CORE
Centre for Ocular Research & Education

UNIVERSITY OF WATERLOO
FACULTY OF SCIENCE
School of Optometry & Vision Science

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Protocol

REFITTING DAILY DISPOSABLE CONTACT LENS WEARERS WITH DRY EYE DISEASE WITH A DIFFERENT DAILY DISPOSABLE LENS TYPE (CORGI)

Funding source: ALCON (IIT)

Funding study number: IIT Proposal [redacted]

CORE protocol number: P/678/19/L

Protocol authors: [redacted]

Principal investigator: Lyndon Jones

Role & printed name	Reviewed and approved (sign)	Date DD/MMM/YYYY
Principal investigator: [redacted]	[redacted]	
Lead investigator: [redacted]		
Protocol author: [redacted]		
Quality assurance: [redacted]		

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Version date	Author	Description of change(s)
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Confidentiality

This is a private document and the property of the Centre for Ocular Research & Education. 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 Ocular Research & Education. 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

Contact lens (CL) discomfort affects up to 50% of contact lens wearers.[1] Patients with signs and symptoms of dry eye disease (DED) have significantly increased odds of dropping out of CL wear.[1] It is likely that symptomatic CL wearers also have DED, either due to evaporative causes, aqueous deficiency or, most often, a combination of both.

To date, there are no CL studies characterizing dry eye in CL wearers using the TFOS DEWS II guidelines.[2]

2 OBJECTIVES

The objectives of the study are:

- To examine and classify DED subtypes in a group of symptomatic CL wearers who are already wearers of daily disposable (DD) CLs (excluding Dailies Total1 (DT1)).
- To assess subjective ratings, cumulative comfort scores, average wear time and comfortable wear time while symptomatic CL wearers use their habitual DD CLs.
- To refit participants with DT1 CLs and assess subjective ratings, cumulative comfort scores, average wear time and comfortable wear time after wearing DT1 for one month.

Primary Endpoint:

- Subjective ratings of end-of-day comfort and dryness (with CLs; 0 to 100 scale)
- Average wear time (hours)
- Comfortable wear time (hours)

3 RATIONALE

Refitting symptomatic CL-wearing patients into daily disposable (DD) CLs is one problem-solving strategy that has been frequently reported.

To explore if the unique ‘water gradient’ material of DT1 allows symptomatic daily disposable contact lens wearers to comfortably wear these contact lenses for a longer period than possible in their habitual DD lenses.

4 HYPOTHESIS

DT1 CLs will provide equivalent or better end-of-day comfort and longer comfortable wear time for DD CL wearers who suffer from DED compared to their habitual lenses.

5 MATERIALS AND METHODS

5.1 STUDY DESIGN

5.1.1 OVERALL DESIGN

This is a prospective, single-site, non-randomized, participant masked (study lenses are over-labelled), comparative study (habitual DD vs DT1) including 43 symptomatic DD CL wearers with DED. Clinical signs and subjective symptoms with habitual lenses will be assessed at the screening visit and these results will be compared to the study lens after 1 month of wear.

5.1.2 RANDOMIZATION

There will be no randomization in this study.

5.1.3 MASKING

Participants will be masked to the lens type (brand) they will be wearing during the study in order to reduce bias towards or against this product. Lens packages/ blister will be overlabeled.

5.2 STUDY POPULATION

5.2.1 SAMPLE SIZE CALCULATION

The sample size required for a 2-tailed matched paired t-test to detect a difference of at least 5 points in subjective ratings, with α=0.05, power = 0.95, and diff/SD = 0.60 is 39 (Figure 1). Therefore, a sample size of 43 is being proposed to account for possible dropouts and screen failures (for which not all visits are required).

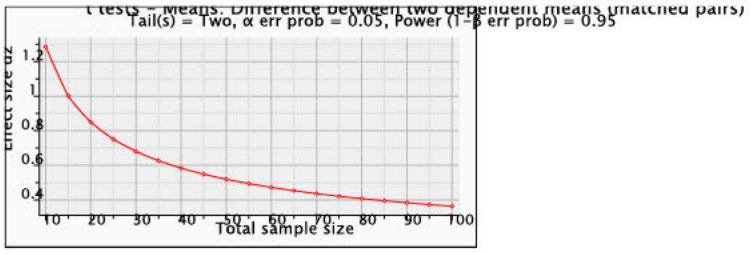

Figure 1: Sample size calculation

5.2.2 NUMBER OF PARTICIPANTS

Up to 60 participants may be screened using CORE records and advertising approved by the UW Office of Research Ethics. Approximately 43 participants will be dispensed / randomized with study products, with a target of number of 39 participants 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 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. As per TFOS DEWS II[2], have dry eye symptoms (without CL wear) as determined by an OSDI score of ≥13 and at least **one** of the following:
    a. Tear osmolarity ≥ 308mOsm/L or interocular difference >8 mOsm/L
    b. Non-invasive tear breakup time of < 10 seconds in at least one eye
    c. More than 5 spots of corneal staining OR > 9 conjunctival spots in at least one eye
5. Reports dryness while wearing DD CLs with CLDEQ-8 score ≥ 12 and ≤ 20[3]
6. Habitually wears soft spherical DD CLs with a power between +6.00D and -10.00D
7. Manifest spectacle cyl ≤1.00DC in either eye
8. BCVA ≤0.20 log MAR each eye with habitual & DT1
9. Acceptable fit with habitual & DT1
10. Willing to wear DT1 CLs at least 3 days per week and 6 hours per day throughout the study

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

1. Is participating in any concurrent clinical or research study;
2. Has any known active* ocular disease and/or infection;
3. Has a systemic condition that in the opinion of the investigator may affect a study outcome variable;
4. Is using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable;
5. Has known sensitivity to the diagnostic pharmaceuticals to be used in the study;
6. Is pregnant, lactating or planning a pregnancy at the time of enrolment (by self-report);

7. Is aphakic;
8. Has undergone refractive error surgery;
9. Has taken part in another clinical research study within the last 14 days;
10. Current habitual wearer of DT1
11. Any ocular and/or systemic conditions or concomitant medication to contraindicate contact lens wear or be expected to interfere with the primary outcome variables.

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

5.2.4 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 (per subject) will be 3.

5.3 STUDY MATERIALS

5.3.1 LENSES

Details on the lens type used in this study are listed in Table 1.

Table 1: Lens characteristics

Lens	Lens name
Material	Dailies Total1
Manufacturer	Alcon
HC licence #	87774
Dk/t (barrer/cm)	156 (-3.00D)
Sphere power (D)	+6.00D to -10.00D
Base curve (mm)	8.5
Diameter	14.1
Replacement schedule	daily

5.3.2 LENS CARE SYSTEM

A lens care system is not needed, because the lenses will be worn on a daily disposable basis and will be discarded at the end of each lens wear day.

5.3.3 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 each visit.

5.3.4 ORDERING CONSUMABLES

DT1 lenses will be supplied by Alcon for the use in this study. Osmometry chips will be invoiced for upon completion of the study and are a direct consumable cost that is not included in the budget.

5.3.5 DISPOSING OF CONSUMABLES

Worn lenses collected during study visits will be discarded as per University of Waterloo regulations.

5.3.6 PRODUCT ACCOUNTABILITY

Accountability logs will be kept to include the number of lenses received, dispensed and unused. All products dispensed to participants will be recorded in the study binder.

5.4 SCHEDULED AND UNSCHEDULED VISITS

This study has a total of 3 study visits, including the screening visit.

Pre-screening:

Potential participants who show an interest in the study will be provided with more details about the study over the phone as well as in writing (Recruit 01 Recruitment email). Two prescreening questionnaires (Appendix 4 CLDEQ-8: Symptoms with lens wear and Appendix 5 OSDI: Dry-eye symptoms without lens wear) will be attached to the email script and sent to participants in the CORE database or to participants expressing an interest in the study. These completed questionnaires will be used to determine whether the subject is likely to meet the dry eye symptom eligibility criteria. If interested, potential participants can return both questionnaires to CORE, in order to determine whether they may generally be suitable for the study based on the severity of their dry eye symptoms. Participants meeting the dry eye symptom criteria, according to the questionnaires, will be invited to a screening visit where their full eligibility will be determined. Questionnaires completed prior to the consent procedure will not be included in the analysis, instead the questionnaires will be completed again during the Screening visit. Participants may also be accepted to participate in the study without previously completing the questionnaires, however in order to save time and to avoid screen failures due to insufficient symptoms, completing the questionnaires prior to the screening visit is preferred.

5.4.1 SCREENING

The investigator will determine participant eligibility using the inclusion and exclusion criteria. All participants who sign the consent letter will be assigned a study ID number. Ineligible participants will be discontinued from the study.

5.4.2 STUDY VISITS

Table 2 shows the summary of the 3 study visits.

Table 2: Summary of visits

Visit code	Visits
1	Screening (1.5 hours)
2	Review habitual DD lenses and dispense DT1, 6-14 days after V1 (1.0 hour)
3	Review DT1 and study exit, 29-34 days after V2 (1.0 hour)

Visit 1 (Day 0 for habitual DD): Screening (1.5 hours)

- Informed consent procedure

- Participants will attend this visit wearing their habitual spectacles. They will be asked to stop lens wear for ≥ 12 hours prior to the visit and will be asked to bring a new pair of their habitual lenses with them.
- The purpose of this visit is to determine participant eligibility and to classify the type of DED exhibited by the participant, using TFOS DEWS II guidelines. These tests will include:
    - OSDI questionnaire (with participant reflecting on their ocular symptoms without CL wear);
    - Tear osmolarity (TearLab);
    - Non-invasive tear break-up time (using the Oculus K5M);
    - Tear meniscus height assessment (using the Oculus K5M);
    - Meibomian gland assessment (to calculate a meibomian gland score) using the meibomian gland evaluator (Johnson & Johnson Vision);
    - Ocular surface staining assessment and lid wiper staining;

      To minimize disruption of the ocular surface, these tests will be conducted in the order of the least invasive, through to the most invasive.

- Participants will complete a CLDEQ-8 questionnaire to review their experience with their habitual lenses over the past two weeks.
- A full slit lamp biomicroscopy examination will also be performed to determine ocular health, including ocular hyperemia and surface staining with fluorescein.
- Participants will undergo a subjective refraction (Distance High Contrast High Illumination [HIHC] visual acuity, OD, OS & OU) and will be fit with DT1 to confirm acceptable visual acuity and lens fit.
- Participants will be asked to insert their habitual lenses to confirm acceptable visual acuity and lens fit.
    - Distance HCHI visual acuity with habitual lenses, OD, OS & OU
- If the participant meets all inclusion / exclusion criteria, the participant will be instructed to wear their habitual DD CLs as usual until their next scheduled visit.
- Participants will be provided with a subjective rating questionnaire (related to comfort, dryness, handling, onset time of discomfort, total wear times and reasons for lens removal) to be completed at home on Days 1, 3 and 5. Participants will be instructed that they must wear the lenses on the days where they are required to complete the ratings, and will be scheduled to return for their next visit between 6 and 14 days after the screening visit.

Visit 2 (Day 0 for DT1): Review habitual DD lenses and dispense DT1, 6-14 days after V1 (1.0 hour)

- Participants will attend this visit wearing their habitual DD CLs for ≥ 2 hours prior to the visit.
- The subjective ratings completed at home will be reviewed.
- In-office subjective ratings of a typical day for comfort, dryness, vision and handling (with CLs; 0 to 100 scale), plus total wear time and comfortable wear time (onset time of discomfort) per day over the last month.

- The following assessment of the habitual lenses will be made:
    - Distance HCHI visual acuity, OD, OS & OU;
    - Lens surface characteristics: wettability and deposition;
    - Lens fit.
- After lens removal, a slit lamp biomicroscopy examination (including assessments for ocular surface staining and hyperemia) will be performed.
- DT1 will be dispensed and the following assessments will be made:
    - Distance HCHI visual acuity, OD, OS & OU;
    - Lens surface characteristics: wettability and deposition;
    - Lens fit.
- Participants will be provided with a 1 month supply of overlabeled DT1 CLs (for masking) and instructed to wear the lenses at least 3 days per week and 6 hours per day throughout the study.
- Participants will be provided with a subjective rating questionnaire (related to comfort, dryness, handling wear times and reasons for lens removal) to complete at home on Days 1, 3, 5, 7, 21, 28. Participants will be instructed that they must wear the study lenses on the days where they are required to complete the ratings, and will be scheduled to return for their next visit between 29 and 34 days after V2.

Visit 3: Review DT1 and study exit, day 29-34 days after V2

- Participants will attend this visit wearing the study CLs for ≥ 2 hours prior to the visit.
- Participants will be asked to complete a CLDEQ-8 questionnaire to review their experience with the DT1 study lenses.
- The subjective ratings completed at home will be reviewed.
- In-office subjective ratings of comfort, dryness, vision and handling (with CLs; 0 to 100 scale), total wear time and comfortable wear time (onset time of discomfort) over the last month.
- The following assessment of the study lenses will be made:
    - Distance HCHI visual acuity, OD, OS & OU;
    - Lens surface characteristics: wettability and deposition;
    - Lens fit.
- Slit lamp biomicroscopy examination (including assessments for ocular surface staining and hyperemia).
- Study exit documentation & reimbursement.

5.4.3 UNSCHEDULED VISITS

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

5.5 STUDY PROCEDURES

Table 3 summarizes the procedures at each visit. The order of procedures is described in sections 5.4.2.

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

Procedure	Screening Visit 1	Dispense Visit 2	Follow-up Visit 3
Informed consent	X		
Participant demographics (age, sex, ethnicity)	X		
Contact lens history	X		
Medical history and medications	X		
Changes in medical history/ medications		X	X
HCVA (logMAR) (habitual Spectacles)	X		
OSDI questionnaire	X		
CLDEQ-8 questionnaire	X (habitual CL)		X (study CL)
Comfort, dryness, vision, handling ratings, comfortable & total CL wear time over last month	X (habitual CL)		X (study CL)
Non-invasive tear break-up time (Oculus K5M)	X		
Tear meniscus height (Oculus K5M)	X		
Tear osmolarity (TearLab)	X		
Meibomian gland score (MG evaluator)	X		
HCVA (logMAR) (Contact lenses)	X (habitual and study CL)	X (habitual and study CL)	X (study CL)
Biomicroscopy (incl. staining assessment)	X	X	X
Auto refraction/auto keratometry: horizontal and vertical K readings	X		
Subjective refraction	X		
Lens performance (fit, wettability, deposition)	X (habitual CL)	X (habitual and study CL)	X (study CL)
Review of compliance (CL wear, completion of home ratings)		X	X
Subjective at-home ratings provided	X	X	
Study lens fitting	X		
Study lens dispense		X	
Collection of unused study lenses			X
Study Exit			X

5.5.1 CASE HISTORY

Demographics:

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

Medical History:

At screening, information will be obtained from participants about the current medication, allergies, and any medical conditions. At visits 2 and 3 participants will be asked about changes in their medication or health.

Contact Lens History:

Information will be obtained from the participant about the current contact lens type (lens name, brand), lens power, lens wear days and use of artificial tears. Participants will be asked how many years of lens wear experience they have and how long they have been wearing DD lenses.

5.5.2 QUESTIONNAIRES AND SUBJECTIVE RATINGS

Questionnaires:

At the screening visit (Visit 1), participants will complete the OSDI questionnaire to reflect their dry eye symptoms.

At visits 1 and 3, participants will complete the CLDEQ-8 questionnaire, reporting their experience with their habitual and study contact lenses, respectively, over the past 2 weeks.

Subjective ratings:

Participants will be provided with subjective rating 0-100 questionnaires related to comfort, dryness, vision, lens handling and will be asked for times of lens insertion and removal and reasons for lens removal as well as onset of discomfort on that day and reason for lens removal. This questionnaire will be completed at home on Days 1, 3, 5 after visit 1 and on Days 1, 3, 5, 7, 21, 28 after visit 2. Participants will be instructed that they must wear the study lenses on the days where they are required to complete the ratings, and will be scheduled to return for their next visit.

The same questionnaire will be provided to the participants during visit 1 and 3 to reflect their overall 'typical day' experience over the previous month.

5.5.3 VISUAL ACUITY

Visual acuity will be measured using high contrast computer-generated acuity charts. Participants will be asked to read letters that progressively decrease in size on a computer screen located at a distance of 6 meters. Measurements will be taken during the subjective refraction, with habitual lenses, study lenses and habitual spectacles.

5.5.4 AUTOREFRACTION

Participants will be asked to focus on a target while seated at an instrument that measures their approximate spectacle prescription and corneal shape.

5.5.5 SUBJECTIVE REFRACTION

Participants will be asked to read a letter chart from a distance through lenses placed in front of their eyes. They will also be asked to compare clarity of your vision between different lenses placed in front of your eyes. This procedure aids to determine their spectacle and/or contact lens prescription.

5.5.6 NON-INVASIVE BREAK-UP TIME

The participant will be seated in front of a device (OCULUS Keratograph (K5M) that will project rings of light (Placido discs) onto the tear film. The participant will be asked to keep their eyes open for as long as they can and the time until the rings first begin to distort or break will be recorded. Three measurements will be taken for each eye to obtain an average value.

5.5.7 TEAR MENISCUS HEIGHT

The participant will be seated in front of the OCULUS Keratograph (K5M) with their chin on the chin rest and head against the forehead rest. The investigator will select the Tear meniscus height feature and will take images of the ocular surface of each eye.

5.5.8 TEAR OSMOMETRY

The participant will be asked to lean their head back and gaze towards the ceiling. The TearLab™ pens are loaded with sterile test cards. The pen will be used to gather ~50nL of tears

from one eye at a time, from the lower lateral tear meniscus without making direct contact with the eye. The pen will be docked to the base instrument to determine tear osmolarity.

5.5.9 LENS PERFORMANCE

Contact lens fit:

Lens fit will be assessed to ensure acceptable lens fit with a participant's habitual and study lenses using a 0-4 scale, (0= perfect lens fit).

Contact lens wettability and deposits:

Contact lens wettability and deposits will be graded with participant's habitual and study lenses using e.g. 32x magnification, on a 0-4 scale, 0 = excellent wettability, 0= no deposits.

5.5.10 SLIT LAMP BIOMICROSCOPY

The participant will be seated behind a slit lamp and the following will be assessed:

Cornea:

Any current or past corneal observations (such as infiltrates, old scars, etc) will be documented at each visit.

Corneal and conjunctival staining:

A sodium fluorescein strip, wetted with a few drops of saline, will be applied to the superior bulbar conjunctiva of both eyes. Staining will be graded using the Efron grading scale (0 to 4, 0 = normal) in 0.1 scale increments, while viewing with cobalt blue light through a Wratten no. 12 barrier filter.

Bulbar and limbal hyperemia:

Ocular redness will be assessed for the bulbar and limbal conjunctiva using the EFRON grading scale (0 to 4, 0 = normal; 0.1 increments). Redness will also objectively be assessed using an imaging technique provided by the Oculus K5M.

Palpebral conjunctival hyperemia and roughness:

The redness and roughness of the upper and lower eyelids (tarsal plate zone 2) will be assessed using the Efron grading scale (0 to 4, 0 = normal/ uniform satin appearance).

5.5.11 MEIBOMIAN GLAND EXPRESSIBILITY

Meibomian gland dysfunction results in stagnation of the meibum (oil) within the glands. The ease of expression of the gland and the quality of the expressed contents therefore provides an indication of the functional capabilities of the glands. The MG Evaluator (TearScience/J&J) will be used to apply a pressure of 1.2g/mm^2 to the lower eyelid just inferior to the lid margin in three areas – nasal, central and temporal. Five consecutive glands in each area will be assessed for expressibility. Glands will be graded as follows: 0: blocked, 1: inspissated (toothpaste), 2: cloudy with debris, 3: clear, the results for each location will be summed (Meibomian gland score).

5.5.12 MEIBOGRAPHY

While seated at the Lipiview II instrument the participant will be asked to place their chin on the chin rest and head against the forehead rest. The lower lid will be everted and infrared images will be taken of the exposed palpebral surface. This will be repeated for the superior eyelid. The grading of meibomian gland dropout will be conducted on the images after all participants are completed. The grading scale used will be the one described by Arita et al.[4] the Meiboscore, where: Grade 0: no dropout, Grade 1: < 1/3 total area dropout, Grade 2: 1/3 to 2/3 total area dropout, Grade 3: > 2/3 total area dropout.

6 MONITORING PROTOCOL ADHERENCE

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

7 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

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

Contact lenses in this study will be worn on a daily wear (and daily disposable) basis. Adverse events and/ or complications in daily wear of soft contact lenses can occur (e.g. inflammation and infection). Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The

incidence of infection due to daily-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. Thirty five million Americans who currently wear contact lenses assume this risk.

When contact lenses are worn on a daily wear basis there is a small risk of an adverse event compared to not wearing contact lenses. When contact lenses are worn on an extended wear basis, there is a significantly increased risk of an adverse reaction compared with wearing contact lenses on a daily wear basis.

A dye (fluorescein) normally used for eye exams is being 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.

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

The study lens may provide fewer signs and symptoms of dry eye during wear, however, there is no guarantee that participants will benefit from participating in this study. In addition, participants will have the opportunity to try a different type of soft contact lenses at no cost to them.

Participation in this study may contribute to scientific research information that may be used in the development of new contact lens products. Information from this study may help researchers and the funding company to better understand if the use of specific daily disposable lens types in lens wearers with dry eye disease.

8 ADVERSE EVENTS

See CORE SOP012_v02 for a description of all adverse events, including management and reporting.

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

9 DISCONTINUATION FROM THE STUDY

Participants may be discontinued at the discretion of the investigator in consideration of participant safety or protocol compliance, or at discretion of the participant. Participants discontinued from a study will be reimbursed $20 per hour for their active involvement in the study (including the initial screening visit). Upon discontinuing, a participant will be offered the option of their data being withdrawn from future statistical analysis. The following is a list of possible reasons for discontinuation from the study:

- Screening failure: Participants will be discontinued if they do not meet the inclusion and exclusion criteria outlined in section 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 may 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 CORE or the Office of Research Ethics at the University of Waterloo.

A discontinuation form (ADMIN 3), stating the reason for discontinuation will be completed, which requires the signatures of both the participant and the investigator except where the participant is lost to follow-up in which case only the signature of the investigator is required.

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

10 STUDY COMPLETION AND REMUNERATION

At the last scheduled protocol visit a study completion form (ADMIN 2) will be completed, which requires the signatures of both the participant and the investigator.

Once their involvement in the study is complete, participants will be informed about receiving feedback following study completion in the Letter of Appreciation (ADMIN 1).

Participant remuneration will be $90 for completing the study this includes $70 for active time and $20 for completing the at-home questionnaires.

11 STATISTICAL ANALYSIS AND DATA MANAGEMENT

11.1 STATISTICAL ANALYSIS

All data will be analyzed by CORE at the University of Waterloo. Descriptive statistics will be provided on information regarding baseline variables (e.g. age, gender). Differences between lenses and differences over time will be compared using either Paired t-tests or Wilcoxon matched pairs, or using ANOVA, as applicable; statistical significance will be set at 5%. The appropriate tests will be selected based on tests of normality - non-parametric tests will be used for data not showing a normal distribution. For assessments conducted for each eye separately, the right eye will be used for analysis.

The following statistical tests will be performed for the listed comparisons after 1 month of DT1 wear vs habitual DD CL wear (Table 4).

Table 4: Statistical procedures

Comparison	Statistical test
CLDEQ-8 ratings between lenses (habitual DD vs. DT1)	2-sided paired t-test
Subjective ratings between lenses (habitual DD vs. DT1)	2-sided paired t-test

Subjective ratings over time (from home ratings) for DT1	Repeated Measures ANOVA
Comparisons as above, but on groups stratified by DED subtype (evaporative/aqueous deficient/mixed disease)	2-sided paired t-test

In addition, equivalence and superiority for the test lens (DT1) vs the habitual lens will be evaluated for the primary outcome variables, with a change in subjective ratings of 5 points and a difference of 0.5 hours in average and comfortable wear time being considered as a clinically relevant difference.

11.2 DATA MANAGEMENT

All study data will be recorded on paper CRFs. Data from this study will be entered in an electronic database and retained by CORE for a minimum of 25 years on a password-protected server. After 25 years, data will be disposed of in accordance with the guidelines laid out by the University of Waterloo.

At the completion of the study CORE may provide a copy of the study data to the funding company. 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. Using this method means that data files are only stored on University of Waterloo servers during the transfer.

11.3 COMMENTS ON SOURCE DOCUMENTS

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

12 PROTOCOL TRAINING

All study personnel will be required to complete training prior to their involvement in the study. Records of training will be kept at CORE.

13 STUDY MONITORING

Study monitoring will be conducted throughout the study. In addition study records may be inspected at CORE by the Office of Research Ethics at the University of Waterloo, and by regulatory authorities in Canada and the United States, namely Health Canada and the United States Food and Drug Administration (FDA); however, no records containing identifiable/personal information will be permitted to leave the custody of CORE.

Study monitoring will include, but may not be limited to:

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

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

CORE will register this study with clinicaltrials.gov.

14.4 PROTOCOL DEVIATIONS

Protocol deviations are unanticipated or unintentional changes to a study after it has received 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;
- 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

CORE 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 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.

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 CORE SOP014_v02_Clinical data management.

15 REPORT

A report will be completed after data collection has been completed.

16 REFERENCES

1. Dumbleton K, Caffery B, Dogru M, et al. The TFOS International Workshop on Contact Lens Discomfort: report of the subcommittee on epidemiology. *Invest Ophthalmol Vis Sci.* 2013;54(11):TFOS20-36.
2. Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II Diagnostic Methodology report. *Ocul Surf.* 2017;15(3):539-574.

3. Chalmers RL, Young G, Kern J, Napier L, Hunt C. Soft Contact Lens-Related Symptoms in North America and the United Kingdom. *Optom Vis Sci.* 2016;93(8):836-847.

4. Arita R, Suehiro J, Haraguchi T, Shirakawa R, Tokoro H, Amano S. Objective image analysis of the meibomian gland area. *Br J Ophthalmol.* 2014;98(6):746-755.