9 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 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 regular study updates to the Sponsor).

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

10 STUDY COMPLETION AND REMUNERATION

At the last scheduled protocol visit a study completion form (Appendix 19) will be completed, which requires the signatures of both the participant and the investigator. The participant will also be provided with a Letter of Appreciation (Appendix 17).

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 calculated at $20 per hour of study visits and out-of-office tasks.

11 STATISTICAL ANALYSIS AND DATA MANAGEMENT

11.1 STATISTICAL ANALYSIS

All data will be analyzed by the CCLR at the University of Waterloo. Unmasked data analysis will be conducted using Statistica 12 and/or SPSS 24. Descriptive statistics will be provided on information regarding baseline variables (age, gender, refractive error distribution, etc.). For data completed on each eye individually (e.g. biomicroscopy), results of the right eye will be reported unless a difference between right eye and left eye is found. Table 4 lists the primary outcome variables and anticipated statistical procedures.

Table 4 : Statistical procedures

Variable	Analysis	Statistical test
Numeric rating scales Visual acuity Lens fitting Biomicroscopy (continuous variables)	*Effect of lens type*	Paired t-test Wilcoxon matched pairs test
Biomicroscopy (ordinal variables)	*Effect of lens type*	Friedman Wilcoxon matched pairs test
Subjective preference ratings Investigator refit agreement ratings	*Preference of lens type*	Binomial test

All data will be tested for normality of distribution using Shapiro-Wilk tests. The appropriate statistical test will be selected based on tests of normality. Statistical significance will be set at 5%, with no adjustments for multiple comparisons. In the event of missing data, individual data points will be excluded in the analysis and not extrapolated from the collected data.

A binomial test will be used to analyze the results for the count data of subjective preferences and investigator refit agreement ratings. The number of “no preference” (if featured on the scale) will be evenly distributed to the two options on the basis respondents would be equally likely to choose either.

11.2 DATA MANAGEMENT

Data from this study will be retained by the CCLR 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 the CCLR 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.

11.3 COMMENTS ON SOURCE DOCUMENTS

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

12 DATA QUALITY ASSURANCE

12.1 STUDY MONITORING

Site qualification of the investigative site has been completed to ensure that the site facility is adequate, personnel are qualified and resources are satisfactory to conduct clinical studies for the

Sponsor. The protocol will be reviewed by the investigators prior to enrollment of the first participant. This will involve an overview of the protocol, which includes information on study objectives, inclusion and exclusion criteria, study visits and adverse event reporting. Data collection forms will also be reviewed and this will provide an opportunity to discuss any questions.

Central study monitoring will involve regular study updates from the CCLR to the sponsor. The updates will include the number of participants enrolled, the number eligible, the number completed and whether there have been any unscheduled visits, discontinuations, significant or serious adverse events or major protocol deviations. These updates will be provided weekly.

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 the CCLR 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 the CCLR.

12.2 SPONSOR RESPONSIBILITIES

The Sponsor has the ultimate responsibility for monitoring. The Sponsor is to supply and keep an up-to-date signed protocol and protocol amendments, and provide devices which are the subject of the clinical investigation.

The sponsor should ensure: appropriate information is provided to the Investigators to conduct the study; that deviations are reviewed with the Investigator as needed and included in the final report. Adverse events are reported by the Investigator, and the sponsor in turn will then notify their applicable regulatory authorities, and other investigators as appropriate. The Sponsor is to maintain Sponsor-specific study documentation as required by the regulatory authorities and to ensure the Investigator is aware of their record keeping responsibilities.

12.3 INVESTIGATOR RESPONSIBILITIES

The CCLR is responsible for ensuring participant safety and data quality by: protocol compliance, adherence to GCP and local regulatory requirements, and the Declaration of Helsinki. The Investigator should be appropriately qualified and legally entitled to practice, and be trained in the proper method of obtaining informed consent.

The CCLR must have the appropriate resources to conduct the study, be familiar with the protocol and agree to adhere to it, support monitoring and auditing activities, communicate with the

Sponsor regarding any study issues or need for protocol modifications, make the necessary arrangements to ensure proper conduct and completion of the study, and ensure the protection and welfare of the participant, including arranging any emergency treatment as needed.

The CCLR must ensure written ORE approval is received prior to the start of the study, that the ORE and Sponsor is kept informed of the study progress, including adverse events and deviations as required by them, and that any changes to the protocol are notified to the ORE and review written approval prior to implementation.

12.4 RECORD KEEPING

Detailed records of all study visits will be made using the Case Report Forms (CRFs). All data recorded on forms will be in ink. Any corrections to the forms will be initialed and dated at the time they are modified.

12.5 RETENTION OF STUDY RECORDS AND DATA

Following study completion, data will be available in electronic and/or paper format for audit, sponsor use, or subsequent analysis. The original clinical raw data (including completed CRFs and Informed Consent forms) will be retained according to guidelines set forth in the general work agreement with the site. The Sponsor will be notified and consulted if ever the files are to be destroyed. Copies of raw data will be forwarded to the sponsor at completion of the final report.

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

13 PROTOCOL TRAINING

All study personnel will be required to complete training prior to their involvement in the study. A series of training modules will be developed for the study and records of training will be kept at the CCLR.

14 STUDY MANAGEMENT

14.1 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/

14.2 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.

14.3 CLINICAL TRIAL REGISTRATION

This study will be registered in the clinical trials registry (https://clinicaltrials.gov/) by the study sponsor.

14.4 PROTOCOL DEVIATIONS

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

14.4.1 MAJOR PROTOCOL DEVIATIONS

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

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

- Changes in procedures initiated to eliminate immediate risks/hazards to participants;
- Enrollment of participants outside the protocol inclusion/exclusion criteria whether agreed to or not by the sponsor;
- 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.

14.4.2 MINOR PROTOCOL DEVIATIONS

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

- Logistical or administrative aspects of the study (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).

14.4.3 REPORTING AND DOCUMENTING PROTCOL DEVIATIONS

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

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

14.5 PREMATURE TERMINATION OF THE STUDY

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

14.6 STUDY PARTICIPANT RECORDS

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

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

14.7 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 CCLR SOP014.

15 CONFIDENTIALITY

This study is confidential in nature. All information gathered during this study is proprietary and should be made available only to those directly involved in the study. Information and reports arising from this project are the property of the sponsor.

16 PUBLICATION

Due to the confidential and proprietary nature of the clinical study, any presentation and/or publication including but not limited to those made at scientific meetings, in peer-review journals, professional publications, etc. need to be approved by the sponsor.

17 STUDY COSTS

The sponsor will compensate CCLR for the conduct of this study. CCLR will compensate the participants for their time and participation in this voluntary study.

Expenses incurred by participants 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 and a written report completed indicating the subsequent treatment and resolution of the condition.

18 REFERENCES

1. Diec J, Tilia D, Thomas V. Comparison of Silicone Hydrogel and Hydrogel Daily Disposable Contact Lenses. Eye & contact lens 2017.

2. Papas EB, Keay L, Golebiowski B. Estimating a just-noticeable difference for ocular comfort in contact lens wearers. Invest Ophthalmol Vis Sci 2011;52:4390-4.

19 REPORT

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

20 APPENDICES

Appendix 1 Informed consent letter

Appendix 2 Screening Form

Appendix 3 Dispense Proclear 1 Day

Appendix 4 Baseline Proclear 1 Day

Appendix 5 Dispense Clariti 1 Day

Appendix 6 Review Clariti 1 Day

Appendix 7 Lens fitting characteristics

Appendix 8 Biomicroscopy form

[redacted]

Appendix 15 Medical history form

Appendix 16 Study exit form

Appendix 17 Letter of Appreciation

Appendix 18 Discontinuation form

Appendix 19 Study completion form

Appendix 20 CVI Adverse event notification form

Appendix 21 CVI Adverse event outcome form

Appendix 22 Product observation form

Appendix 23 Protocol deviation form

Appendix 24 CCLR SOP012_v01 Adverse event management and reporting

Appendix 25 Recruitment email script

Appendix 26 Social media advertisements

Appendix 27 Recruitment poster

Appendix 28 Emergency Wallet Card

Appendix 29 Unscheduled visit form