CORE
Centre for Ocular Research & Education

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

Centre for Ocular Research & Education (CORE)
School of Optometry & Vision Science | University of Waterloo, 200 University Avenue West | Waterloo, ON, Canada N2L 3G1
+1 519 888-4742 | CORE.uwaterloo.ca

Protocol

INVESTIGATING ILUX® EFFICACY IN CONTACT LENS WEARERS WITH EVAPORATIVE DRY EYE DISEASE

Funding source: Alcon (IIT)

Funding study number: IIT Proposal [redacted]

CORE protocol number: P/688/19/CORE

Protocol author: [redacted]

Principal investigator(s): Lyndon Jones

[redacted]

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

Study Personnel

Principal investigator:	**Lyndon Jones** *PhD FCOptom* Director, Centre for Ocular Research and Education [redacted]
Head of Clinical Research:	**Jill Woods** *BSc(Hons) MCOptom* [redacted]
Project developer	**Lyndon Jones** **Jill Woods** [redacted]
Protocol author:	[redacted]
Lead investigator:	[redacted]
Quality Control:	[redacted]
Funding source contact:	[redacted]

DOCUMENT CHANGE HISTORY

Version date	Author	Description of change(s)
03sep2019	[redacted]	Original protocol
08oct2019	[redacted]	Minor typographic corrections after ethics review
21oct2019	[redacted]	• Typographic correction in section 4.2.3 Inclusion criteria #12 – removed the word “minimum” • Section 4.5.11 Lid margin cleaning – amended to include the use of topical anesthetic in the procedure. Only lower lids will be cleaned.

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Confidentiality

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Disclaimer

This study will be conducted for research purposes only and is not intended to be used to support the safety of iLux in a regulatory submission.

1 INTRODUCTION

Contact lens (CL) discomfort affects up to 50% of contact lens wearers.[1] Dry eye, in particular changes in meibomian gland (MG) structure and function, significantly increases the odds of CL drop out.[2] Studies have shown that managing meibomian gland dysfunction (MGD) results in positive outcomes for symptomatic contact lens wearers, including increased comfortable CL wear time.[3]

Launched in May 2018, the iLux® Device is a medical device approved in Canada for use by eye care professionals to provide in-office treatment for the management of MGD and evaporative dry eye disease (DED). The handheld device delivers localized heat (38-44°C) to the eyelids to melt meibum and the operator applies pressure to the treatment zone to express melted meibum through the gland orifices. The treatment can be applied to the upper and lower eyelids (sequentially) and takes 8-12 minutes to complete. Patient safety is maintained with the use of iLux® Smart Tips, which are sterile, single-use attachments to the handheld device which make contact with the eyelids during treatment.

The iLux® Device is considered comparable to another commercially available eyelid thermal pulsation system, the LipiFlow® System (Johnson & Johnson Vision). Previous studies have shown that treating MGD with a single LipiFlow® treatment increased mean comfortable CL wear time by 4 hours per day, which was sustained for up to 3 months.[3]

The purpose of this clinical trial is to investigate the efficacy of a single iLux® treatment in symptomatic CL wearers who have DED (according to the TFOS DEWS II diagnostic criteria),[4] of the evaporative dry eye disease subtype (EDE).

2 OBJECTIVES

The objectives of this clinical trial are:

- To assess eye dryness symptoms (using the SPEED questionnaire) at 1- and 3-months post iLux® treatment;
- To assess Meibomian gland secretions (by expression using the Meibomian Gland Evaluator) at 1- and 3-months post iLux® treatment.

Primary endpoint:

- Changes in SPEED questionnaire score at 1 month.

Secondary endpoints:

- Meibomian gland secretion (assessments will be reported as meibomian gland scores (MGS);
- Pre-lens tear break-up time;
- Reported average wear time and comfortable wear time.

Exploratory endpoint:

- Changes in symptoms, determined using CLDEQ-8 and OSDI questionnaires, at 1- and 3-months, and SPEED at 3 months post iLux® treatment.

3 NULL HYPOTHESES

- There will be no difference between treatment and control groups for mean comfortable CL wear time.
- There will be no difference between treatment and control groups for symptoms, determined using SPEED questionnaire, at 1-month.
- There will be no difference between treatment and control groups for Meibomian gland score (MGS) at 1-month.

4 MATERIALS AND METHODS

4.1 STUDY DESIGN

4.1.1 OVERALL DESIGN

This is a prospective, single-site, parallel-group study involving 52 existing CL wearers who have confirmed EDE (according to the TFOS DEWS II diagnostic criteria). This study will involve three visits (Figure 1). Participants will attend CORE for a total of 3.5 hours.

Eligible participants will be randomized in a 1:1 ratio to receive a single, bilateral iLux® treatment at Visit 1 (treatment group), or delayed iLux® treatment provided at Visit 2 (control-treatment group i.e. 1-month no treatment, administer treatment at Visit 2). The treatment group will be reviewed 1- and 3-months after treatment. The control-treatment group will be reviewed at 1-month, at which point they will receive a single, bilateral iLux® treatment. The control-treatment group will be reviewed 1 month (full clinical assessment, including symptom assessment) and 3 months (symptom assessment only) after iLux® treatment. Participants randomized to the treatment group will be involved in the study for 3 months. Participants randomized to the control-treatment group will be involved in the study for 4 months.

Participants will wear their habitual CLs during the study. To ensure compliance, they will be supplied their habitual CLs and, if applicable, their habitual lens care products, for use during their involvement in the study.

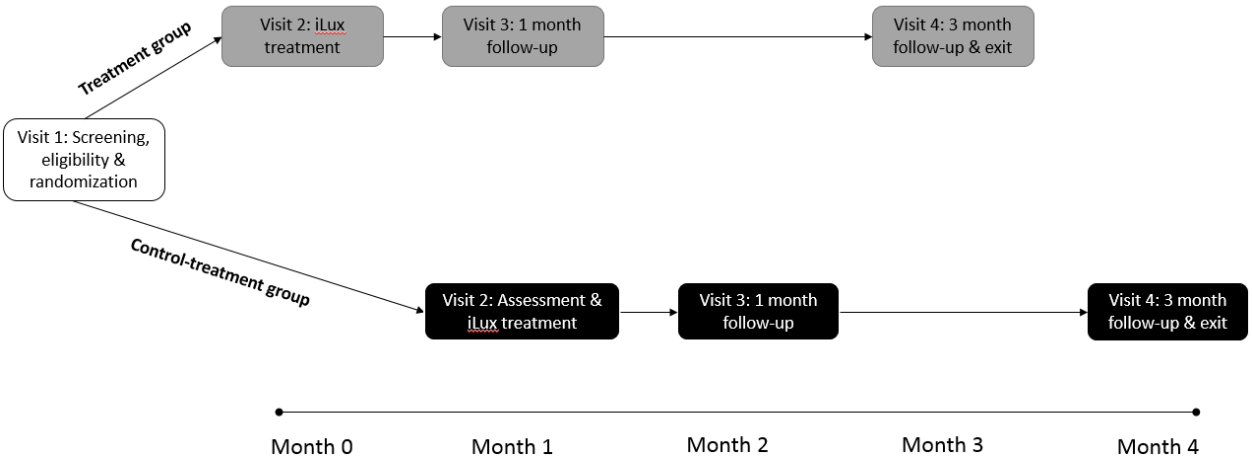

Figure 1: Study flow chart

4.1.2 RANDOMIZATION

A randomization schedule will be generated using a web-based program: (www.randomization.com). The final study randomization schedule will be generated by CORE's Data Team Leader and provided to the research assistants for the study. Study investigators will remain masked to the randomization schedule until the study is completed and the database is locked.

4.1.3 MASKING

There will be no masking in this study.

4.2 STUDY POPULATION

4.2.1 SAMPLE SIZE CALCULATION

There are no current data available regarding the minimally clinically important differences for MGS nor SPEED scores to inform an effect size. Data from Blackie et al[3] show a 12-point improvement in MGS score and 8-point improvement in SPEED scores with small standard deviations, corresponding to very large effect sizes of 1.7 and 1.8, respectively. This data supports a minimum sample of 9 in each group would be required to detect an 8-point mean difference in

SPEED scores at 90% power (alpha=0.05, power analysis = a priori, two-tailed, difference between two independent means).

However, an effect size of 1.7 and 1.8 are ambitious targets in this field. Applying targets of a more realistic effect size of 1.0 and a power of 90%, a minimum sample size of 23 in each group is recommended (alpha=0.05, power analysis = a priori, two-tailed, difference between two independent means). Factoring a 10% dropout, the total suggested sample size is 52 participants.

4.2.2 NUMBER OF PARTICIPANTS

Participants will be recruited using CORE records and advertising approved by the University of Waterloo Office of Research Ethics. Participants expressing an interest in the study will be pre-screened using the CLDEQ-8 questionnaire to assess whether they meet the symptomatic contact lens wear criteria. However, eligibility for the study can only be determined at the screening visit using the inclusion and exclusion criteria. Data from the pre-screening questionnaire will not be considered as study data and will be confidentially disposed of. This questionnaire will be repeated at the screening visit and stored as study data.

Up to 52 eligible participants will be randomized with a target of 46 participants 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 he/she:

1. Is at least 18 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. Has been using the same CL type (brand, material and dimensions) for > 3 months;
5. Wears commercially available soft CLs on average >2 hours per day, 4-7 days per week;
6. Is willing to try to wear their habitual CLs on average ≥ 6 hours per day, 4-7 days per week and maintain this for the duration of their involvement in the study;
7. Demonstrates an acceptable lens fit of their habitual contact lenses;
8. Does not have contact lens discomfort due to contact lens fit, lens material or known solution compatibility issues, in the opinion of the investigator;
9. Has at least one month supply of their habitual contact lens products at the time of the screening visit;
10. Has a CLDEQ-8 score ≥ 12;

11. Has dry eye symptoms without CL wear (OSDI ≥ 13) and has at least one of the two following signs:
    a. Non-invasive tear break-up time (NITBUT) of < 10 seconds in at least one eye;
    b. Fluorescein staining: > 5 spots of corneal staining OR > 9 conjunctival spots OR lid wiper staining (≥ 2mm length, ≥ 25% width) in at least one eye;
12. Has a lipid layer thickness of ≤ 100 nm in both eyes;
13. A meibomian gland secretion score (MGS) of ≤ 15 for 15 glands of the lower lid in both eyes.

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

1. Is participating in any concurrent clinical or research study;
2. Has used any prescription systemic medications or topical treatments for MGD or dry eye for the past 30 days prior to the screening visit and not willing to stop using these for the study duration (excluding over-the-counter artificial tears, dietary supplements and ocular lubricants but includes warm compresses, eyelid massage, eyelid hygiene, manual meibomian gland expression, punctal plug insertion or punctal occlusion, intense pulsed light treatment of the face or eyelids);
3. Has previously received treatment with an eyelid thermal pulsation device;
4. Has a history of any of the following ocular (eye or eyelid) conditions or procedures in either eye within the past 90 days prior to the screening visit:
    a. Ocular trauma
    b. Chemical burns
    c. Ocular *Herpes simplex* or *Herpes zoster* infection
    d. Limbal stem cell deficiency
    e. Recurrent ocular inflammation (e.g. uveitits, iritis, scleritis, episcleritis, keratitis)
5. Has undergone ocular surgery (e.g. intraocular, oculoplastic, corneal or refractive surgery procedure) within the past 12 months prior to the screening visit;
6. Has permanent make-up or tattoos on their eyelids;
7. Has any other known active* ocular disease and/or infection in either eye including: cicatricial lid margin disease or severe (≥ grade 3) blepharitis; moderate to severe (grade 2-4) allergic, vernal or giant papillary conjunctivitis; a hordeolum or stye; ocular surface abnormality that may compromise corneal integrity (e.g. Grade 3 corneal fluorescein staining, recurrent corneal erosion, corneal epithelial defect, map dot fingerprint dystrophy, previously treated chemical burn);

8. Has an eyelid abnormality that affects normal lid function (e.g. entropion, ectropion, oedema, blepharospasm, lagophthalmos, severe trichiasis, severe ptosis);
9. Has a systemic condition that in the opinion of the investigator may affect a study outcome variable;
10. Has any other condition that could compromise treatment or increase the risk of a procedure-related injury;
11. Is using any systemic or topical medications that in the opinion of the investigator may affect a study outcome variable;
12. Has known sensitivity to the diagnostic pharmaceuticals to be used in the study;
13. Has a history of sensitivity to rapidly blinking lights or photosensitive epilepsy;
14. Is pregnant, lactating or planning a pregnancy (by verbal communication) at the time of enrolment;
15. Is aphakic;
16. Is a member of CORE directly involved in the study;
17. Has taken part in a clinical research study within the last 30 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. The participant attends having used any ocular lubricants (including artificial tears, emollients or liposomal sprays), used eye make-up or facial cosmetics around their eyes, rubbed their eyes and has been swimming in a chlorinated pool less than 12 hours prior to attending the screening visit;
2. Incomplete information available at time of screening to determine eligibility (e.g. current lens brands worn, history from current eye care practitioner etc.)
3. Study procedures unable to be completed in time scheduled for visit;
4. Study products not available at the time of the screening visit;

5. A transient health condition which may affect the eye(s) (e.g. a common cold, active allergies, fatigue etc.)
6. The short term use of medications (e.g. antibiotics, antihistamines etc.)
7. Reassessment of baseline ocular conditions (e.g. corneal and/or conjunctival staining, scars etc.)

The maximum total number of screenings permitted per participant will be 3.

4.3 STUDY MATERIALS

4.3.1 ILUX® DEVICE

One iLux® Device will be supplied by the study sponsor for use in this study (Figure 2). This device has been approved by Health Canada as a Class 3 medical device. Details of this device can be found in Table 1. iLux® treatment will be administered to eligible participants at either Visit 1 or Visit 2 (according to the randomization scheme).

Table 1: iLux® device details

	iLux® Device
Manufacturer	TEAR FILM INNOVATION, INC. 12625 High Bluff Drive,, Suite 107 San Diego, CA, US, 92130
Health Canada MDAL License #	101082
Device identifier	2020
Device class	Class 3

Figure 2: iLux® device with Smart Tip

4.3.2 ILUX® SMART TIPS

Single-patient-use, disposable iLux® Smart Tips will be used with the iLux® device (Table 2). These Smart Tips will supplied by the sponsor for use in this study.

Table 2: iLux® Smart Tips details

	iLux® Smart Tips
Manufacturer	TEAR FILM INNOVATION, INC. 12625 High Bluff Drive,, Suite 107 San Diego, CA, US, 92130
Health Canada MDAL License #	101082
Device identifier	2020-D
Device class	Class 3

4.3.3 TOPICAL ANAESTHETIC

Prior to the iLux treatment, a topical anaesthetic eye drop, Alcaine, will be instilled into each eye (Table 3).

Table 3: Topical anaesthetic

Alcaine	
Manufacturer	Alcon Canada Inc., 2665 Meadowpine Blvd, Mississauga, Ontario, Canada L5N 8C7
Health Canada, DIN	00035076
Active ingredient	Proparacaine hydrochloride (0.5%)
Non-medicinal ingredients	Glycerin, hydrochloric acid and/or sodium hydroxide (to adjust pH), purified water
Preservative	Benzalkonium chloride (0.01%)
Dosage	Instill one to two drops to the eye prior to iLux procedure.

4.3.4 CONTACT LENSES AND SOLUTIONS

Participants will wear their habitual contact lens type/ brand throughout the study and will continue to use their habitual lens care, if required. Participants will be instructed to wear their contact lenses for a minimum of 4 days per week, 6 hours per day throughout the study.

Participants will be instructed to bring their lens care system (if applicable) and an unopened package of their current contact lenses to the screening visit. The specifications of the contact lenses and care system will be noted.

Participants will be supplied with contact lenses and lens care solutions (as applicable) at the next scheduled visit after the screening visit.

4.3.5 REWETTING DROPS AND OCULAR LUBRICANTS

Participants are permitted to continue using their habitual over-the-counter (OTC) drops (e.g. rewetting drops, artificial tears, eye lubricants) if they were using the product prior to their

participation in the study. Participants will be instructed not to start using any new OTC products for the study duration.

4.3.6 ORDERING CONSUMABLES

CORE will order contact lenses and contact lens care systems (as applicable) for each participant. The sponsor will supply one iLux® device and sufficient Smart Tips for use in this study.

4.3.7 DISPOSING OF CONSUMABLES

Unused Smart Tips will be returned with the iLux® device at the end of the study.

4.3.8 PRODUCT ACCOUNTABILITY

Accountability logs will be kept to include the number of lenses and lens care system bottles received, dispensed, unused. Accountability logs will also kept to document the number of Smart Tips used and returned to sponsor (if applicable). 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 a total of 4 study visits, including the screening visit. The total time commitment for this study for the treatment group is 3.5 hours. The total time commitment for the control-treatment group is 4.0 hours. Participants randomized to the treatment group will be involved in the study for three months. Participants randomized to the control-treatment group will be involved in the study for four months. Table 4 summarizes the study visits.

Table 4: Summary of visit codes

Visit #	Day/s	Visits	Duration (hours)
For **all participants**			
Visit 1	0	Screening	1.0
For participants randomized to the **treatment group**			
Visit 2A	0	iLux® treatment	0.5
Visit 3A	23 - 37 days after Visit 1	1 month follow-up	1.0
Visit 4A	83 - 97 days after Visit 1	3 month follow-up & study exit	1.0
For participants randomized to the **control-treatment group**			
Visit 2B	23 - 37 days after Visit 1	Assessment & iLux® treatment	1.5
Visit 3B	23 - 37 days after Visit 2	1 month follow-up	1.0
Visit 4B	83 - 97 days after Visit 2	3 month follow-up & study exit	0.5

4.4.2 SCREENING (VISIT 1)

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

Participants will be instructed to refrain from the following for at least 12 hours before the screening visit:

- Used any ocular lubricants, artificial tears, emollients or liposomal sprays
- Using any eye make-up or facial cosmetics around their eyes
- Rubbing their eyes
- Swimming in a chlorinated pool

If participants attend the screening visit having used any of the products or performed any of the tasks listed above, they will be advised to reschedule their screening visit.

The following procedures will be conducted:

1. The participant is expected to attend the screening / baseline visit having refrained from CL wear for at least 12 hours. Participants are expected to bring a new pair of their habitual contact lenses and habitual solutions (if applicable)

2. The participant will be required to read and sign an Informed Consent Letter prior to enrollment. When the participant has signed the consent form, the participant will be considered enrolled in the study.
3. Participant demographics and medical history (age, sex, medical conditions, medications, allergies, management of dry eye symptoms).
4. Contact lens history: collect information regarding the participant's habitual CLs and lens care systems (if applicable). Also collect information on the participant's CL wear habits:
    a. Average total wear time (number of days per week, number of hours per day)
    b. Average comfortable wear time (number of hours per day).
5. The participant will complete the CLDEQ-8 questionnaire, SPEED questionnaire and OSDI questionnaire.
6. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual spectacles.
7. Non-invasive tear break-up time.
8. Lipid layer assessment (LipiView II)
9. Meibomian gland secretion assessment using the Meibomian Gland Evaluator.
10. Meibomian gland imaging of the upper and lower eyelids to determine meibomian gland drop out;
11. Ocular health assessment, including ocular surface staining.
12. Rinse eyes with saline to flush out any residual stain prior to lens insertion.
13. The participant inserts a new pair of their habitual contact lenses.
14. Contact lens fit assessment:
    a. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination)
    b. Lens wettability
    c. Lens deposition
    d. Centration
    e. Movement
    f. Tightness (push-up test)
    g. Overall fit
15. After the lenses have been on eye for 10 minutes, pre-lens tear breakup time will be assessed.
16. The investigator will confirm that the participant meets the eligibility specifications set out in the inclusion criteria and exclusion criteria and is eligible to continue in the study.

17. If the participant meets all the inclusion criteria and none of the exclusion criteria, the participant will be randomized.
18. If the participant is randomized to the control-treatment group, the participant is advised to continue wearing their contact lenses on average ≥ 6 hours per day, 4-7 days per week until their next scheduled visit and to refrain from using any new OTC products or medications to manage their dryness and/or contact lens discomfort symptoms.
19. If the participant is randomized to the treatment group, the participant will immediately proceed to Visit 2.

The remaining visits outlined are separated according to treatment group assignment.

4.4.3 TREATMENT GROUP

4.4.3.1 ILUX® TREATMENT (VISIT 2A)

Visit 2 occurs immediately after Visit 1 for participants that have been randomized to the treatment group. The following procedures will be conducted:

1. The participant will remove their contact lenses.
2. The participant's eyelids will be cleaned by the investigator.
3. The iLux® treatment will be administered to both eyes by the investigator.
4. A slit lamp biomicroscope examination will be performed as a safety check.
5. The participant will be provided with verbal and written instructions on how to complete blinking exercises. One round of blinking exercises will be completed with the investigator to ensure the participant understands the instructions.
6. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual spectacles as a safety check.

4.4.3.2 1 MONTH FOLLOW-UP (VISIT 3A)

Participants will attend this visit 23-37 days after iLux® treatment administered at Visit 2. Participants will attend this visit wearing a new pair of their habitual CLs for ≥ 4 hours prior to the visit. Participants who attend not meeting this criteria will be rescheduled (unless they report problems when wearing their lenses). The following procedures will be conducted:

1. Review medical history (changes in medication, adverse events)
2. Collect information on participant's CL wear habits:
    a. Average total wear time (number of days per week, number of hours per day)

b. Average comfortable wear time (number of hours per day).

3. The participant will complete the CLDEQ-8 questionnaire, SPEED questionnaire and OSDI questionnaire.
4. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual CLs.
5. Assess pre-lens tear film break-up time.
6. The participant will remove their CLs.
7. Meibomian gland secretion assessment using the Meibomian gland evaluator.
8. Ocular health assessment including ocular surface staining.
9. The participant will be allowed to reapply their habitual CLs or wear their own spectacles. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with visual correction.

4.4.3.3 3 MONTH FOLLOW-UP VISIT AND STUDY EXIT (VISIT 4A)

Participants will attend this visit 83-97 days after iLux® treatment administered at Visit 2. Participants will attend this visit wearing a new pair of their habitual CLs for ≥ 4 hours prior to the visit. Participants who attend not meeting this criteria will be rescheduled (unless they report problems when wearing their lenses). The following procedures will be conducted:

1. Review medical history (changes in medication, adverse events)
2. Collect information on participant's CL wear habits:
    a. Average total wear time (number of days per week, number of hours per day)
    b. Average comfortable wear time (number of hours per day).
3. The participant will complete the CLDEQ-8 questionnaire, SPEED questionnaire and OSDI questionnaire.
4. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual CLs.
5. Assess pre-lens tear film break-up time
6. The participant will remove their CLs.
7. Meibomian gland secretion assessment using the Meibomian gland evaluator.
8. Ocular health assessment including ocular surface staining.
9. The participant will be allowed to reapply their habitual CLs or wear their own spectacles. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with visual correction.
10. Study exit documentation and remuneration.

4.4.4 CONTROL-TREATMENT GROUP

4.4.4.1 ASSESSMENT AND ILUX® TREATMENT (VISIT 2B)

Participants will attend this visit 23-37 days after Visit 1. Participants will attend this visit wearing a new pair of their habitual CLs for ≥ 4 hours prior to the visit. Participants who attend not meeting this criteria will be rescheduled (unless they report problems when wearing their lenses). The following procedures will be conducted:

1. Review medical history (changes in medication, adverse events)
2. Collect information on participant's CL wear habits:
    a. Average total wear time (number of days per week, number of hours per day)
    b. Average comfortable wear time (number of hours per day).
3. The participant will complete the CLDEQ-8 questionnaire, SPEED questionnaire and OSDI questionnaire.
4. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual CLs.
5. Assess pre-lens tear film break-up time.
6. The participant will remove their CLs.
7. Meibomian gland secretion assessment using the Meibomian gland evaluator.
8. Ocular health assessment including ocular surface staining.
9. Confirm the participant is suitable to receive iLux® treatment.

If the participant is suitable to receive treatment, the following procedures will be conducted:

1. The participant will remove their contact lenses.
2. The participant's eyelids will be cleaned by the investigator.
3. The iLux® treatment will be administered to both eyes by the investigator.
4. A slit lamp biomicroscope examination will be performed as a safety check.
5. The participant will be provided with verbal and written instructions on how to complete blinking exercises. One round of blinking exercises will be completed with the investigator to ensure the participant understands the instructions.
6. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual spectacles as a safety check.

4.4.4.2 1 MONTH FOLLOW-UP VISIT (VISIT 3B)

Participants will attend this visit 23-37 days after iLux® treatment administered at Visit 2. Participants will attend this visit wearing a new pair of their habitual CLs for ≥ 4 hours prior to the visit. Participants who attend not meeting this criteria will be rescheduled (unless they report problems when wearing their lenses).The following procedures will be conducted:

1. Review medical history (changes in medication, adverse events)
2. Collect information on participant's CL wear habits:
    a. Average total wear time (number of days per week, number of hours per day)
    b. Average comfortable wear time (number of hours per day).
3. The participant will complete the CLDEQ-8 questionnaire, SPEED questionnaire and OSDI questionnaire.
4. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with habitual CLs.
5. Assess pre-lens tear film break-up time
6. The participant will remove their CLs.
7. Meibomian gland secretion assessment using the Meibomian gland evaluator.
8. Ocular health assessment including ocular surface staining.
9. The participant will be allowed to reapply their habitual CLs or wear their own spectacles. Monocular & binocular distance logMAR visual acuity (high contrast, high illumination) with visual correction.

4.4.4.3 3 MONTH FOLLOW-UP VISIT & STUDY EXIT (VISIT 4B)

Participants will attend this visit 83-97 days days after iLux® treatment administered at Visit 2. Participants will attend this visit wearing a new pair of their habitual CLs for ≥ 4 hours prior to the visit. Participants who attend not meeting this criteria will be rescheduled (unless they report problems when wearing their lenses).The following procedures will be conducted:

1. Review medical history (changes in medication, adverse events)
2. Collect information on participant's CL wear habits:
    a. Average total wear time (number of days per week, number of hours per day)
    b. Average comfortable wear time (number of hours per day).
3. The participant will complete the CLDEQ-8 questionnaire, SPEED questionnaire and OSDI questionnaire.
4. Study exit documentation and remuneration.

4.4.5 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

The study procedures are summarized in Table 5.

Table 5: Summary of procedures to be conducted at scheduled visits

	All	Treatment group			Control-treatment group		
Procedure	**Visit 1**	**Visit 2A**	**Visit 3A**	**Visit 4A**	**Visit 2B**	**Visit 3B**	**Visit 4B**
Informed consent	x						
Participant demographics	x						
Medical history and medications	x						
Contact lens history	x						
Comfortable & total contact lens wear time	x		x	x	x	x	x
CLDEQ-8, SPEED questionnaire, OSDI questionnaire	x		x	x	x	x	x
Visual acuity	x		x	x	x	x	
Non-invasive tear break-up time	x						
Lipid layer assessment	x						
Meibomian gland secretion assessment	x		x	x	x	x	
Meibomian gland imaging	x						
Slit lamp biomicroscopy	x		x	x	x	x	
Contact lens assessment	x						
Pre-lens tear break-up time	x		x	x	x	x	
Lid margin cleaning		x			x		
iLux® treatment		x			x		
Blink exercises - teach & practice		x			x		
Study exit				x			x

4.5.1 DEMOGRAPHICS

Demographic information from participants will be obtained, including age, sex, medical conditions, medications, allergies, management of dry eye symptoms. Medical history questions to determine any medical conditions, prior/concomitant medications and any allergies will be asked and documented.

4.5.2 CONTACT LENS HISTORY

Information will be obtained from the participant about the current contact lens type (lens name, brand), lens power, contact lens care solution, number of lens wear days, lens wear time (total and comfortable) and use of rewetting drops.

4.5.3 QUESTIONNAIRES

4.5.3.1 CLDEQ-8

The Contact Lens Dry Eye Questionnaire (CLDEQ-8) is a validated questionnaire recommended by the 2013 TFOS Workshop on Contact Lens Discomfort as the best approach for detecting contact lens discomfort (CLD).[5] A cut-off score ≥ 12 suggests CLD is present and the CL wearer would benefit from clinical management of the CL-related symptoms.[6]

4.5.3.2 SPEED

The Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire (TearScience, Morrisville, NC) is a dry eye questionnaire developed to assess the frequency (0-3 scale) and severity (0-4 scale) of patient symptoms and reviews the presence of symptoms within the past 72 hours and past 3 months.[7] Scores range from 0-28, with higher values indicating more severe dryness.

4.5.3.3 OSDI

The Ocular Surface Disease Index (OSDI) questionnaire (Allergan, Irvine, CA) is a dry eye questionnaire that asks the participant to reflect and rate over the past week, their symptoms of eye dryness in different working conditions and environments. A higher composite score indicates more severe dryness.[8]

4.5.4 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.

4.5.5 NON-INVASIVE TEAR BREAK-UP TIME AND PRE-LENS TEAR BREAK-UP TIME

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.

4.5.6 LIPID LAYER ASSESSMENT (LIPIVIEW II)

The participant will be seated at the LipiView II instrument which will image and compute the lipid layer thickness of the tear film. Prior to the commencement of this test, no history of seizures or discomfort with rapidly blinking lights will be reconfirmed.

4.5.7 MEIBOMIAN GLAND SECRETION ASSESSMENT

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/mm2 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: No secretion (includes capped orifices), 1: inspissated (toothpaste), 2: colored/cloudy with debris, 3: clear liquid oil. The results for each location will be summed (Meibomian gland secretion score, MGS, range = 0 to 45). A score of ≤ 15 (on a scale of 0 to 45) for 15 glands of the lower lid in both eyes is required to be eligible for this study. In addition, the total number of functional Meibomian glands, defined as having a liquid section with a grade 2 or 3, will be counted (range = 0 to 15).

4.5.8 MEIBOMIAN GLAND IMAGING

While seated at the OCULUS Keratograph 5M, 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 upper eyelid.

The grading of Meibomian gland dropout will be conducted on the images after all participants are completed. Images will be graded according to Pult's 5-grade meiboscale (Figure 3).[9]

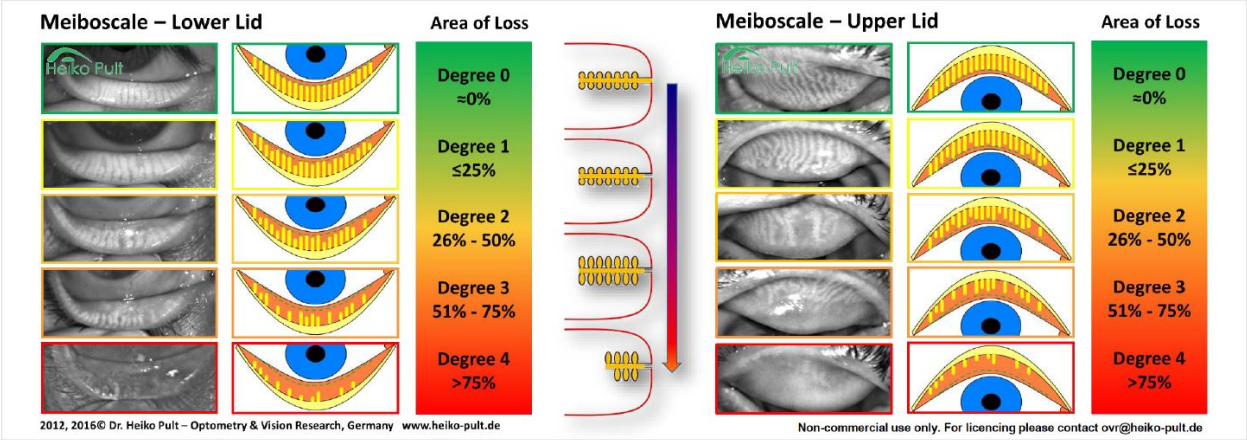

Figure 3: Meiboscale for grading the percentage of Meibomian gland dropout[9]

4.5.9 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 the 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. If detected, the anomaly will be described.

Lids

The presence or absence of the following findings will be recorded:

- Erythematous lid margins
- Thickened lid margins
- Significant telangiectasia
- Irregular or serrated lid margins
- Blepharitis
- Other lid conditions: entropion, ectropion, significant lid oedema, trichiasis, ptosis, lagophthalmos, blepharospasm

Bulbar and limbal hyperemia

The redness of the bulbar and limbal conjunctiva of both eyes will be assessed.

Cornea

The presence or absence of scars or other corneal observations will be recorded and described.

Endothelium abnormalities:

The presence or absence of endothelium abnormalities will be recorded and described.

Anterior chamber

The presence or absence of anterior chamber reaction will be recorded and described.

Other abnormalities

The presence or absence of other abnormalities will be recorded and described.

Corneal and conjunctival staining

A sodium fluorescein strip, wetted with a few drops of saline, will be applied to the inferior temporal tarsal conjunctiva of both eyes. Staining will be graded while viewing with cobalt blue light through a Wratten no. 12 barrier filter.

Palpebral conjunctival hyperemia and papillae (roughness)

The redness and roughness of the upper and lower eyelids will be assessed.

4.5.10 CONTACT LENS FIT ASSESSMENT

Contact lens fit:

Lens fit will be assessed to ensure acceptable lens fit with the participant's habitual contact lenses. The following will be assessed:

- Monocular & binocular distance logMAR visual acuity (high contrast, high illumination)
- Centration in primary gaze (scale: optimal, slight decentration, moderate decentration but not encroaching limbus, excessive & occasionally encroaching limbus)
- Post-blink movement in primary gaze (mm)
- Lens tightness (push-up test) in primary gaze (0-100, where 0= falls from the cornea without lid support, 50 = optimum, 100 = no movement)
- Overall fit (0-4, where 0=lens should not be worn at all, 4= perfect)

Contact lens wettability and deposits:

Contact lens wettability and deposits will be graded with participant's habitual and study lenses using 32x magnification, on a 0-4 scale in 0.25 steps where 0 = excellent wettability, 0= no deposits.

4.5.11 LID MARGIN CLEANING

The lower lid margins of both eyes, including the area directly over the Meibomian gland orifices, will be cleaned prior to administering iLux® treatment. Cleaning the lid margins will remove any devitalized cellular material and other accumulated buildup along the lid margins.[10, 11] A golf club spud is used to gently remove debris, with anesthetic. This procedure is not intended to remove tissue that cannot be removed with gentle motion and gentle pressure of the golf club spud. The participant should not experience discomfort. The "wet" conjunctiva will not be debrided. The following steps will be taken:

1. Instill one drop of Alcaine (0.5% proparacaine hydrochloride). Soak a cotton tip with Alcaine and dab the cotton tip along the lid margins.
2. A sodium fluorescein strip, wetted with a few drops of saline, will be applied to the inferior temporal bulbar conjunctiva of both eyes to aid visualization of the Line of Marx.
3. With the participant seated at the slit lamp (16x magnification), the participant will be instructed to look up.
4. The golf club spud will be placed onto the lid margin, directly over the Line of Marx which should be stained with fluorescein.
5. The golf club spud will be gently maneuvered in small wiping motions (nasal to temporal or vice versa) with mild pressure across the entire length of the Line of Marx.
6. After cleaning the Line of Marx, examine the lid margin to ensure there are no stained cells visible.
7. After cleaning the Line of Marx, any remaining accumulated debris on the keratinized lid margin and any accumulated material potentially obstructing the Meibomian gland orifices will be removed. The golf club spud will be placed onto the keratinized lid margin with **the tip of the spud placed at the edge of the Line of Marx** which was previously cleaned.
8. The golf club spud will be gently maneuvered in small wiping motions (nasal to temporal or vice versa) with mild pressure across the entire length of the keratinized lid margin surface, covering all areas **from the edge of the Line of Marx to the base of the lashes at the lash line**.

9. After cleaning the keratinized lid margin, examine the lid to ensure that little to no sheen is visible on the lid margin surface, and any functional Meibomian gland orifices are exposed.
10. For the upper lid, the participant will be instructed to look downwards during the procedure.
11. The participant is instructed to notify the investigator if they experience any discomfort during any part of this procedure.

4.5.12 ILUX® TREATMENT

The upper and lower eyelids of both eyes will be treated with the iLux device using a single disposable Smart Tip. Each eyelid will be divided into two treatment zones: nasal-central, central-temporal. Each zone will be treated for all eyelids of both eyes. The same procedure is applied for each zone. A new Smart Tip will be used for each new participant. One drop of Alcaine (0.5% proparacaine hydrochloride) will be instilled to each eye immediately before iLux® treatment.

The following steps will be taken:

1. With the participant reclined, instruct the participant to look up (if treating the lower lids) or down (if treating the upper lids).
2. Slide the inner pad behind the eyelid positioned to the treatment zone. Confirm the appropriate position by looking through the magnification panel of the device.
3. Slide the Heater Control Switch forward to slide the outer pad gently hold the eyelid in position and deliver heat to the treatment zone.
4. Deliver heat to the treatment zone for 40-90 seconds (indicated by the “melting time” value on the screen display) while looking through the magnifying lens. The duration of heat application is dependent on the quantity of meibum expressed from the glands in the treatment zone.
5. After the application of heat, slide the Heater Control Switch to deactivate the heating LED lights and to move the device to the expression phase.
6. Perform 4 rounds of compression, lasting 5 seconds each. Keep visualizing the quantity and quality of meibum expressed from the glands.
7. Gently remove the inner pad from the eyelid and repeat the process on the remaining treatment zones for each eyelid.
8. Participants will be instructed that they can resume contact lens wear one hour after completion of iLux® treatment unless there is an adverse event, as determined by the investigator and participant. In the case of an adverse event (e.g. ocular surface irritation,

inflammation or discomfort), participants will be advised when to resume contact lens wear following resolution of the event.

4.5.13 BLINKING EXERCISES

After the administration of the iLux® treatment, the participant will be instructed on how to perform blinking exercises. These exercises will be performed daily, every hour for a minimum 10 times per day until the 1 month follow-up visit to ensure the flow of oils from the Meibomian glands is sustained. The exercises will practiced with the participant before they leave after their treatment, and will also receive the information on a printed handout. Participants will be instructed to:

1. Place their fingers at the corner of their eyes to feel the lid movement.
2. Close their eyelids together with the upper and lower lids completely touching for a count of 2. When the lids are closed correctly, the participant should not feel like movement under their fingers.
3. Squeeze their eyelids lightly for a count of 2. When squeezing their eyelids lightly, they should feel slight lid movement under their fingers. With a moderate squeeze, they should feel the contraction of the lid muscles under their fingers.
4. Open their eyelids for a count of 2.
5. Repeat the cycle nine more time to reach a total of 10 repetitions: CLOSE and count 1 and 2 - SQUEEZE and count 1 and 2 - OPEN and count 1 and 2.

5 MONITORING PROTOCOL ADHERENCE

All study personnel, including investigators, will undergo training on the protocol and their specific role. Procedures for monitoring and reporting protocol deviations are described in the protocol (Section 13.4).

6 POTENTIAL RISKS AND BENEFITS TO HUMAN PARTICIPANTS

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

Contact lenses in this study will be worn on a daily wear basis, for at least 5 days per week and at least 6 hours per day. 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. As participants will be

wearing their habitual contact lens type in this study, there is no increased risk from wearing the lenses in this study. Due to the daily wear nature of the study, this study considered a non-significant risk study based on United States Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines.

This study will provide participants with one treatment with the iLux® device. A safety study has found that iLux® treatment does not cause excessive heating of the cornea, outer eyelid or surrounding surface. It is possible that participants may experience: eyelid/eye pain requiring discontinuation of the treatment procedure, eyelid irritation or inflammation, temporary reddening of the skin, ocular surface irritation or inflammation (e.g., corneal abrasion, conjunctive oedema or conjunctival hyperemia), and ocular symptoms (e.g., burning, stinging, tearing, itching, discharge, redness, foreign body sensation, visual disturbance, sensitivity to light).

Additionally, it is possible that participants may experience temporary discomfort associated with the other study procedures including: burning and stinging, blurred vision, sandiness or grittiness, light sensitivity, dryness, itching, crusty eyes and foreign body sensation. The use of topical numbing (anaesthetic) eye drops may also cause stinging, burning or an allergic reaction. A dye (fluorescein) normally used for eye exams is being used in this study. Although rare, it is possible that participants may have any allergic reaction to the dye. This could cause discomfort to their eye.

Participants may benefit directly from taking part in this study as they will receive a treatment that will manage their dry eye disease that may improve their contact lens wear experience. Information from this study may help researchers come up with new management options to help others with contact lens discomfort in the future. Participation in this study may contribute to scientific research information that may be used in the development of new treatments for dry eye disease and contact lens discomfort.

7 ADVERSE EVENTS

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

An ‘adverse event’ (AE) refers to any untoward medical occurrence in a subject administered an investigational product or subjected to an investigational study procedure. 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

therefore be any unfavorable and unintended sign, symptom, or disease temporarily associated with the investigational product / study procedure, whether there is a causal relationship or not.

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). Data will not be included in statistical analysis, unless permission is granted by the participant at the time of discontinuation. 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 $70 for completing the study for the treatment group and $80 for the control-treatment group. This reflects a reimbursement rate of $20 per hour.

10 STATISTICAL ANALYSIS AND DATA MANAGEMENT

10.1 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, sex). The appropriate tests will be selected based on tests of normality; non-parametric tests will be used for data not showing a normal distribution. Analysis of variables will be conducted separately on each eye, and data will not be pooled. For assessments conducted for each eye separately, the right eye will be used for analysis if there is no difference between eyes.

The following planned comparisons of the key endpoints (SPEED scores, MGS, pre-lens tear break-up time, reported average wear time and comfortable wear time) will be made:

- Within group comparisons:
    - Baseline vs. 1 month [2-sided paired t-test or Wilcoxon signed rank test]
    - For treatment group only: Baseline vs. 1 month vs. 3 month [Repeated measures ANOVA or Friedman test]
    - Baseline vs. 1 month pooled data (i.e. treatment group and control-treatment group after 1 month treatment) [2-sided paired t-test or Wilcoxon signed rank test]
- Between group comparisons:
    - 1 month post-treatment vs. 1 month control (i.e. no treatment) [2-sided independent t-test or Mann-Whitney U test]

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.

At the completion of the study CORE may provide a copy of the study data to the funder. Data will typically be sent using a secure file share system operated by the University of Waterloo called Sendit which uses 128bit (or 256bit) SSL encryption. This system provides a secure way to transfer files when email is not appropriate, whether because of file size, file type or concerns over security. Sendit includes features such as password protection, a restricted time period for download, IP logging and email notification of download. Files may be encrypted prior to transmission at the request of the sponsor. Using this method means that data files are only stored on University of Waterloo servers during the transfer.

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. Documentation of training will be kept at CORE.

12 STUDY MONITORING

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 two people and the entries will be compared. All adverse events and protocol deviations will be reviewed by the Lead Investigator. All serious adverse events and major protocol deviations will be reviewed by the Principal Investigator.

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.

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), 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/

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 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.

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_v02_Clinical data management.

14 REPORT

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

15 REFERENCES

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3. Blackie CA, Coleman CA, Nichols KK, et al. A single vectored thermal pulsation treatment for meibomian gland dysfunction increases mean comfortable contact lens wearing time by approximately 4 hours per day. Clin Ophthalmol 2018;12:169-83.

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