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Centre for Ocular Research & Education

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

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Protocol

PERFORMANCE OF DAILIES TOTAL1 DAILY DISPOSABLE CONTACT LENSES IN HABITUAL SOFT LENS WEARERS WHO REPORT SUBSTANTIAL DIGITAL DEVICE USE

(CODENAME: FOX)

Funding source: Alcon (IIT)

Funding study number: IIT Proposal # [redacted]

CORE protocol number: P/853/23/L

Protocol author: [redacted]

Principal investigator(s): Lyndon Jones

Role & printed name	Reviewed and approved (sign)	Date DD/MMM/YYYY
[redacted]	[redacted]	

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Disclaimer

This study will be conducted for research purposes only.

1 INTRODUCTION

A review published in 2020 reported that an average of 21.7% of contact lens (CL) wearers stop wearing lenses,[1] with discomfort being the main reason for discontinuation.[2-5] One study reported 26.6% of new soft CL wearers stopped wearing lenses over the first year. The most common reasons for discontinuing CL wear were poor distance vision (38%), poor near vision (24%), handling problems (23%) and discomfort (21%).[2] A study conducted in Canada found 23% permanently discontinued lens wear, with the main reasons being discomfort (24%) and dryness (20%). As we spend an increasing amount of time on digital devices in our daily lives, the number of people potentially dropping out of CL wear may be affected by the use of digital devices. CL wearers suffer from computer vision syndrome more frequently than those who do not wear lenses (65% to 50%), with lens wearers who use computers for >6 hours per day more likely to be symptomatic.[6] Symptoms related to use of digital devices may be due to multiple reasons, including a decreased blink rate, incomplete blinking, or poor wetting of the lens.[7-9]

The importance of choosing a suitable contact lens for digital device users was demonstrated in a recent study. Lens wearers who used digital devices for an average of 9.7 hours per day were refit with verofilcon A (PRECISION1®) daily disposable CLs.[10] After two weeks of wear, participants were asked to rate the overall comfort, dryness, and clarity of vision using 0 to 100 scale (where 100 was the best rating). Verofilcon A lenses performed well, with mean ± standard deviation ratings of 91 ± 11 for comfort, 88 ± 11 for dryness, and 92 ± 9 for clarity of vision. Most participants felt verofilcon A provided all-day good comfort (88%) and vision (91%). The majority of participants were also satisfied with the comfort (84%), vision (91%), and overall performance (81%) of the lenses when using digital devices for at least 6 hours.

The purpose of this study is to evaluate the performance of delefilcon A (DAILIES TOTAL1®) in habitual contact lens wearers who report substantial digital device use (≥ 8 hours on a typical day).

2 OBJECTIVES

The objective of the study is:

- To refit habitual soft lens wearers, who use digital devices ≥8 hours on a typical day, with DAILIES TOTAL1® daily disposable CLs, and to assess their subjective ratings (0-100) for overall comfort, overall dryness, and overall clarity of vision during a typical day when using digital devices ≥8 hours while wearing DAILIES TOTAL1® CLs, reported after two weeks of wear.

The primary outcome variables for this study are:

- Subjective ratings (0-100, where 100=best) of overall comfort, overall dryness and overall clarity of vision with DAILIES TOTAL1® CLs during a typical day when using digital devices ≥8 hours (reported after two weeks of wear).

Other outcome variables of interest include:

- Likert type questions exploring the satisfaction with DAILIES TOTAL1® CLs when using digital devices (after two weeks of wear)
- Subjective ratings (0-100, 100=best) of comfort, dryness, and clarity of vision collected using an at home questionnaire on days 1, 7, and 14±1) at three time-points each day: after lens insertion, after 8 hours of digital device use, and at the end of day
- Lens wear time
- Lens fit

3 HYPOTHESIS

DAILIES TOTAL1® will provide a satisfactory performance for substantial digital device users as reflected in subjective ratings of ≥75 (0-100 scale, 100=best) for overall comfort, dryness, and clarity of vision during a typical day when using digital devices for ≥8 hours, reported after two weeks of wear.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

4.1.1 OVERALL DESIGN

This is a prospective, non-masked, open-label dispensing study with three study visits on two study days. CL wearers who use digital devices for ≥8 hours on a typical day will be enrolled. Eligible participants will be fit and dispensed with DAILIES TOTAL1® study lenses for 14+2 days, to be worn for at least 5 days a week and at least 13 hours per day.

- **Visit 1**: Screening and fitting of study lens (approx. 1.0 hour)
- **Visit 2**: Baseline & Dispense (approx. 0.5 hours; same day as and directly after Visit 1)
- **Visit 3**: Day 14 Follow-up and study exit (approx. 1.0 hour)

4.1.2 RANDOMIZATION

There will be no randomization in this study because all participants will be dispensed with DAILIES TOTAL1®.

4.2 STUDY POPULATION

4.2.1 SAMPLE SIZE

The sample size in this study is based on the previous study with a similar aim and design, involving PRECISION1® contact lenses (PUG, Kuali# 41694).[11] That study found meaningful results with a sample size of 32 and therefore the sample size for this study is planned to be the same, with a minimum of 32 participants to complete the study.

4.2.2 NUMBER OF PARTICIPANTS

Participants will be recruited using CORE database and advertising approved by the UW Office of Research Ethics. Up to 35 participants may be dispensed with study products, with a target of 32 completing the study. Informed consent will be obtained for all participants prior to their enrolment in the study.

4.2.3 INCLUSION AND EXCLUSION CRITERIA

A person is eligible for inclusion in the study if they:

1. Are between 18 and 40 years of age (inclusive) and has full legal capacity to volunteer;
2. Have read and signed an information consent letter;
3. Are willing and able to follow instructions and maintain the appointment schedule;
4. Are a digital device user (at least 8 hours on a typical day using any combination of digital devices such as PC, laptop, smartphone or tablet);
5. Are a habitual wearer of daily wear, spherical, soft contact lenses (no bifocal or multifocal contact lenses, no extended wear or monovision) for at least 5 days/week and at least 13+ hours/day on a typical day during the month prior to enrolment;
6. The habitual lens type brand will be restricted such that a maximum of 7 participants will be included in the study for each lens brand/material;
7. Have a vertex corrected spherical equivalent distance refraction within -0.50D to -9.00D in each eye;
8. Have a vertex corrected refractive cylinder ≤ -0.75 cylindrical correction in each eye after vertexing to the corneal plane;
9. Demonstrate an acceptable fit and achieves best corrected visual acuity of at least 0.10 logMAR in each eye with DAILIES TOTAL1® contact lenses;

10. Are willing to wear DAILIES TOTAL1® contact lenses at least 5 days per week and 13+ hours per day throughout the study.

A person will be excluded from the study if they:

1. Are participating in any concurrent clinical or research study involving intervention or invasive ocular tests;
2. Are presbyopic or habitually use a reading addition for close work;
3. Have any known active* ocular disease and/or infection;
4. Meet the diagnosis of dry eye disease as per the following combination:
    - Meets the symptom criteria of CLDEQ-8 score ≥12
    - And they show 1 of the following 2 signs:
        - Either NaFl staining (either [cornea >5 dots] or [conjunctiva >9 dots] or [lid margin >2mm length AND ≥25% width]);
        - Or NITBUT (no contact lens) <10 seconds.
5. Have a systemic condition that in the opinion of the investigator may affect a study outcome variable;+
6. Are using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable;
7. Are a current wearer of DAILIES TOTAL1® daily disposable contact lenses;
8. Have known sensitivity to the diagnostic pharmaceutical sodium fluorescein to be used in the study;
9. Have undergone refractive error surgery;
10. Are a member of CORE directly involved in the study.

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

+ Any potential exclusion will be reviewed with the Lead Investigator or Principal Investigator prior to final decision making.

Age >40 years is excluded because presbyopia and pre-presbyopia is highly prevalent in this population and will cause eyestrain and impact vision irrespective of the contact lens material, thus impacting subjective ratings.

4.2.4 VULNERABLE POPULATION

This study will not be conducted in vulnerable populations.

4.2.5 REPEATED SCREENINGS

In some circumstances a repeated screening may need to be scheduled (V1-R). 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 the 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. 2 re-screens are permitted.

4.3 STUDY MATERIALS

4.3.1 LENSES

The study lens is approved by Health Canada. Lenses will be worn bilaterally, and on a daily disposable basis.

Table 1: Lens characteristics

Lens	DAILIES TOTAL1®
Material	delefilcon A
HC licence #	87774
Medical device class	2
Dk/t (barrer/cm) at -3.00D	156
Water content	core 33%, surface ≥ 80%
Sphere power (D)	+0.50 to +6.00 (in 0.25 steps) -0.50 to -6.00 (in 0.25 steps) -6.50 to -12.00 (in 0.50 steps)
Base curve (mm)	8.5
Diameter	14.1
Replacement scheduled	daily disposable

4.3.2 LENS CARE SYSTEM

No lens care system is required because the lenses are daily disposable lenses.

4.3.3 DRUGS

No drugs will be used on the study.

4.3.4 REWETTING DROPS

Participants will not be encouraged to use rewetting drops; however, those who habitually used rewetting drops will be allowed to continue using their normal drops. Rewetting drop use will be recorded at each visit.

4.3.5 ORDERING CONSUMABLES

DAILIES TOTAL1® study lenses will be supplied by Alcon for use in this study.

4.3.6 DISPOSING OF CONSUMABLES

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

4.3.7 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 individual participant logs in the study binder.

4.4 SCHEDULED AND UNSCHEDULED VISITS

This study has a total of three study visits on two separate days, including the screening visit (V1) which will typically be conducted immediately prior to the baseline/dispense visit (V2). Participants will attend the clinical site for a total of approximately 2.5 hours. Participants will also be asked to complete at home ratings on Day 1, Day 7, and Day 14±1 to assess their experience with the study CLs.

4.4.1 STUDY VISITS

A summary of the study visits is shown in Table 2.

Table 2: Summary of visits

Visit code	Day	Visits	Duration (hours)
V1	0	Screening	1.0
V2	0	Baseline & Dispense Provide instructions on at-home ratings.	0.5
Given to participant at V2	1, 7, 14±1	Subjective at-home ratings	0.5
V3 & Exit	14 + 2 after V2	Day 14 Follow-up	1.0
Total			**3.0**

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

4.4.2 PRE-SCREENING

A pre-screening questionnaire will be attached to the recruitment email script sent out to participants in the CORE database or to participants expressing an interest in the study to assess whether they would meet the criteria of a habitual soft lens wearer who uses digital devices for ≥8 hours on a typical day and to determine if their level of symptoms while wearing CLs aligns with inclusion/exclusion criteria. If interested, potential participants can return the questionnaires to CORE, or answer the questions over the phone, if preferred. The pre-screening questionnaire is used to minimise screen failures and is not considered study data. Participant eligibility will be determined at a scheduled screening visit, using the inclusion/exclusion criteria listed in Section 4.2.3 **after** informed consent has been obtained. All study data questionnaires will be completed **after** informed consent has been obtained.

4.4.3 SCREENING (VISIT 1)

A documented informed consent process will be conducted with all participants prior to their enrolment in the study and prior to any data collection of measurements.

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

The procedures to be performed are listed below and are explained in more detail in Section 4.5.:

Participants will attend the visit wearing spectacles. Participants will not have worn their contact lenses for at least 12 hours prior to the visit.

1. Informed consent;
2. Participant demographics (age, sex);
3. Participant history:
    - *Medical history/medications;*
    - *Habitual contact lens wear;*
    - *Digital device use.*
4. CLDEQ-8 questionnaire;
5. logMAR distance high illumination, high contrast visual acuity (HIHC VA) with habitual spectacles for OD, OS, and OU;
6. Auto-refraction/auto-keratometry;
7. Non-invasive break-up time;
8. Biomicroscopy examination:
    - *External adnexa anomalies;*
    - *Cornea & anterior eye assessment for scars, infiltrates;*
    - *Bulbar & limbal redness;*
    - *Corneal & conjunctival staining with fluorescein dye;*
    - *Palpebral conjunctival hyperemia and roughness;*
    - *Lid margin staining (horizontal length and sagittal width 0-3 scale; 1 increment).*
9. Subjective sphero-cylindrical refraction, monocular and binocular logMAR distance HIHC VA;
10. Best sphere refraction, monocular and binocular logMAR distance HIHC VA;

11. DAILIES TOTAL1® fitting:
    i. *The contact lens power will be chosen based on the vertexed best sphere refraction;*
    ii. *The participant will insert the lenses which will be allowed to settle for 5 minutes;*
    iii. *Monocular over-refraction will be performed. If a different lens power is needed, the new power CL will be inserted and steps ii and iii will be repeated;*
    iv. *The final lens powers for OD and OS will be recorded with the monocular and binocular logMAR distance HIHC VA;*
    v. *Acceptability of lens fit (movement, centration; YES/NO) will be confirmed.*
12. Confirm eligibility.

4.4.4 BASELINE AND DISPENSE, DAY 0 (VISIT 2)

1. Participants who successfully meet all the eligibility criteria will proceed directly to Visit 2, while continuing to wear the pair of study lenses that were just fit in Visit 1.
2. logMAR distance HIHC VA with study lenses for OD, OS, OU;
3. Subjective post-insertion ratings (0-100 integer scale, where 100 means best performance; both eyes rated together) to assess the initial impression of DAILIES TOTAL1® regarding:
    - *Comfort;*
    - *Clarity of vision.*
4. Lens fit and surface evaluation:
    - *Lens centration;*
    - *Lens movement in primary gaze;*
    - *Lens tightness on push-up test;*
    - *Surface wettability;*
    - *Surface deposits.*
5. At-home rating scales: Participants will receive at-home rating scales to be completed on Day 1, Day 7, and Day 14±1.
6. Lens wear instructions. The participants will be asked to:
    - *Wear the lenses at least 5 days per week and >13 hours per day throughout the study;*
    - *Complete the subjective at-home ratings to reflect their lens wear experience on Day 1 (the day after V2), Day 7, and Day 14±1 using a 0-100 scale. Ratings will be completed after insertion, after 8 hours of digital device use, and at the end of the day just before lens removal. The final at-home questionnaire will be*

completed the evening before their scheduled Visit 3. Variables to be assessed are:

- *Comfort;*
- *Dryness;*
- *Clarity of vision.*

- *Attend V3 after 8 hours or more of DAILIES TOTAL1® study lens wear.*

7. Dispense lenses.

4.4.5 DAY 14 FOLLOW-UP VISIT AND EXIT, DAY 14+2 (VISIT 3)

Participants will attend the visit after 8 hours of DAILIES TOTAL1® study lens wear.

1. Collect unused study CLs;
2. Changes in medication history/medications;
3. Compliance with # of CL wear days/hour per day with typical # hours of digital device use over the past 2 weeks and for V3 visit day;
4. Collect and review at-home ratings;
5. logMAR distance HIHC VA with study lenses for OD, OS, and OU;
6. Subjective ratings (0-100 scales, where 100 means better performance; integer steps, both eyes rated together), to assess a typical day in the past 2 weeks 5 minutes after insertion, after 8 hours of digital device use, at the end of the day just prior to removal, and overall for:
    - *Comfort;*
    - *Dryness;*
    - *Clarity of vision.*
7. Subjective satisfaction;
8. Lens fit and surface evaluation:
    - *Lens centration;*
    - *Lens movement in primary gaze;*
    - *Lens tightness on push-up test;*
    - *Surface wettability and deposits.*
9. Biomicroscopy examination:
    - *External adnexa anomalies;*
    - *Cornea & anterior eye assessment for scars and infiltrates;*
    - *Bulbar & limbal redness;*
    - *Corneal & conjunctival staining with fluorescein dye;*

- *Palpebral conjunctival hyperemia & roughness.*

10. logMAR distance HIHC VA with habitual spectacles or CLs for OD, OS, and OU.

4.4.6 STUDY EXIT

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

Exit monocular and binocular distance (HIHC VA logMAR) will be recorded with either the participant's spectacles, refraction or habitual contact lenses. An exit biomicroscopy assessment will be conducted if biomicroscopy has not already completed on the same day for a concurrent study visit.

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

4.4.7 UNSCHEDULED VISITS

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

4.5 STUDY PROCEDURES

A summary of the study procedures to be conducted at the different scheduled visits is listed in Table 3. Most procedures are in described in more detail in the following sub-sections.

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

Procedure	Visit 1	Visit 2	Visit 3
	Screening	Baseline & Dispense	Day 14 Follow-up
Informed consent	X		

Participant demographics (age, sex)	X		
Medical history and medications	X		
Changes in medical history/medications			X
Contact lens history	X		
Digital device use history	X		
CLDEQ-8 questionnaire	X		
HIHC VA (logMAR) (habitual spectacles)	X		
Auto-refraction/auto-keratometry: horizontal and vertical K readings	X		
Non-invasive tear film break-up time	X		
Biomicroscopy	X		
Biomicroscopy (without lid margin staining)			X
Subjective refraction	X		
HIHC VA (logMAR) (study CL)	X	X	X
Study lens fitting	X		
Eligibility	X		
Subjective ratings (post-insertion comfort & vision)		X	
Subjective ratings (comfort, dryness, & vision)			X
Satisfaction ratings (Likert scale)			X
Lens assessment (fit, wettability, deposits)		X	X

Provide at-home ratings (comfort, dryness, & vision)		X	
Collect unused study lenses			X
Review of compliance (CL wear, digital device use, completion of at-home ratings)			X
HIHC VA (logMAR) (habitual spectacles or contact lenses)			X

4.5.1 CASE HISTORY

Demographics:

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

Medical History:

At screening, information will be obtained from the participant about the current medication, allergies, and any medical conditions. At the beginning of the Follow-up visits and end of study visits, the participant 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 brand name, lens power), replacement frequency, contact lens care solution (if applicable), typical number of lens wear days per week, typical lens wear time per day (total and comfortable), years of lens wear and use of artificial tears, plus confirmation that that the subject uses contact lenses ≥13 hours per day;

Digital device use:

Participants will be asked about their typical use of digital devices (total hours/day of all devices combined) and to identify the type of devices (e.g. smartphone, computer, laptop, tablet) they use, with confirmation that the subject uses digital devices ≥8 hours per day.

4.5.2 CLDEQ-8 QUESTIONNAIRE

The Contact Lens Dry Eye Questionnaire (CLDEQ-8) is a validated questionnaire recommended by the 2013 TFOS Workshop on Contact Lens Discomfort[12] as the best approach for detecting

contact lens discomfort (CLD). Instructions for completion are present on the source documents and will be reviewed with the participant prior to completion. The CLDEQ-8 score ranges from 0 to 37, with higher scores indicating increased symptoms.

4.5.3 VISUAL ACUITY

Visual acuity for distance will be measured using high contrast computer-generated acuity charts in high illumination. Participants will be asked to read letters that progressively decrease in size on a computer screen located at a distance of 6 meters.

4.5.4 NON-INVASIVE TEAR FILM BREAK-UP TIME (NITBUT)

The participant will be seated in front of a device 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 to obtain an average value. The assessment will be carried out without study contact lenses.

4.5.5 AUTO-REFRACTION AND AUTO-KERATOMETRY

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

4.5.6 SUBJECTIVE REFRACTION

The participant 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 the clarity of their vision between different lenses placed in front of their eyes. This procedure aids in determining their spectacle and/or contact lens prescription.

4.5.7 SLIT LAMP BIOMICROSCOPY

A slit lamp biomicroscopy examination will be conducted to assess anterior segment ocular health. The participant will be seated behind a slit lamp and the ocular findings will be graded using Efron grading scale (0-4, 0.1 steps – unless otherwise stated).

External adnexa anomalies

The presence or absence of external adnexa anomalies will be recorded.

Bulbar and limbal hyperemia

The redness of each quadrant of the bulbar and limbal conjunctiva of both eyes will be assessed (Efron 0-4 scale; 0.1 increments).

Assessment of cornea and anterior eye for scars, infiltrates and any other abnormalities

The presence or absence of scars, infiltrates, or other abnormalities will be recorded. The size (diameter) of the largest infiltrate (0-4 where 0 = none, 1 = < 0.5mm, 2 = 0.5 – 1mm, 3 = 1 – 1.5 mm, 4 = >1.5 mm) and the depth of the largest infiltrate will be graded (0-4, 0 = none, 1 = epithelial, 2 = sub-epithelial, 3 = mid-stromal, 4 = deep stromal).

Corneal, conjunctival and lid margin staining

A sodium fluorescein strip, wetted with a few drops of saline, will be applied to the superior bulbar conjunctiva of both eyes. Staining of all five zones of the cornea and four zones of the conjunctiva will be graded while viewing with cobalt blue light through a Wratten no. 12 barrier filter (Efron 0-4 scale; 0.25 increments). The horizontal length (0-3 where 0 = <2mm, 1 = 2-4mm, 2 = 5-9mm, 3 = ≥10m) and sagittal width (0-3 where 0 = <25%, 1 = 25-49%, 2 = 50-74%, 3 = ≥75%; 1 increment) of the staining of the upper and lower lid margins will be assessed.

Palpebral conjunctival hyperemia and roughness

The redness and roughness of the upper and lower eyelids (tarsal plate zone 2) will be assessed (Efron 0-4 scale; 0.25 increments).

4.5.8 LENS FIT & SURFACE ASSESSMENT

CL fit:

Lens fit will be assessed to ensure acceptable lens fit (centration and movement) with study lenses at the screening visit (V1).

At V2 and V3, lens centration and movement will be assessed as follows:

- *Lens centration (0-3 scale; 0 = optimal, 1 = slight decentration, 2 = moderate decentration but not encroaching limbus; 3 = excessive & occasionally encroaching limbus);*
- *Lens movement for primary gaze (+2 to -2 scale; -2 = unacceptably tight, -1 = slightly tight but acceptable, 0 = optimal, +1 = slightly loose but acceptable, +2 = unacceptably loose);*
- *Lens tightness on push-up test (0-100 scale; 0 = falls from cornea without lid support; 50 = optimal, 100 = no movement).*

CL surface wettability and deposits:

Contact lens wettability and deposits will be graded with study lenses at V2 and V3:

- *Surface wettability (0-4 scale in 0.25 steps; 0 = excellent); very low illumination, external diffuser in place, x32 magnification, viewing the quality of the Purkinje image;*
- *Surface deposits (0-4 scale in 0.25 steps; 0 = excellent); using low illumination and a moderate beam with direct illumination to scan the contact lens for deposits, x32.*

4.5.9 SUBJECTIVE RATINGS

Subjective ratings:

At visit 2, participants will be provided with subjective rating questionnaires using a 0-100 scale (where 100 = best performance; integer steps, both eyes rated together) to assess their first impression with the study CLs post-insertion regarding comfort and clarity of vision.

At the end of Visit 2, participants will be provided with at-home questionnaires to subjectively rate the experience with study lenses regarding comfort, dryness, and clarity of vision using a 0-100 scale (integer steps; both eyes together), where 100 means better performance. This questionnaire will be completed on Days 1, 7, and 14±1 after Visit 2 (i.e. Day 0), at three different time-points on each of these days: after insertion, after 8 hours of digital device use, and at the end of the day just before lens removal. The final at-home questionnaire will be the evening before their scheduled Visit 3. In addition, times of lens insertion, first notice of discomfort, and lens removal will be collected. There will also be a diary entry for the number of hours of cumulative digital device use that day.

At Visit 3, participants will be provided with subjective rating questionnaires to assess a **typical** day over the past 2 weeks, to report their experiences i) 5 minutes after insertion, ii) after 8 hours of digital device use, iii) at the end of the day just prior to lens removal, and iv) overall. For each typical timepoint, comfort, dryness, and clarity of vision will be assessed using a 0-100 scale (integer steps; both eyes together), where 100 means best performance.

Satisfaction with study CL:

Satisfaction (5-point Likert scale: strongly disagree, slightly disagree, neither disagree or agree, slightly agree, strongly agree) with DAILIES TOTAL1® CLs overall and while using digital devices on a **typical** day in the past 2 weeks will be assessed for the following questions:

- *The study lenses provide good vision all day long.*
- *The study lenses provide good comfort all day long.*

- *I am satisfied with the comfort the study lenses provide when I use digital devices for ≥8 hours.*
- *I am satisfied with the vision the study lenses provide when I use digital devices for ≥8 hours.*
- *I don't experience eye strain when I wear the study lenses and use digital devices for ≥8 hours.*
- *I don't experience eye fatigue (tired eyes) when I wear the study lenses and use digital devices for ≥8 hours.*
- *I don't experience episodes of blurred vision when I wear the study lenses and use digital devices for ≥8 hours.*
- *I don't experience dryness with digital device use.*
- *Overall, these lenses provide good performance when using digital devices for ≥8 hours.*

5 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 and significant adverse events and major protocol deviations will be reviewed by the Principal Investigator and Head of Clinical Research.

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 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.

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.

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.

This study will be conducted during the ongoing COVID-19 pandemic. Therefore, risks of infection with COVID-19 exist through participation. These risks arise due to possible exposure during commute to and from the study visit as well as during the study visit, particularly due to the closeness of the investigator and participant (within 2m for some assessments). The potential effects of COVID-19 are not yet fully known and may include long-term health consequences. In a small percentage, infection with COVID-19 can lead to serious illness, hospitalization, and in rare cases to complications leading to death. Individuals aged 60 and above and those with underlying medical conditions are considered at a greater risk for severe illness from the COVID-19 virus however they are excluded from this study for different reasons.

In consideration of risks associated with COVID-19, CORE has implemented a series of on-site safety procedures which have been reviewed and approved by the University of Waterloo. These include, but are not limited to, self-screening of investigators, maintaining physical distancing as much as possible, frequent handwashing, wearing of face masks by the investigator and participant as per University guidelines, and frequent room and equipment hygiene. In addition, members of CORE and participants will follow any University policies regarding Covid-19 vaccination.

Participants may not benefit directly from taking part in this study. Information from this study may help researchers come up with new soft contact lens designs to help others in the future. This study may help the research team to better understand the performance of the product being used in this study, particularly during digital device use.

7 ADVERSE EVENTS

See CORE SOP012 AE Reporting for a description of the reporting of adverse events.

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

8 DISCONTINUATION FROM THE STUDY

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

- Screening failure: Participants will be discontinued if they do not meet the inclusion and exclusion criteria outlined in Section 4.2.3.
- Unacceptable performance with products to be used in study: Participants may be discontinued if they are unable to achieve acceptable comfort and /or vision with the study products.
- Positive slit lamp finding: Participants may be permanently discontinued from the study depending on the severity of the condition and on the judgement of the investigator.
- Adverse event: If a participant experiences an adverse event during the study they may be discontinued based on the clinical judgement of the investigator.
- Symptoms: If the participant has persistent symptoms they may be discontinued based on the clinical judgement of the investigator.
- Disinterest, relocation or illness: The participant may choose to discontinue due to reasons within or beyond their control.
- Violation of protocol or non-compliance: The participant will be discontinued if they are unable or unwilling to follow the protocol specified visit schedules and/or study procedures.
- Instillation of topical ocular medication: The participant will be discontinued if they elect to use a topical ocular medication during the study unless that topical ocular medication is prescribed for a limited duration (less than two weeks) to treat a transient condition; in this case the participant may remain an active participant (at the discretion of the investigator) after stopping topical ocular medication following resolution of the ocular condition).

- Lost to follow-up: The participant will be discontinued if they cannot be contacted and do not return for a final exit visit, and if the investigator has made a reasonable effort to contact the participant for a final study visit.
- Premature termination of the study by the sponsor, CORE or the Office of Research Ethics at the University of Waterloo.

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

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

9 STUDY COMPLETION AND REMUNERATION

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

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

Participant remuneration will be $60 for completing the study. This is calculated at $20 per hour for the 2.5 hours of scheduled visits plus the 30 minutes of time required to complete the at-home ratings. Full details are given in the information consent letter. A cheque will be provided at the final visit.

10 STATISTICAL ANALYSIS AND DATA MANAGEMENT

10.1 STATISTICAL ANALYSIS

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

Descriptive statistics will be provided for all primary and exploratory outcomes as well as information regarding baseline variables (e.g. age, sex).

Subjective ratings and lens fit assessments will be compared between Visit 2 (Dispense) and Visit 3 (2-week follow-up) 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 if there is no difference between the eyes.

Binomial testing will be conducted to analyze Likert questionnaires. For example, agreement questionnaires (strongly disagree, slightly disagree, neither disagree nor agree, slightly agree, strongly agree) to determine whether participants had a positive or negative experience with the test lens.

Additional analysis may be conducted.

10.2 DATA MANAGEMENT

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

At the completion of the study CORE will 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, or REDCap. These systems provide a secure way to transfer files when email is not appropriate, whether because of file size, file type or concerns over security. Sendit and REDCap include 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 funding company. Using this method means that data files are only stored on University of Waterloo servers during the transfer.

10.3 COMMENTS ON SOURCE DOCUMENTS

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

11 PROTOCOL TRAINING

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

12 STUDY MONITORING

Status reports will be provided to the study funding company by email on a regular basis.

Status reports will include:

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

Study monitoring will be conducted by CORE personnel. Consent documentation will be reviewed by a person not involved in the consent process. To improve data integrity, data entry will be conducted by one person and a second person will visually compare the data entry to the source documents to facilitate data monitoring. All adverse events and protocol deviations will be reviewed by the Lead Investigator. All serious and significant adverse events and major protocol deviations will be reviewed by the Principal Investigator and Head of Clinical Research.

13 STUDY MANAGEMENT

13.1 STATEMENT OF COMPLIANCE

This clinical study is designed to be in compliance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for Good Clinical Practice (GCP) (ICH E6 R2), with ISO 14155:2020 Clinical Investigation of Medical Devices for Human Subjects, 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, TCPS2 (2022).

- Declaration of Helsinki
- ICH E6 - International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guidelines for Good Clinical Practice
- Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2022)
- https://uwaterloo.ca/research/office-research-ethics/research-human-participants

13.2 ETHICS REVIEW

This protocol will be submitted to and reviewed through the Office of Research Ethics (ORE) at the University of Waterloo. Notification of ethics clearance of the application is required prior to the commencement of the study.

13.3 CLINICAL TRIAL REGISTRATION

CORE will register this study with clinicaltrials.gov.

13.4 PROTOCOL DEVIATIONS

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

13.4.1 MAJOR PROTOCOL DEVIATIONS

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

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

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

13.4.2 MINOR PROTOCOL DEVIATIONS

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

- Logistical or administrative aspects of the study (e.g., study participant missed appointment, change in appointment date);

- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would not impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

13.4.3 REPORTING AND DOCUMENTING PROTCOL DEVIATIONS

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

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

13.5 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.

13.6 STUDY PARTICIPANT RECORDS

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

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

13.7 RETENTION OF STUDY RECORDS AND DATA

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

14 REPORT

A report will be sent to the funding company after data collection and statistical analysis have been completed, in accordance with the agreements.

15 REFERENCES

1. Pucker AD, Tichenor AA. A review of contact lens dropout. *Clin Optom (Auckl)*. 2020;12:85-94.
2. Sulley A, Young G, Hunt C, et al. Retention rates in new contact lens wearers. *Eye Contact Lens*. 2018;44 Suppl 1:S273-S282.
3. Young G, Veys J, Pritchard N, et al. A multi-centre study of lapsed contact lens wearers. *Ophthalmic Physiol Opt*. 2002;22(6):516-27.
4. Dumbleton K, Woods CA, Jones LW, et al. The impact of contemporary contact lenses on contact lens discontinuation. *Eye Contact Lens*. 2013;39(1):93-9.
5. Pritchard N, Fonn D, Brazeau D. Discontinuation of contact lens wear: a survey. *Int Contact Lens Clin*. 1999;26(6):157-162.
6. Tauste A, Ronda E, Molina MJ, et al. Effect of contact lens use on computer vision syndrome. *Ophthalmic and Physiological Optics*. 2016;36(2):112-119.
7. Truong TN, Graham AD, Lin MC. Factors in contact lens symptoms: evidence from a multistudy database. *Optometry and Vision Science*. 2014;91(2):133-141.
8. Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. *Bmj Open Ophthalmology*. 2018;3(1).
9. Guillon M, Theodoratos P, Patel K, et al. Pre-contact lens and pre-corneal tear film kinetics. *Contact Lens & Anterior Eye*. 2019;42(3):246-252.
10. Schulze MM, Fadel D, Luensmann D, et al. Evaluating the performance of verofilcon A daily disposable contact lenses in a group of heavy digital device users. *Clinical Ophthalmology*. 2023;17:3165-3176.
11. Schulze M. Evaluating the performance of Precision1 daily disposable contact lenses in a group of heavy digital device users protocol. 2019.
12. Dumbleton K, Woods CA, Jones LW, et al. The impact of contemporary contact lenses on contact lens discontinuation. *Eye & Contact Lens - Science and Clinical Practice*. 2013;39(1):93-99.