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Protocol

Protease and cytokine composition in post lens tear reservoir of scleral lenses for Keratoconic eyes

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Table of Contents

Confidentiality

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Disclaimer

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

14 INTRODUCTION

Scleral contact lenses are rigid gas permeable lenses designed to rest on the sclera while vaulting over the cornea with a fluid reservoir. (1) The use of scleral contact lenses has become the current standard of practice as a nonsurgical management of corneal ectasia and ocular surface diseases.(1–3) Currently, the long term impact which scleral contact lens wear has on the physiology of the cornea and limbus is not known. Tear film analysis of changes in levels of proteinases and cytokines have helped researchers gain a better understanding of pathophysiology in complications in soft contact lenses wearers (4,5), dry eye (6), and keratoconus (7,8). Understanding factors that influence tear film composition may aid in better understanding of the impact of scleral contact lenses on the health of the cornea, specifically, the mechanism of complications commonly associated with the usage of these large gas permeable lenses.

14 PURPOSE AND HYPOTHESIS

The purpose of this study is to investigate changes in the level of inflammatory mediators in the tear film of scleral contact lenses wearers. The hypothesis is that scleral contact lens wear is associated with inflammation in the tear film. Furthermore, the level of proteases and cytokines will be altered in samples collected post scleral lens wear compared to those collected pre-lens wear. Additionally, the amount of alteration will correlate to the fitting characteristics in the limbal zone of the scleral lenses.

14 OBJECTIVES

We propose to take a sample of keratoconic participants and fit them in scleral lenses and:

1. To collect and examine tear samples before and after 6-8 hours of scleral lens wear.
2. To measure the level proteases and cytokines in each of the samples using enzyme-linked immunosorbent assays (ELISA)
3. To compare the results of varying limbal clearance in scleral lens fit.

14 MATERIALS AND METHODS

13.1 STUDY DESIGN

12.1.1 OVERALL DESIGN

This will be a prospective cross-over, dispensing study design. The study will involve up to 20 keratoconic participants.

Participants will attend 1 screening/fitting visit wearing their habitual contact lenses where the two test lens designs will be fitted. There then will be a dispensing visit for each design (randomly selected) and a single follow up visit 2 weeks later after 6-8 hours of scleral lens wear. A washout period of a minimum of 72 hours will be applied between the cross-over of each lens design.

Lenses to be worn in this study will be made of Boston XO material and are approved by Health Canada. The lenses will have a diameter of 14.8 to 17.8mm with a high and low sagittal depth at the limbal zone. As to which of the two lenses is being assessed, both the investigator and the participant will be masked.

13.2 STUDY POPULATION

12.2.1 SAMPLE SIZE CALCULATION

A sample of 15-20 participants was chosen according to historical data on tear assessment in this group of participants.

12.2.2 NUMBER OF PARTICIPANTS

Recruitment: Up to 20 participants will be enrolled. Participants who are patients of the University of Waterloo Contact Lens Clinic (UW-CLC) will be invited to participate in this study by their attending doctor. With the patient's permission, the investigators will initiate recruitment according to the in-person script approved by the Office of Research Ethics (Appendix 1). The investigators will discuss the project where any questions regarding the study procedures and any risks associated with the study can be answered. Eligibility will be determined using the inclusion and exclusion criteria. Informed consent will be obtained for all participants prior to their enrollment in the study (Appendix 2).

INCLUSION CRITERIA

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

- Had been diagnosed with keratoconus in at least one eye.

- Is at least 18 years of age and has full legal capacity to volunteer.
- Has read and understood the information consent letter.
- Is willing and able to follow instructions and maintain the appointment schedule.

EXCLUSION CRITERIA

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

- Is using any topical medications that will affect ocular health.
- Has any ocular pathology or severe insufficiency of lacrimal secretion (severe dry eyes) that would affect the wearing of contact lenses.
- Has persistent, clinically significant corneal or conjunctival staining using sodium fluorescein dye.
- Has any clinically significant lid or conjunctival abnormalities and active neovascularization.
- Is aphakic.
- Has undergone any corneal surgery.
- Is participating in any other type of eye related clinical or research study.
- Has any known allergies or sensitivity to the diagnostic pharmaceuticals or products, such as fluorescein, used in this study.

13.3 STUDY MATERIALS

12.3.1 VISANTE OCT

The Visante OCT Optical Coherence Tomographer, a standard optometric class II medical device, commercially available in Canada (Health Canada licence #69113), will be used to measure the shape of the eye for contact lens fitting.

12.3.2 PENTACAM

The Oculus Pentacam®, a standard optometric class II medical device, commercially available in Canada (Health Canada licence #69466) will be used for the measure the corneal curvature.

12.3.3 KERATOGRAPH 4

The Oculus Keratograph® 4, a standard optometric class II medical device, commercially available in Canada (Health Canada licence #90001) will be used for the limbal and bulbar redness evaluation and pre-lens non-invasive tear break-up time (NITBUT) measurements.

12.3.4 SEMI-SCLERAL LENSES

The lenses used in this study are approved by Health Canada, with Health Canada license # 29758, and are commercially available. All lenses will be worn during the day only. Lenses will be fitted according to manufacturer's recommended guidelines and participants will proceed in the study only if a suitable fit with the lenses can be obtained. Appendices 9 (Package insert for Boston XO) and 10 (Custom Stable Fitting Guide) are included.

12.3.5 TEAR FILM ANALYSIS

Tear film analysis is performed using antigen capture enzyme linked immunosorbent assay (ELISA). (5) After collection, the tear samples are stored at -80ºC until analysis. Preparation of the samples includes dilution with phosphate buffered saline (PBS) containing 1% (w/v) bovine serum albumin and incubation with specific antigen. The tears are assayed for specific proteinase and cytokines using commercially available ELISA kits. Preparation and analysis of samples are as per instructions supplied by manufacturers.

13.4 SCHEDULED AND UNSCHEDULED VISITS

This study has a total of 6 study visits, including the screening visit (see Table 1).

12.4.1 SCREENING

The investigator will determine participant eligibility by reviewing the inclusion and exclusion criteria. Ineligible participants will be advised they do not meet the criteria for the study.

12.4.2 STUDY VISITS

This study will involve 6 visits over 5 study days. The total time commitment for all study visits is approximately 6 hours. The total study visit time commitment may be different for each participant, as the needed visit time will depend on how easily the lenses can be fitted.

The first visit will involve screening of the participants and baseline measurements. The investigator will determine the eligibility of the participant using the inclusion/ exclusion criteria. Ineligible participants will be discontinued from the study. The investigator will also perform baseline tear collection.

At the lens fitting appointment, the participants will be fitted with the scleral contact lenses based on the baseline measurement obtained at the screening appointment. Participants will be instructed on insertion, removal, and proper handling of the lenses.

At each of the lens delivery appointments, the researcher will deliver the study lenses. Measurements, including bulbar hyperemia and pre-lens NITBUT, will be obtained while the participants are wearing the lenses.

After the participant has worn the lenses during the day for two weeks, the participant will return for a follow up visit. At each of the follow up appointments, the lens fit and measurements, including bulbar hyperemia and pre-lens NITBUT, will be repeated while the participants are wearing the lenses. Tear samples will be collected from the study lenses after lens removal.

A wash-out period of minimum of 72 hours is required between the first follow up visit and the second lens delivery visit.

Table 1 provides a summary of the study visits.

Table 1: Summary of visits

Visit code	Visits	Time
0-0	Screening and baseline measurements	1hr±½ hr
1-1	Lens fitting	1hr±½ hr
2-1	Lens Delivery visit - Lens 1	1hr±½ hr
2-2	Follow-up visit - Lens 1	1hr±½ hr
3-1	Lens Delivery visit - Lens 2	1hr±½ hr
3-2	Follow-up visit - Lens 2	1hr±½ hr

12.4.3 UNSCHEDULED VISITS

Unscheduled visits will be performed if necessary.

13.5 STUDY PROCEDURES

12.5.1 SCREENING, BASELINE AND EXPERIMENTAL MEASUREMENTS

Screening & Baseline procedure: Participants will present to the screening visit. Their corneal sagittal depth which will be measured with the Visante OCT, auto-refraction and associated visual acuity measurements and corneal topography carried out and biomicroscopy performed, along with hyperemia imaging and pre-lens non-invasive tear break up time. Eligibility will be confirmed and a baseline biomicroscopy assessment will be performed. (Visit 0-0)

Bulbar and Limbal Redness assessment: The eyes of the participants will be imaged using the Keratograph® 4. Participants will be asked to be seated at the Keratograph 4 instrument and will be asked to blink 2-3 times and hold their eye open for a few seconds until the instrument software takes a picture of the eye. This image will be repeated three times.

Flush tear collection method: This procedure entails the instillation of a small amount non-preserved saline, 60µL, into the inferior palpebral fold. After which, the fluid can be collected with a micro-capillary tube. (9,10) All samples are collected by the researcher. (Visit 0-0)

Fitting of the semi-scleral lenses: Participants will be fitted each of the two sets of semi-scleral lenses of varying sagittal depth at the limbal zones. Fittings will be done using the corneal sagittal depth which was measured at the screening/baseline visit with the Visante OCT. The lenses will be made of the same gas permeable lens material Boston XO. The lens fit will be evaluated; over-refraction and visual acuity determined. Participants will be instructed on insertion, removal, and proper handling of lenses. (Visits 1-1)

Video Imaging procedure with test lenses: The lens fitting will be imaged using a video-slit lamp and the Visante OCT after the lens delivery appointment (Visits 2-1 & 3-1) and at the follow up appointment. (Visits 2-2 & 3-2)

Pre-lens Non-invasive tear break up time (NITBUT) with test lenses: Pre-lens NIBUT will be measured with the study lens after lens delivery (Visits 2-1 & 3-1) as well as at the follow up visits (Visits 2-2 & 3-2). Participants will be asked to be seated at the Keratograph 4 instrument and will be asked to blink 2-3 times and hold their eye open for a few seconds until the instrument software takes a measurement of the NITBUT. This measurement will be repeated three times.

Subjective ocular symptom assessment: At the follow up appointment, participants will be asked to rate their ocular comfort, dryness, burning and vision with the contact lenses (Appendix 5). (Visits 2-2 & 3-2)

Table 2 lists a summary of procedures to be conducted at scheduled visits.

Table 2: Summary of procedures to be conducted at scheduled visits

Visit	Procedure	Instrument/ application	Form (Appendix #)
Screening & Baseline visit (0-0)	Informed Consent	-	ICL (2)
	Demographics & History, incl. health, meds, contact lens details	-	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Baseline Tear Collection	-	Biomicroscopy Form (4)
	Sagittal depth measurement	Visante OCT	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Auto-refraction/ topography	Auto-refractor/ Pentacam	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Vision assessment	Vision charts	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Slit-lamp biomicroscopy (Corneal integrity & staining)	Slit-lamp	Biomicroscopy Form (4)
	Hyperemia / NITBUT	Keratograph 4	Biomicroscopy Form (4)
Lens Fitting (Visits 1-1)	Lens Insertion	-	-
	Lens examination	Slit lamp	Screen/Fitting and Study Visit Form for GP Lenses (3)
Lens Delivery (Visits 1-1 & 2-1)	Lens examination	Slit lamp	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Auto-refraction/ topography	Auto-refractor /Pentacam	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Vision with study lens	Vision charts	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Subjective Best Sphere	Vision charts	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Hyperemia / NITBUT	Keratograph 4	Biomicroscopy Form (4)
	Ocular Symptom Questionnaire	-	Ocular Symptom Questionnaire (5)
Follow-up visit (Visits 1-2 & 2-2)	Lens examination	Slit lamp	Screen/Fitting and Study Visit Form for GP Lenses (3)
	Hyperemia / NITBUT	Keratograph 4	Biomicroscopy Form (4)
	Ocular Symptom Questionnaire	-	Ocular Symptom Questionnaire (5)
	Lens Removal	-	-
	Slit-lamp biomicroscopy (Corneal integrity & staining)	Slit-lamp	Biomicroscopy Form (4)
	Tear Sample Collection from Lens after Lens Removal	-	Biomicroscopy Form (4)

14 POTENTIAL RISKS AND BENEFITS TO HUMAN SUBJECTS

There may be direct benefits to the participants in this study as they will experience a new lens fitting modality. Participation in this study may contribute to scientific research information that may be used in the development of new contact lens products.

This study is considered to be a non-significant risk study based on United States Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines due to the daily wear nature of the study.

The lenses used in this study are approved by Health Canada and commercially available. The lenses are intended for daily wear (NOT extended wear). This study is a dispensing study. The participants' lens wear will be monitored closely by the investigators as participants will be able to be in close contact with the investigator by phone at any time.

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 with gas permeable rigid lenses, the possibility does exist. The occurrence rate of incurring a bacterial infection for patients that wear rigid gas permeable lenses is approximately two/10,000 per year. (11)

If the participant should experience any pain or discomfort during lens wear, any of the symptoms described above, or there is any health concern or a case of emergency, they are instructed to contact Dr. Yeung or Dr. Sorbara at (416)-624-7167 or (519) 888-4567 extension 33085, respectively.

Although participants with any known allergies or sensitivity to the diagnostic pharmaceuticals or products, drops such as fluorescein, used in this study would have been excluded, if any irritation occurs the participant will be instructed to contact the investigators.

14 UNINTENDED EVENTS

The imaging procedures outlined in this protocol will be carried out with instruments that are typically used in any optometric practice and therefore, there are no anticipated unintended events.

14 DISCONTINUATION FROM THE STUDY

Participants discontinued from a study will be compensated $20 for each attended visit in the study. Participants will be discontinued at the discretion of the investigators or participant. 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 4.2.2.
- 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.
- Unexpected adverse event: If a participant experiences an adverse event (excessive redness or dryness), at the discretion of the investigator, the participant may be excluded from the study.
- Symptoms: If the participant has persistent symptoms (excessive redness or dryness), the participant may be discontinued from the study 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.
- Lost to follow-up: The participant will be discontinued if they cannot be contacted and does 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 Office of Research Ethics at the University of Waterloo.

14 STUDY COMPLETION AND REMUNERATION

Once their involvement in the study is complete, participants will be informed about receiving feedback following study completion in the Letter of Appreciation (Appendix 6).

Participant remuneration will be up to $120 for completing the study and is typically paid at the end of the study (Appendix 7).

14 STATISTICAL ANALYSIS AND DATA MANAGEMENT

13.1 STATISTICAL ANALYSIS

All data described above will be analysed at the University of Waterloo from the eye(s) wearing the semi-scleral contact lens(es). Data analysis will be conducted using Statistica 12. Descriptive statistics will be provided on information regarding baseline variables (age, gender, sagittal depth distribution, etc.). Table 3 lists the primary outcome variables and anticipated statistical procedures.

Table 3: Statistical procedures

Variable	Analysis	Statistical test
Parametric (tear clearance, NIBUT, comfort ratings, tear components)	Comparison of lens 1 to lens 2	ANOVA Paired t-test

13.2 DATA MANAGEMENT

At the completion of the study, a report will be generated. Data from this study will be referred to only using study number and will be retained by the PI's for a minimum of 25 years on a password-protected server held by Dr Sorbara. After 25 years, data will be disposed of in accordance with the guidelines laid out by the University of Waterloo.

14 PROTOCOL TRAINING

Training of the research assistant will be conducted for this study to educate her about the testing procedures.

14 STUDY MONITORING

Study records may be inspected by the investigator's supervisor, the Office of Research Ethics at the University of Waterloo, and by regulatory authorities in Canada (Health Canada); however, no records containing identifiable/personal information will be permitted to leave the School of Optometry and Vision Science, Contact Lens Clinic.

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 the Office of Research Ethics (ORE) at the University of Waterloo and reviewed by the Clinical Research Ethics Committee. Notification of ethics clearance of the application is required prior to the commencement of the study.

13.3 ADVERSE EVENTS

12.3.1 ADVERSE EVENT DEFINITIONS

An 'adverse event' refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not. Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' as defined below.

Classification	Definition
Serious Adverse Event	Those events that are life-threatening, or result in permanent impairment of a body function, or permanent damage to a body structure or necessitate medical (therapeutic) or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
Significant Adverse Event	Those non-serious adverse events that occur with contact lens usage that are not sight-threatening but are usually symptomatic and may warrant therapeutic management and /or temporary or permanent discontinuation of contact lens wear.
Non-Significant Adverse Events	Those less severe non-serious adverse events that occur with contact lens usage that are not sight-threatening, may or may not be symptomatic and may warrant palliative management, such as ocular lubricants or temporary interruption of contact lens wear.
Unanticipated Adverse Device Effect	Adverse events in a clinical trial that were not previously identified in the protocol in terms of nature, severity, or degree of incidence. An Unanticipated Serious Adverse Device Effect is an unanticipated adverse event that is serious in nature and caused by or associated with the device and is considered reportable.

AE classification, coding and examples are provided in the following table used for reporting.

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

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

12.3.1.1 NORMAL OR ADAPTIVE SYMPTOMS

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

12.3.2 PROCEDURES FOR ADVERSE EVENTS

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the participant may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the test device or a result of other factors. An Adverse Event Form (Appendix 8) will be completed for each adverse event. If both eyes are involved, a separate Adverse Event Form will be completed *for each eye*. Whenever possible, the adverse event will be photo-documented.

Expenses incurred for medical treatment as part of study participation will be paid by the investigator (bills and prescription receipts kept). The participant must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

12.3.2.1 REPORTING ADVERSE EVENTS

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to participant participation will be reported to the Principal Investigator's supervisor within 24 hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the ORE as soon as possible (by fax, mail/delivery, phone, or email) following the University of Waterloo Office of Research Ethics reporting guidelines. All fatal or life threatening events will be reported immediately to the ORE.

Significant and Non-Significant Adverse Events will be reported to the ORE as soon as possible, but no later than 5 working days after the occurrence.

13.4 PROTOCOL DEVIATIONS

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

12.4.1 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 ethics committee;
- 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.

12.4.2 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).

12.4.3 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

The PI's or the Office of Research Ethics at the University of Waterloo may terminate the study at any time for any reason.

14 QUALITY ASSURANCE

13.1 STUDY PARTICIPANT RECORDS

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

- Study number;
- Participant ID;
- Date enrolled;
- Confirmation by lead investigator that participant meets eligibility criteria;
- Confirmation that participant received a signed and dated copy of informed consent;

13.2 RETENTION OF STUDY RECORDS AND DATA

Records and data from this study will be retained for a minimum of 25 years. Paper copies of study data will be safely held in a secure storage cabinet in a locked office at the School of Optometry and Vision Science, University of Waterloo and will be only available to personnel involved in the data collection of this study. The electronic research data will be encrypted as per Guidelines laid out by UW Information and Systems Technology and be stored on a password protected server held in a locked office at the School of Optometry and Vision Science. The images we acquire, with all identifying information removed, will be kept on a secure password protected server stored in a locked office at the School of Optometry and Vision Science. Image data will be saved using a coded file name associated with each participant, and the list of the participants' names and corresponding numbers will be stored in a separate file at UW. Access to electronic data, images, photographs and videos is limited to authorized study personnel.

Records will be confidentially disposed of in accordance with the guidelines laid out by the University of Waterloo. More information regarding the University of Waterloo's policies on information security is available on the following website: https://uwaterloo.ca/secretariat-general-counsel/policies-procedures-guidelines/policy-8.

14 CLINICAL TRIAL REGISTRATION

Because this protocol is intended to test the early feasibility of the device and/or concept(s) being studied, it is not considered as an applicable clinical trial for clinical trials registry (www.ClinicalTrials.gov or equivalent). As such, this clinical trial will not be registered.

15 REPORT

A report will be generated within 4 weeks after the completion of the study for inclusion in the PI's thesis.

16 APPENDICES

Appendix 1A and 1B Email recruitment script
Appendix 2 Information consent letter
Appendix 3 Screening/Fitting and Study Visit Form for GP Lenses
Appendix 4 Biomicroscopy form
Appendix 5 Ocular Symptom Questionnaire
Appendix 6 Feedback and appreciation letter
Appendix 7 Study Completion/Remuneration Form
Appendix 8 Adverse Event Form (ORE)
Appendix 9 Package Insert Boston XO Material
Appendix 10 Fitting Guide for Custom Stable lenses

17 REFERENCES

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