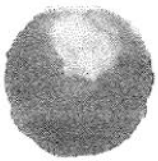

CooperVision

Protocol:

A TWO-WEEK CROSSOVER DISPENSING EVALUATION OF ORION DAILY WEAR SOFT CONTACT LENSES

Sponsor Study Code:	CV-20-18
Version Number:	1.0
Protocol Date:	20 Aug 2020
Sponsor Company:	CooperVision, Inc.
Study Category:	Design Validation
Clinical Sites:	CORL, Indiana University School of Optometry 800 E. Atwater Avenue, Bloomington, IN 47405
Sponsor:	**CooperVision, Inc.** 5870 Stoneridge Drive, Suite 1 Pleasanton, CA, USA 94588

Study Sponsor Representative: [redacted] Date: [redacted]

[redacted]

CooperVision Sponsor Management [redacted] Date: [redacted]

[redacted]

Site Principal Investigator: [redacted] Date: [redacted]

[redacted]

Protocol:

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Site Principal Investigator: [redacted] Date: [redacted]

TABLE OF CONTENTS

DOCUMENT CHANGE HISTORY

Version	Originator	Description of Change(s)	Date
1.0	[redacted]	Original Protocol	20-Aug-2020

1 Introduction

CooperVision is evaluating the clinical performance of Orion (riofilcon A with DAB) Test lens compared to Gemini ([redacted]) Control lens when worn on a daily wear, daily disposable modality in a randomized, bilateral crossover dispensing study.

2 Study Objective

This is a feasibility study to evaluate the clinical performance of a new silicone hydrogel formulation lens (Orion) in comparison with Gemini A[redacted] over a period of two weeks of wear.

The primary variables of interest are:

- Vision

The secondary variables of interest are:

- Comfort/comfort preference
- Surface wettability performance
- Lens fit
- Lens handling
- Anterior ocular health

2.1 Study Hypothesis

The primary hypothesis is that there will be no difference in vision performance between the Orion Test lens and the Gemini Control lens.

The secondary hypothesis is that there will be no difference in performance between the Orion Test lens and the Gemini Control lens for any of the secondary variables.

3 Study Design

This will be a double-masked, randomized, bilateral, two-week crossover, dispensing study, comparing the Orion Test lens against Gemini Control lens, such that each daily replacement lens type will be worn on a daily wear, single use basis for two weeks each. Each subject will be randomized to wear either the Test lenses or the Control lenses potentially as an unmatched pair (with regards to power), according to a predetermined randomization schedule. All lenses will be

replaced daily. Electronic (e.g. email or SMS text survey link) comfort questionnaires will be administered during the course of the study.

It is anticipated that this study will involve up to 4 scheduled visits:

- Visit 1a: Enrollment / Screening / Baseline Visit (Day 0)
- Visit 1b: Dispensing of Pair 1 (Day 0)
- Visit 2: Two-week follow-up of Pair 1 (-1/+4 days) and Dispensing of Pair 2
- Visit 3: Two-week follow-up of Pair 2 (-1/+4 days) and Exit

3.1 Study Design & Comparator Justification

The study design was chosen since the influence of counfounding covariates is reduced in crossover designs, as each subject acts as his or her own control. Crossover study designs are also statistically more efficient.

The choice of comparator was made since the aim of the project is to match the clinical performance of the Gemini (Acquiane) lens, which is CE-marked / already approved in Europe.

4 Ethics Review / Statement of Compliance

4.1 Relevant Standards / Guidelines

This protocol has been developed in accordance with 21 CFR Part 812: Investigational Device Exemptions and with the ethical principles of:

- ISO 14155 Clinical Investigation of Medical Devices for Human Subjects
- Declaration of Helsinki

4.2 Institutional Review Board

This study will be conducted in accordance with Institutional Review Board regulations (U.S. 21CFR Part 56.103) or applicable IEC regulations. Copies of all IRB/IEC correspondence with the investigator/sponsor will be kept on file.

The conduct of this study will be approved by Sterling Institutional Review Board. Approval will be received prior to undertaking the study. Any additional requirements imposed by the Ethics Commitee/IRB or separate regulatory authority will be followed.

4.3 Informed Consent

Informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is carried out.

5 Clinical Trial Registration

This Study will be registered with ClinicalTrials.gov in accordance with Section 801 of the Food and Drug Administration Act (FDAA) which mandates the registration of certain clinical trials of drugs and medical devices.

6 Potential Risks and Benefits to Human Subjects

There might not be direct benefits to the subjects in this study. However, participation in a study may contribute to scientific research information that may be used in the development of new contact lens products. In addition, subjects will receive an examination of the front part of their eyes and may have the opportunity to try a different type of soft contact lenses and/or different lens care products at no cost to them.

This study is considered to be a non-significant risk study based on United State Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines due to the daily wear nature of the study. The risks to the subjects are also reduced based on the results of biocompatability testing.

Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The incidence of infection due to day-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. This risk is assumed by 35-million Americans who currently wear contact lenses.

Routine clinical procedures including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and contact lens fitting will be used. In addition, high magnification imaging of the lens fit may be made using 35 mm or digital cameras, in vivo confocal microscopy, and/or specular microscopy.

7 Materials and Methods

7.1 Participants

Up to 70 subjects will be enrolled and dispensed in order for approximately 60 subjects to complete the study. Each subject will be given a unique ID number. ID numbers will not be reused in event of screen failure or discontinuation. Additionally, all subjects must meet the study inclusion and exclusion criteria listed below.

Inclusion criteria

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

- Is at least 18 years of age and has full legal capacity to volunteer.
- Is no greater than 55 years of age.
- Has read and understood the information consent letter.
- Is willing and able to follow instructions and maintain the appointment schedule.
- Is an adapted soft contact lens wearer having worn lenses for a minimum of 4 weeks prior to the study.
- Has spectacle cylinder ≤1.00D in both eyes.
- Has spherical contact lens power requirement between -1.00D and -6.00D in both eyes.
- Has manifest refraction visual acuities (VA) equal to or better than logMAR equivalent of 20/20 in each eye.
- Wears CLs in both eyes (monovision acceptable, but not monofit)
- Has clear corneas and no active ocular disease.
- Has not worn lenses for at least 12 hours before the examination.
- Is willing to wear the study contact lenses for a minimum 8 hours per day/6 days per week

Exclusion Criteria

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

- Has never worn contact lenses before.
- Has any systemic disease affecting ocular health.
- Is using any systemic or topical medications that will affect ocular health.
- Has any ocular pathology or severe insufficiency of lacrimal secretion (moderate to 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, active neovascularization or any central corneal scars.
- Is aphakic.
- Has strabismus/amblyopia.
- Has undergone corneal refractive surgery.
- Is pregnant, lactating or planning a pregnancy.
- Is participating in any concurrent clinical or research study.

7.2 Study Materials

7.2.1 Contact lens

Subjects will be randomized to receive the Test and Control lenses bilaterally potentially as an unmatched pair (with regards to power), per a predetermined randomization schedule. The daily disposable/single use lenses used in this study will be provided by the Sponsor. Details of the contact lenses are shown in Table 1.

Table 1: Study lenses

	Test Orion	**Control Gemini** [redacted]
Labelling	Masked Investigational	Masked Investigational
Manufacturer	Coopervision, Inc.	Coopervision, Inc.
Material	riofilcon A with DAB	riofilcon A
Water Content	8.60	8.60
Base curve (mm)	14.00	14.00
Power (D)	-1.00 to -6.00 (0.25 steps)	-1.00 to -6.00 (0.25 steps)

7.2.2 Contact Lens care

No contact lens care is required for this study as lenses are to be worn for a single day only.

7.2.3 Storage of Lenses and Lens Care Solutions

The study materials must be stored in a secured area. All lenses and lens care solutions should be stored at controlled room temperature (59-86°F).

7.2.4 Clinical Supply Inventory

The investigator must keep an accurate accounting of the study product during the study. A detailed inventory must be completed for study supplies. The study supplies are to be used in accordance with the protocol by subjects who are under the direct supervision of an investigator.

7.2.5 Disposal of Consumables

This study dispenses consumables (lenses) to participants for use during the study. Subjects will be asked to retain their lens foils each day for return to the study investigator, for lens accountability purposes. Additionally, study lenses worn by participants at the 2-week follow-up visits will be collected and stored in either an unbuffered or phosphate buffered (not borate) saline for return to the Sponsor.

7.2.6 Masking and Control of Study Materials

The contact lenses coding will be masked to both the investigator and subject.

7.2.7 Ordering and Accountability of Study Materials

The Test and Control lenses will be provided by the Sponsor. The investigator must complete an accurate accounting of the study product at the completion of the study. A detailed inventory must be completed for study supplies. All unused and used materials will be returned to the Sponsor at the end of the study unless the investigator is otherwise directed by the study Sponsor.

7.3 Visit Schedule and Procedures

7.3.1 Visit 1a: Baseline / Screening Visit

Procedures to be Performed

The following evaluations will be performed to assess eligibility according to the Inclusion and Exclusion Criteria at the baseline visit only:

- The patient is expected to attend the baseline visit not wearing their habitual contact lens products.
- The subject will be required to read and sign an Informed Consent Form prior to enrolment. When the subject has signed the consent form, the subject will be considered enrolled onto the study.
- Habitual lens wearing time (average, maximum, average comfortable). Also, habitual type of comfort / re-wetting drops and frequency of use, if any, will be recorded.

- Sphero-cylindrical refraction will be conducted and baseline monocular and binocular High Illumination High Contrast (**HIHC**) and High Illumination Low Contrast (**HILC**) logMAR distance visual acuities recorded.
- Slit lamp biomicroscopy will be assessed according to the guidelines set out in the CVI Grading scales [redacted]
- The investigator will confirm that the patient meets the criteria set out in the inclusion criteria.

7.3.2 Visit 1b: Dispensing Visit (Pair 1)

Dispensing visit may occur on same day as Visit 1a. If Visit 1b is conducted on a different day to Visit 1a, slit lamp biomicroscopy should be conducted again to confirm eligibility.

- HVID (mm) and palpebral aperture size (mm) measurements using slit lamp oculars.
- The first study pair of contact lenses will be selected by the investigator according to the randomization table ([redacted] insertion by the subjects. Subjects will be dispensed the lens power nearest to their refractive error requirement.
- Lenses should be allowed to settle for 10 minutes.
- An initial fit assessment will be made to ensure lens fit is acceptable (Y/N). The subject should be discontinued and exited if the lens fit is found unacceptable and the primary reason for poor fit recorded on the CRF and video footage of the fit collected.
- Monocular spherical over-refraction (SOR) will be conducted to determine if a different lens power is required.
- Monocular and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (SOR will be used if the subject is wearing monovision).
- Final lenses will be inserted and allowed to settle for a further 10 minutes, if applicable.
- [redacted]
  - [redacted]

- Lens surface will then be assessed and graded after settling per guidelines detailed in the CVI grading scales ([redacted])
  - [redacted]
  - Wettability (0-4 scale)
  - [redacted]
  - [redacted]
- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales ([redacted]).
  - Lens centration (0.1mm steps)
  - [redacted]
  - Post-blink movement (0.1mm steps)
  - Mobility rating (0.50 steps)
  - Overall lens movement (-2 to +2 scale)
  - Overall lens fit acceptance and investigator reason, if unacceptable (0.25 steps). Video will be recorded in the event of poor fit. Video will be recorded in the event of poor fit.
- The subject will be instructed to wear the study lenses for a minimum of 8 hours per day / 6 days per week.
- The subject will be dispensed adequate lenses (including spares) to last them until the next study visit.
- The subject will be discharged and scheduled to return for Visit 2 within the required study visit window.

7.3.3 Visit 2: Two-Week Follow-up Pair 1 (-1/+4 days) & Dispensing Pair 2

*Subjects will be asked to wear lenses for **at least 3 hours** prior to the visit appointment.*

- Subjective responses will be collected per the Final Questionnaire [redacted] including:
  - Overall satisfaction (7-point Likert scale)
  - Comfort satisfaction & comfort rating (7-point Likert & 100-point scales)
  - [redacted]

- [redacted]
- Lens handling (7-point Likert & 100-point scales)
- [redacted]
- [redacted]
- Lens holding/handling (5-point Likert scales)
- Vision (7-point Likert & 100-point scales)

- The following information will be collected from the subject by the investigator:
  - Wear time at visit (hours).
  - Average time of insertion and removal during previous week, i.e. average time (hours).
  - Maximum wear time during previous week (hours).
  - Average time of day lenses become uncomfortable, if at all, i.e. average comfortable wear time (hours).
  - Use and frequency of comfort / re-wetting drops during past week (if any).

- Monocular and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (a spherical over-refraction will be performed for the distance eye and recorded first if the subject is wearing monovision).

- Lens surface will then be assessed and graded per guidelines detailed in the CVI grading scales [redacted]
  - [redacted]
  - Wettability (0-4 scale)
  - [redacted]
  - [redacted]

- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales [redacted]
  - Lens centration (0.1mm steps)
  - [redacted]
  - Post-blink movement (0.1mm steps)
  - Mobility rating (0.50 steps)
  - Overall lens movement (-2 to +2 scale)
  - Overall lens fit acceptance and investigator reason, if unacceptable (0.25 steps). Video will be recorded in the event of poor fit.

- The lenses will be removed and stored in either an unbuffered or phosphate buffered (not borate) saline for return to the Sponsor.

- Slit lamp biomicroscopy will be assessed according to the CVI approved study biomicroscopy CRF [redacted]

Dispensing Visit (Pair 2)

- The subject will undergo a saline washout.
- The second study pair of contact lenses will be selected by the investigator according to the randomization table [redacted] for insertion by the subjects. Subjects will be dispensed the lens power nearest to their refractive error requirement.
- Lenses should be allowed to settle for 10 minutes.
- An initial fit assessment will be made to ensure lens fit is acceptable (Y/N). The subject should be discontinued and exited if the lens fit is found unacceptable and the primary reason for poor fit recorded on the CRF and video footage of the fit collected.
- Monocular spherical over-refraction (SOR) will be conducted to determine if a different lens power is required.
- Monocular and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (SOR will be used if the subject is wearing monovision).
- Final lenses will be inserted and allowed to settle for a further 10 minutes, if applicable.
- Subjective responses will be collected per the Post-Settling Questionnaire [redacted], including:
  - [redacted]
  - Lens movement/awareness (5-point Likert scales)
  - Vision (7-point Likert & 100-point scales)
- Lens surface will then be assessed and graded after settling per guidelines detailed in the CVI grading scales [redacted]
  - [redacted]
  - Wettability (0-4 scale)
  - [redacted]
  - [redacted]

- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales ([redacted]).
    - Lens centration (0.1mm steps)
    - [redacted]
    - Post-blink movement (0.1mm steps)
    - Mobility rating (0.50 steps)
    - Overall lens movement (-2 to +2 scale)
    - Overall lens fit acceptance and investigator reason, if unacceptable (0.25 steps). Video will be recorded in the event of poor fit.
- The subject will be instructed to wear the study lenses for a minimum of 8 hours per day / 6 days per week.
- The subject will be dispensed adequate lenses (including spares) to last them until the next study visit.
- The subject will be discharged and scheduled to return for Visit 3 within the required study visit window.

7.3.4 Visit 3: Two-Week Follow-up on Pair 2 (-1/+4 days) & Exit

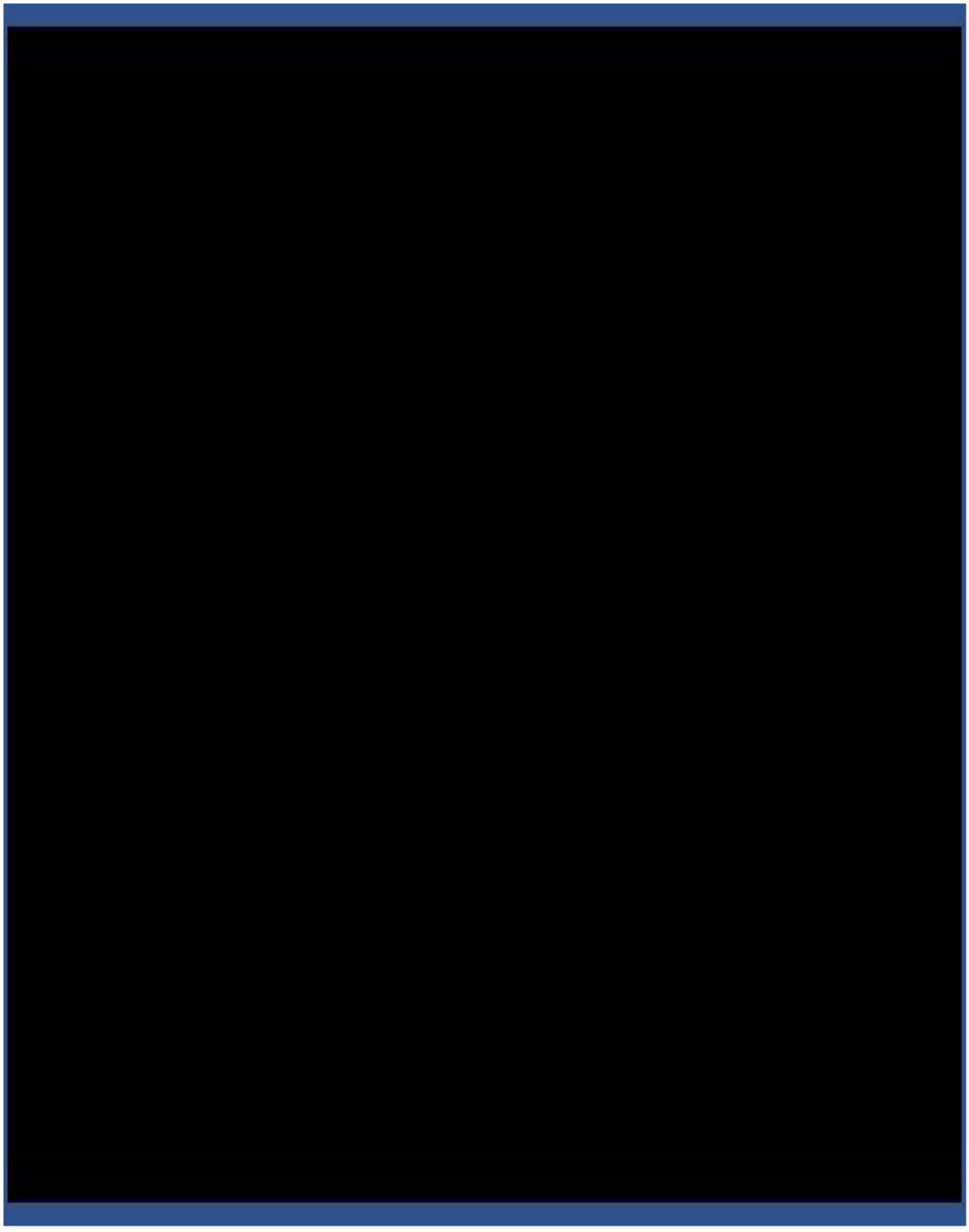
*Subjects will be asked to wear lenses for **at least 3 hours** prior to the visit appointment.*

- Subjective response will be collected per the Final Questionnaire [redacted] including:
    - Overall satisfaction (7-point Likert scale)
    - Comfort satisfaction & comfort rating (7-point Likert & 100-point scales)
    - Comfort on insertion (7-point Likert & 100-point scales)
    - Comfort at end of day (7-point Likert & 100-point scales)
    - [redacted]
    - [redacted]s)
    - [redacted]
    - [redacted]
    - [redacted]
    - Lens handling (7-point Likert & 100-point scales)
    - [redacted]
    - [redacted]
    - Lens holding/handling (5-point Likert scales)
    - Vision (7-point Likert & 100-point scales)
- The following information will be collected from the subject by the investigator:

- Wear time at visit (hours).
- Average time of insertion and removal during previous week, i.e. average time (hours).
- Maximum wear time during previous week (hours).
- Average time of day lenses become uncomfortable, if at all, i.e. average comfortable wear time (hours).
- Use and frequency of comfort / re-wetting drops during past week (if any).

- Monocular and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (a spherical over-refraction will be performed for the distance eye and recorded first if the subject is wearing monovision).
- Lens surface will then be assessed and graded after settling per guidelines detailed in the CVI grading scales (Appendix 4).
  - [redacted]
  - Wettability (0-4 scale)
  - [redacted]
  - [redacted]
- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales [redacted]
  - Lens centration (0.1mm steps)
  - Corneal coverage (Yes / No / Borderline)
  - [redacted]
  - Mobility rating (0.50 steps)
  - Overall lens movement (-2 to +2 scale)
  - Overall lens fit acceptance and investigator reason, if unacceptable (0.25 steps). Video will be recorded in the event of poor fit.
- The lenses will be removed and stored in either an unbuffered or phosphate buffered (not borate) saline for return to the Sponsor.
- Slit lamp biomicroscopy will be assessed according to the CVI approved study biomicroscopy CRF [redacted]
- Subjective response will be collected per the Lens Preference Questionnaire [redacted]
- Exit HIHC monocular distance logMAR visual acuities will be recorded with baseline sphero-cylindrical refraction in place (OD/OS).
- The subject will be discharged and will sign the exit statement.

7.3.5 Email Link or SMS Text Based Comfort Throughout the Day Questionnaire



7.3.6 Training for Use of the Study Products

The study subject willt be instructed by the investigator as to the proper handling, insertion and removal techniques, proper use of the lenses, and the proper accounting and disposal of the used lenses.

Training will be in accordance with the information provided in a separate Subject Instruction Guide. The Subject Instruction Guide will be provided to the subject at the time of initial lens dispensing.

7.3.7 Summary of Visits and Procedures

Table 2 summarizes the visits and procedures for the study.

Table 2: Summary of Visits and Procedures

	Visit 1a *Screening / Baseline*	**Visit 1b** *Dispense Pair 1*	**Visit 2** *2-week follow-up Pair 1 & Dispensing of Pair 2*	**Visit 3** *2-week follow-up Pair 2 & Exit*
Informed consent	✓	-	-	-
Meet inclusion/exclusion criteria	✓	-	-	-
History at baseline	✓	-	-	-
Demographics	✓	-	-	-
Wearing time	✓	-	✓	✓
HVID / palpebral aperture size	-	✓	-	-
Auto-refraction & keratometry	✓	-	-	-
Sphero-cylindrical refraction	✓	-	-	-
HIHC & HILC VAs with sphero-cylindrical refraction	✓	-	-	-
Slit lamp biomicroscopy	✓	✓*	✓	✓
Instillation of lens at office	-	✓	✓	-
Subjective assessments	-	✓	✓	✓
Lens surface assessments	-	✓	✓	✓
Lens fit assessments	-	✓	✓	✓
Spherical over-refraction (SOR)	-	✓	✓	-
HIHC & HILC Distance VAs (with CLs)	-	✓	✓	✓
Lens Preference Questionnaire	-	-	-	✓
Exit VAs	-	-	-	✓
Study Exit	-	-	-	✓

** Not applicable if Visit 1b occurs on the same day as Visit 1a*

8 Adverse Event Reporting

8.1 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 (for reporting to the sponsor) and examples are provided in the following table of Contact Lens Adverse Event Classification and Reporting table:

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	Notify sponsor as soon as possible, **within 24 hours;** IRB reporting as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		

11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	
17	Any sign and/or symptom for which subject is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	
10	Other significant event	

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

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.***

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as Adverse Events.

8.2 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 subject 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 will be completed for each adverse event. If both eyes are involved, a

separate Adverse Event Form will be completed *for each eye*. Whenever possible, the adverse event will be photo documented.

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

8.3 Reporting Adverse Events

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to subject participation will be reported to the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the IRB as soon as possible (by fax, mail/delivery, phone, or email). All fatal or life-threatening events will be reported immediately to the IRB.

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

Sponsor contact details are:

Contact: [redacted]
Email:
Phone:
Address: 5870 Stoneridge Dr.
Suite 1
Pleasanton, CA 94588

A Data Monitoring Committee will not be necessary for this study. The Sponsor will review adverse events per SOP-526, and an impact assessment conducted if required.

8.4 Discontinuation from the Study

A subject's study participation may be discontinued at any time if, in the opinion of the sponsor or the investigator it is in the best interest of the subject. All discontinuations will be fully documented on the appropriate study forms and the Discontinuation Form will be completed.

8.5 Premature Study Termination or Suspension

The clinical study may be suspended or terminated by the Sponsor and/or the reviewing IRB at any time if, in the opionion of the Sponsor or the IRB, it is in the best interests of the study participants.

If the decision is made to terminate the study, the site will be notified to call in the study subjects, perform a final study examination, collect all of the study materials and complete study exit forms and documentation.

9 Device Malfunctions

A device malfunction means the failure of the device to meet its performance specification or otherwise perform as intended. *Any defective lens that is likely to cause or contribute to a Serious Adverse Event should be reported to the Principal Investigator and the sponsor* ***within 24 hours*** *of the investigator becoming aware of the malfunction.*

Other defective lenses should be reported to the Sponsor as soon as possible.

10 Statistical Analysis Plan

10.1 Sample size

Based on historical data, a sample size of 14 completing subjects is sufficient to detect a non-inferiority margin of 0.1 logMAR for the primary variable, visual acuity, assuming α=0.05 and a power of 80% (Table 3).

Table 3: Primary variable (acuity) sample size calculation

Non-inferiority margin for logMAR visual acuity	Mean individual standard deviation	Sample size, Power 80% (p = 0.05)
-0.1	0.07	14

Based on historical data, a sample size of 53 completing subjects is sufficient to detect a non-inferiority margin of -0.75 for the secondary variable, comfort, assuming α=0.05 and a power of 80% (Table 4).

Table 4: Secondary variable (comfort) sample size calculation

Non-inferiority margin for comfort	Mean individual standard deviation	Sample size, Power 80% (p = 0.05)
-0.75	1.3	53

Consequently, a sample size of approximately 60 completing subjects is sufficient for this study.

10.2 Statistical analysis

Summary statistics will be produced (e.g. mean, standard deviation). Paired t-test will be used to compare slit lamp biomicroscopy, lens fit and subjective scores between study lens types. Repeated Measures Analysis of Variance (ANOVA) or paired analysis will be used to compare the variables between study visits. The critical alpha level for statistical significance will be set at $p \leq 0.05$, with adjustment for multiple comparisons.

All participants who were evaluated will be used in the analysis. In the event of missing data, individual data points will be excluded in the analysis and not extrapolated from the collected data.

11 Data Quality Assurance

11.1 Study monitoring

Site qualification of the investigative site has been completed to ensure that the site facility is adequate, personnel are qualified, and resources are satisfactory to conduct clinical studies for the Sponsor. The protocol will be reviewed by the investigators prior to enrollment of the first subject. This will involve an overview of the protocol, which includes information on study objectives, inclusion and exclusion criteria, study visits and adverse event reporting. Data collection forms will also be reviewed, and this will provide an opportunity to discuss any questions.

During the course of the study, remote monitoring will be conducted to verify that written informed consent was obtained using the IRB approved ICF prior to each subject's participation in the study.

Prior to final data freeze, a remote close-out visit/discussion may be warranted to check for accuracy and completeness of records. The sponsor or sponsor's representatives will be authorized to gain access to the source documentation for the purposes of monitoring and auditing the study.

11.2 Record keeping

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

11.3 Record retention

Following study completion, data will be available in electronic and/or paper format for audit, sponsor use, or subsequent analysis. The original clinical raw data (including completed CRFs and Informed Consent forms) will be retained according to guidelines set forth in the general work agreement with the site. The Sponsor will be notified and consulted if ever the files are to be destroyed. In the event that this Study Protocol is indicated for design verification and validation purposes, as indicated on the title page, all original raw data forms and completed CRF's will be forwarded to the sponsor at completion of the final report.

11.4 Data Entry / Data Management

Data will be entered into an electronic spreadsheet. Study staff will only be able to modify the data file via password entry. The investigators will be responsible for the data integrity, and complete data entry for each visit as well as for any questionnaires. The investigator will send the data collected to the study sponsor within approximately 5 business days after the last subject completes the final visit.

11.5 Confidentiality

This study is confidential in nature. Both Indiana University and Sponsor agree to hold in confidence, in accordance with the conditions laid out in the [redacted] Agreement [redacted] any information disclosed to the other party under that Agreement and identified verbally or in writing as confidential.

All records will also be handled in accordance with HIPAA (1996) standards.

11.6 Publication

Indiana University may publish the results of this study, subject to the conditions laid out in the [redacted] Agreement, [redacted]

12 Study Costs

The sponsor will compensate the clinical site and the subjects for their time and participation in this voluntary study.

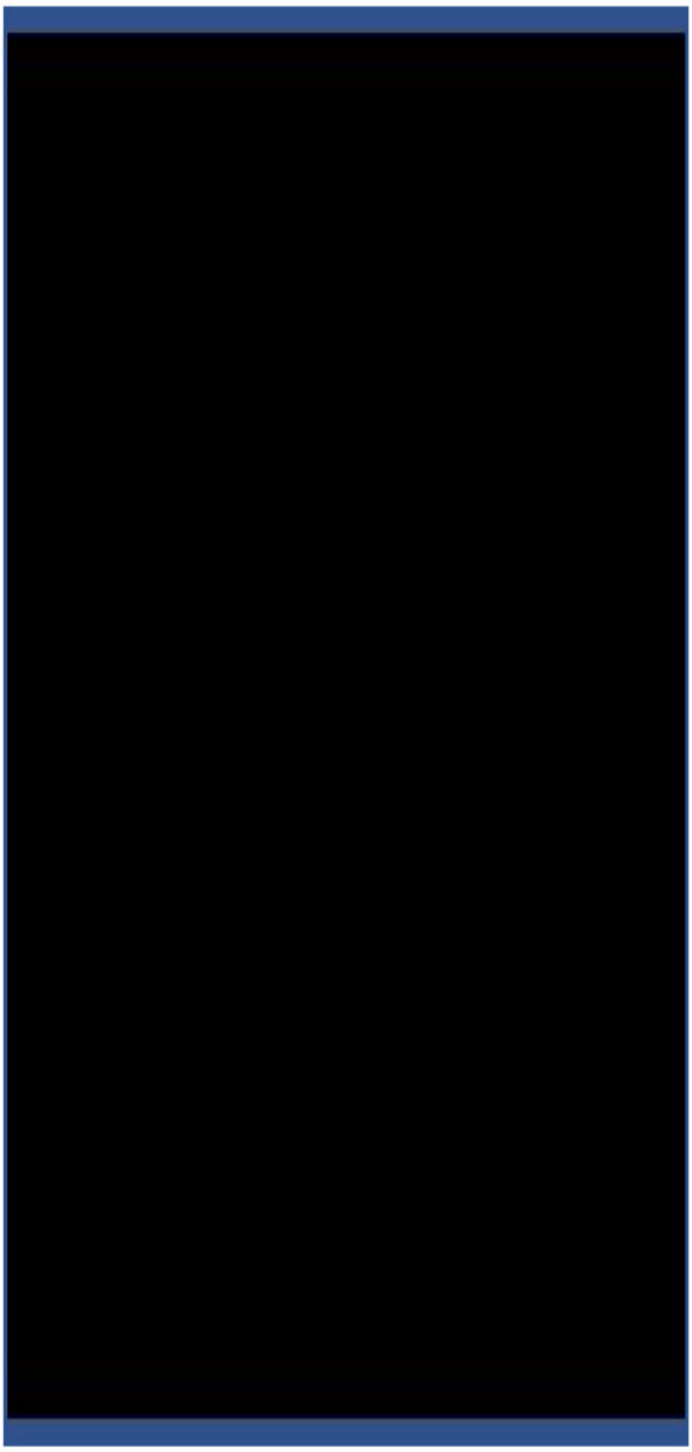
Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The participant must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

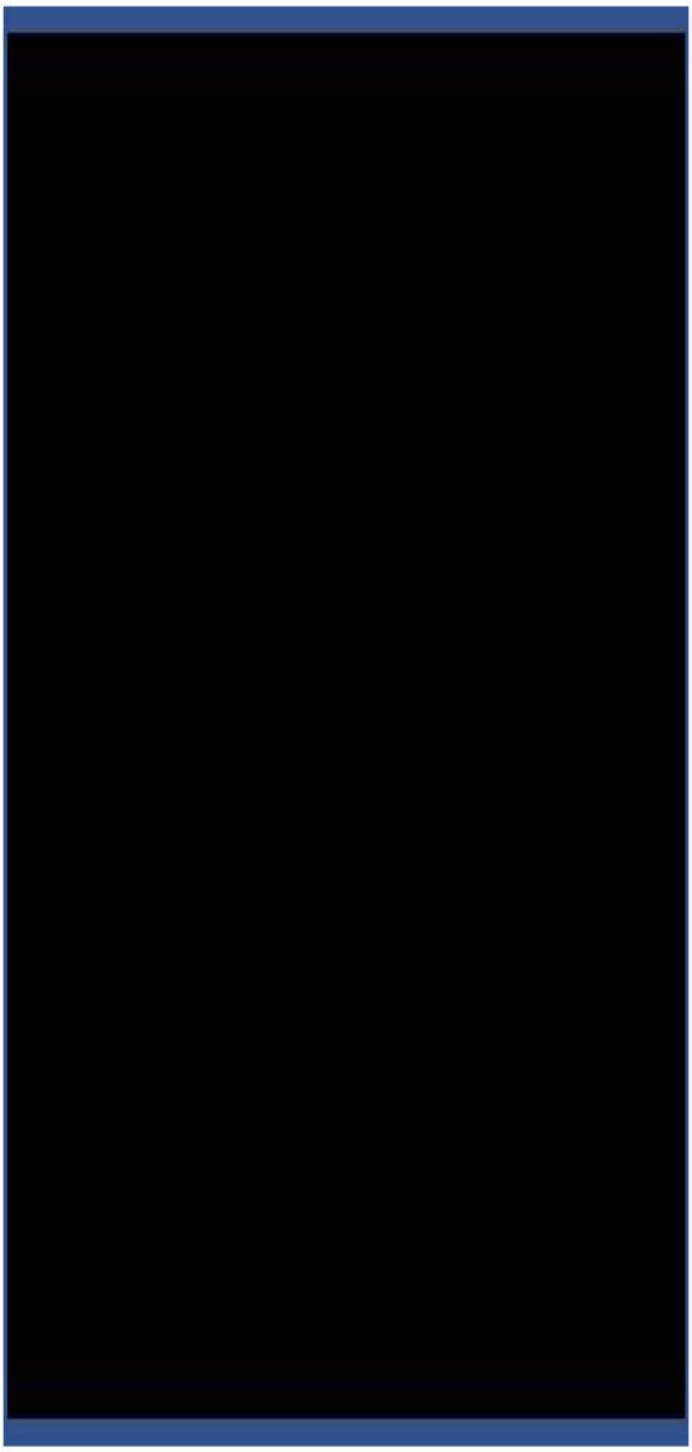
APPENDIX 1

Slit Lamp Biomicroscopy Grading Scales

APPENDIX 2

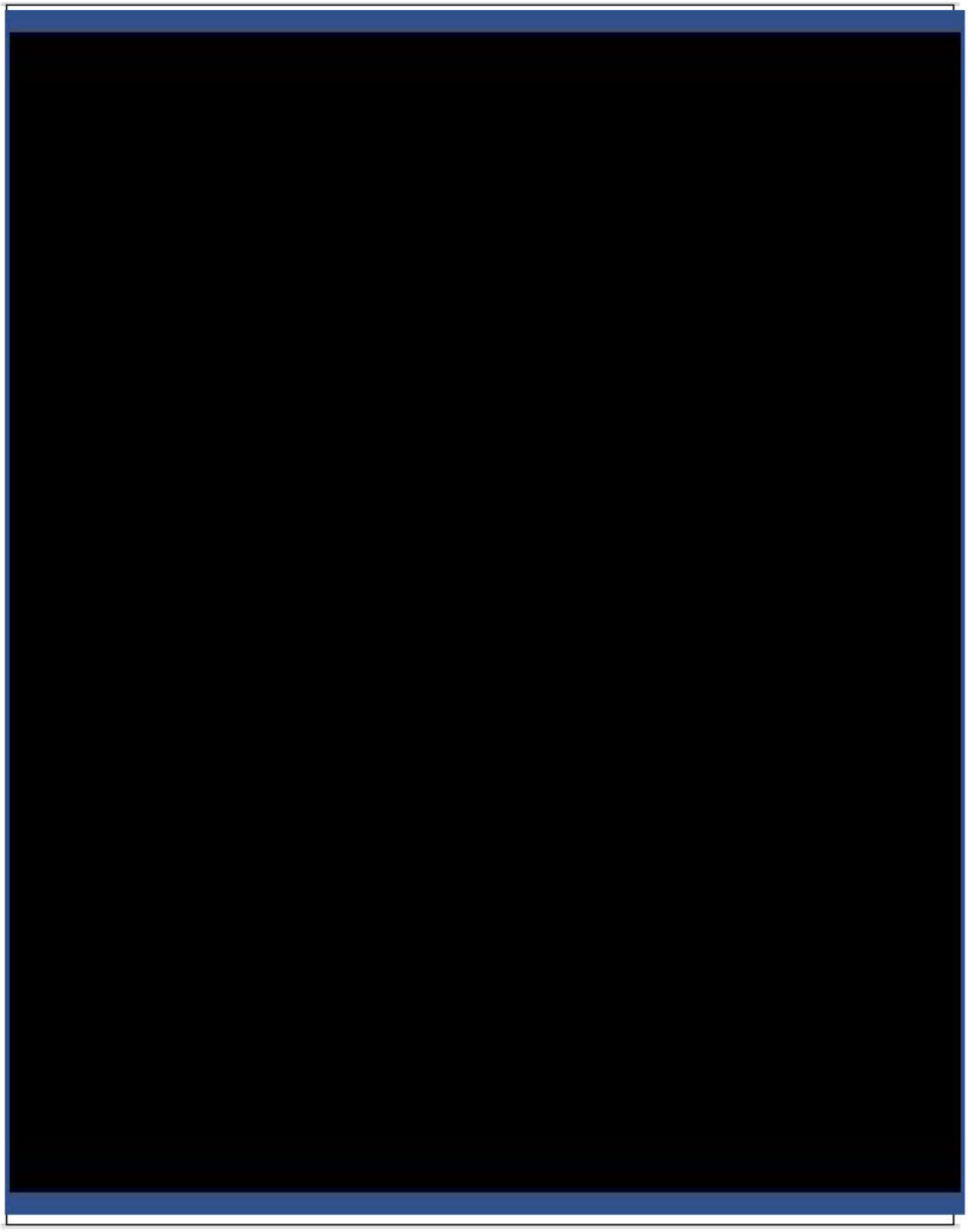
Randomization





APPENDIX 3

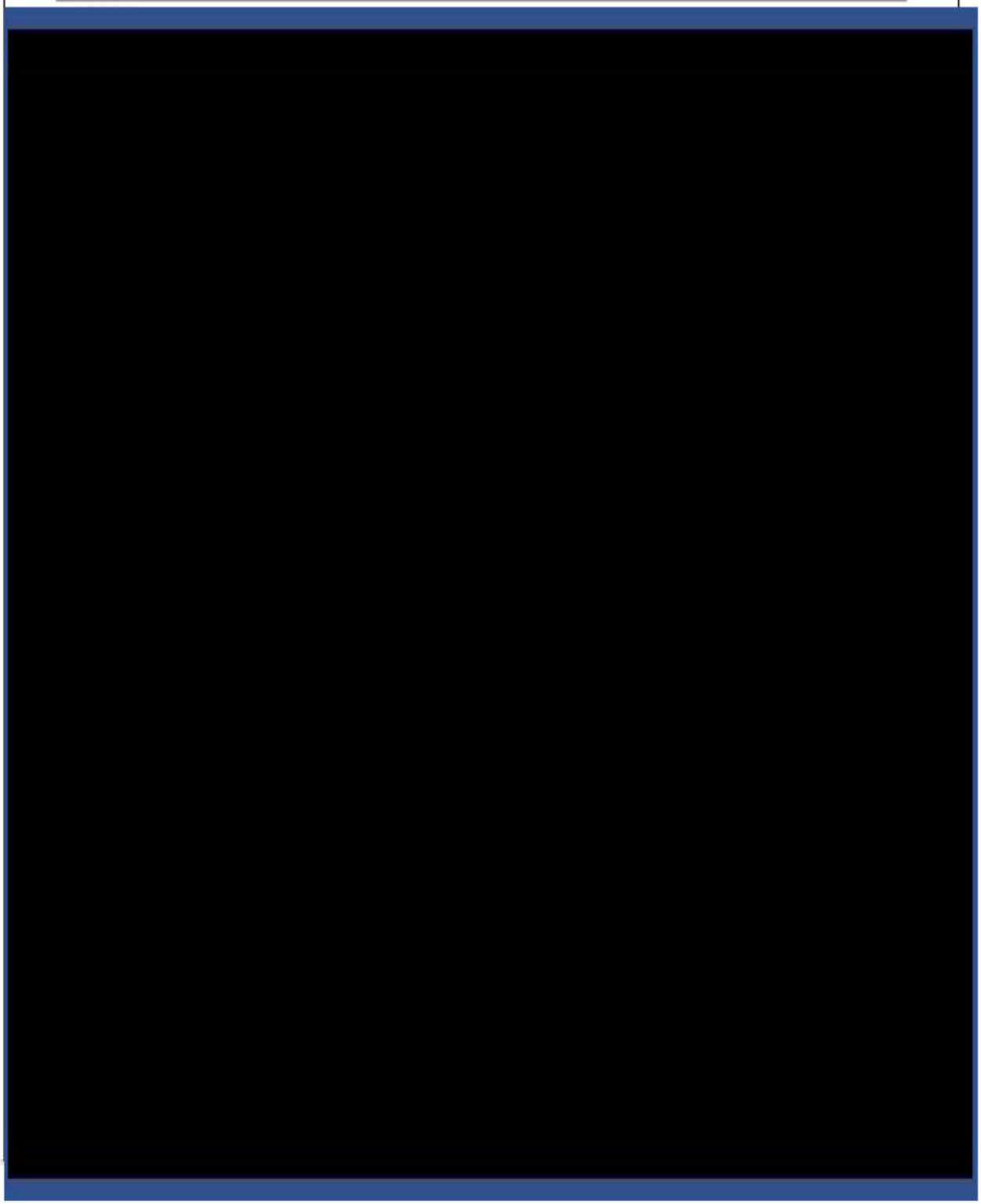
Post-Settling Subjective Questionnaire



CooperVision Bilateral Subjective Questionnaire - *Post-Settling*

[redacted]

CooperVision Bilateral Subjective Questionnaire - *Post-Settling*



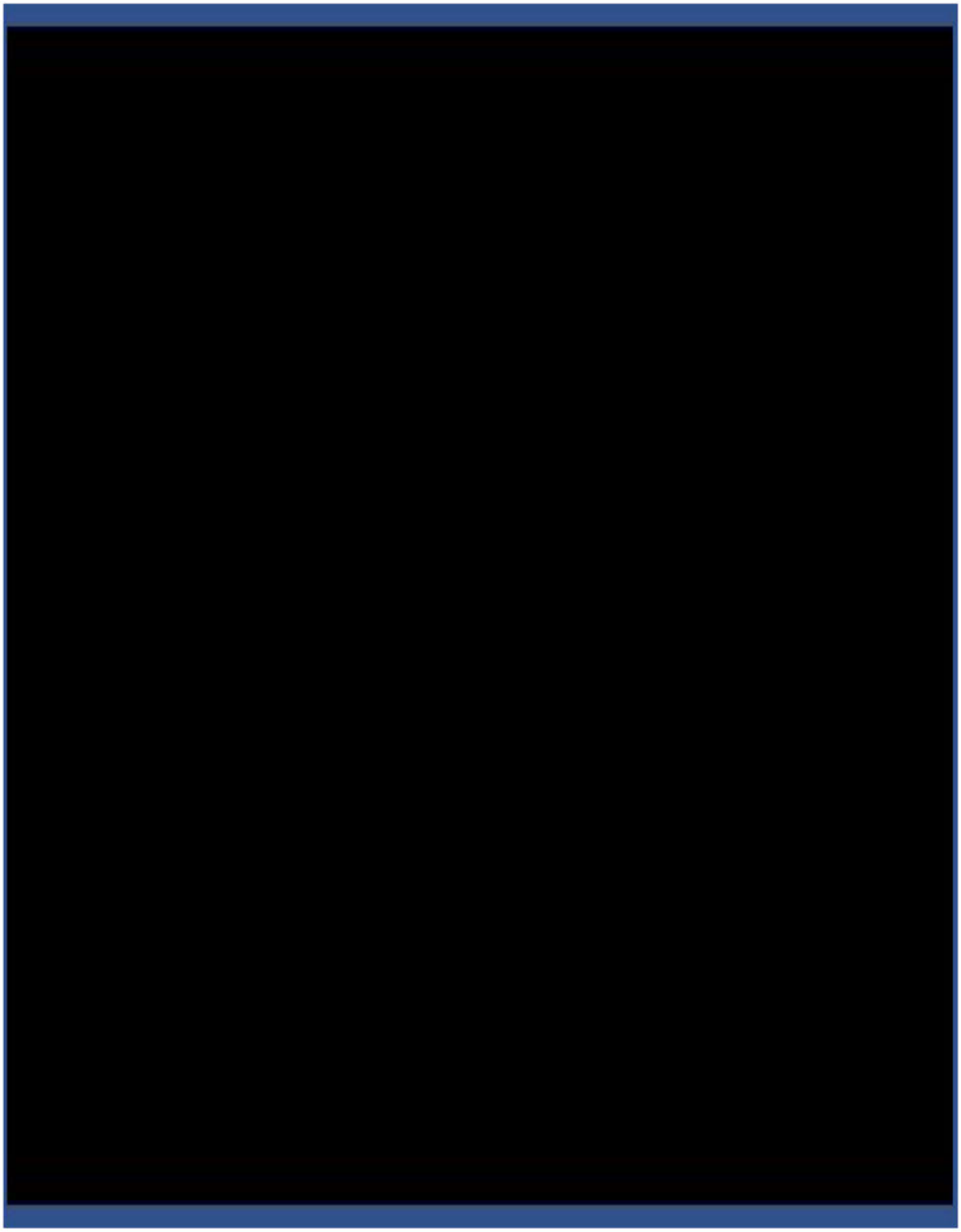
APPENDIX 4

Objective Assessments: Lens Surface and Lens Fit Grading Scales

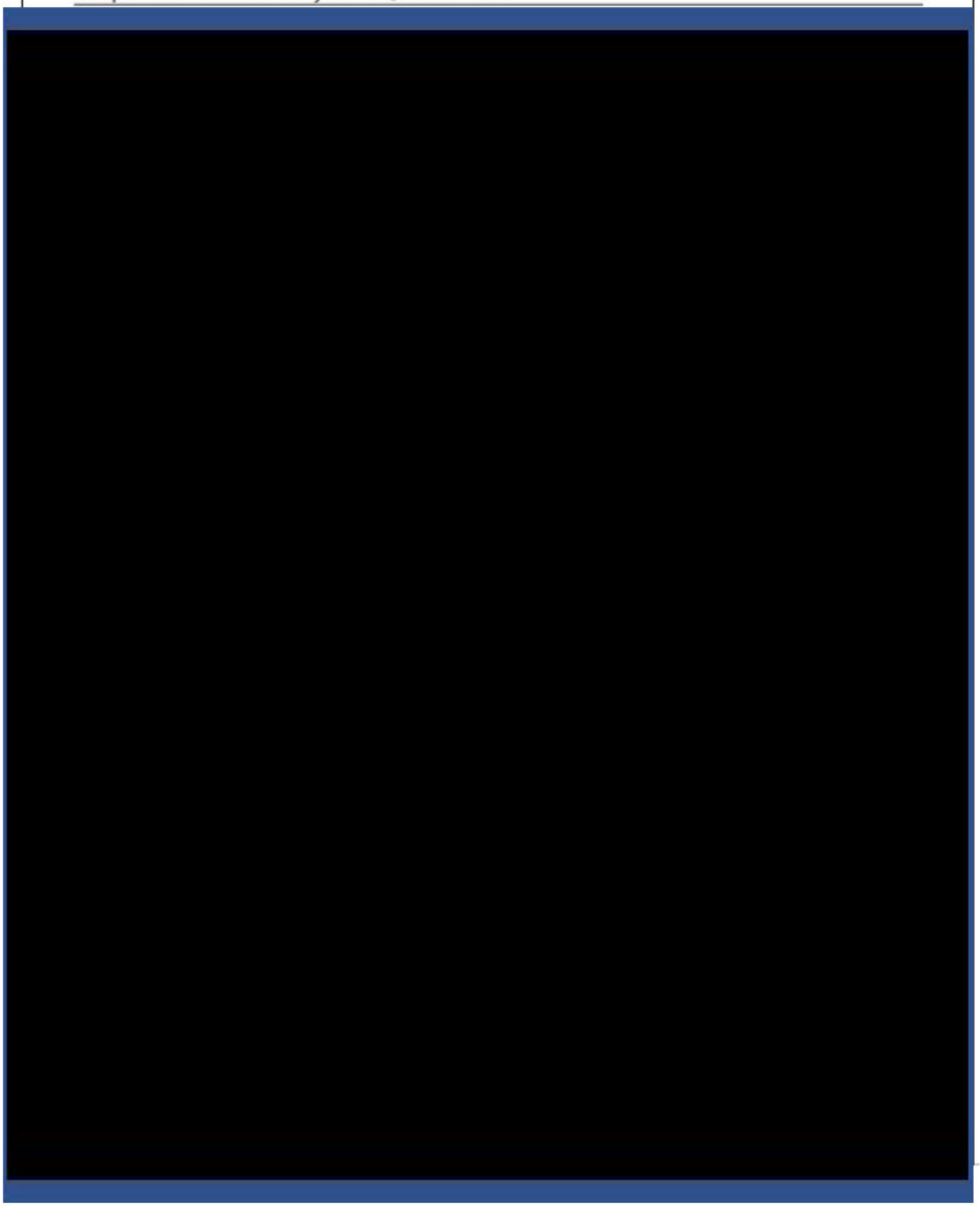
Lens Fit Grading

APPENDIX 5

(Two Week) Final Subjective Questionnaire



CooperVision Bilateral Subjective Questionnaire



CooperVision Bilateral Subjective Questionnaire

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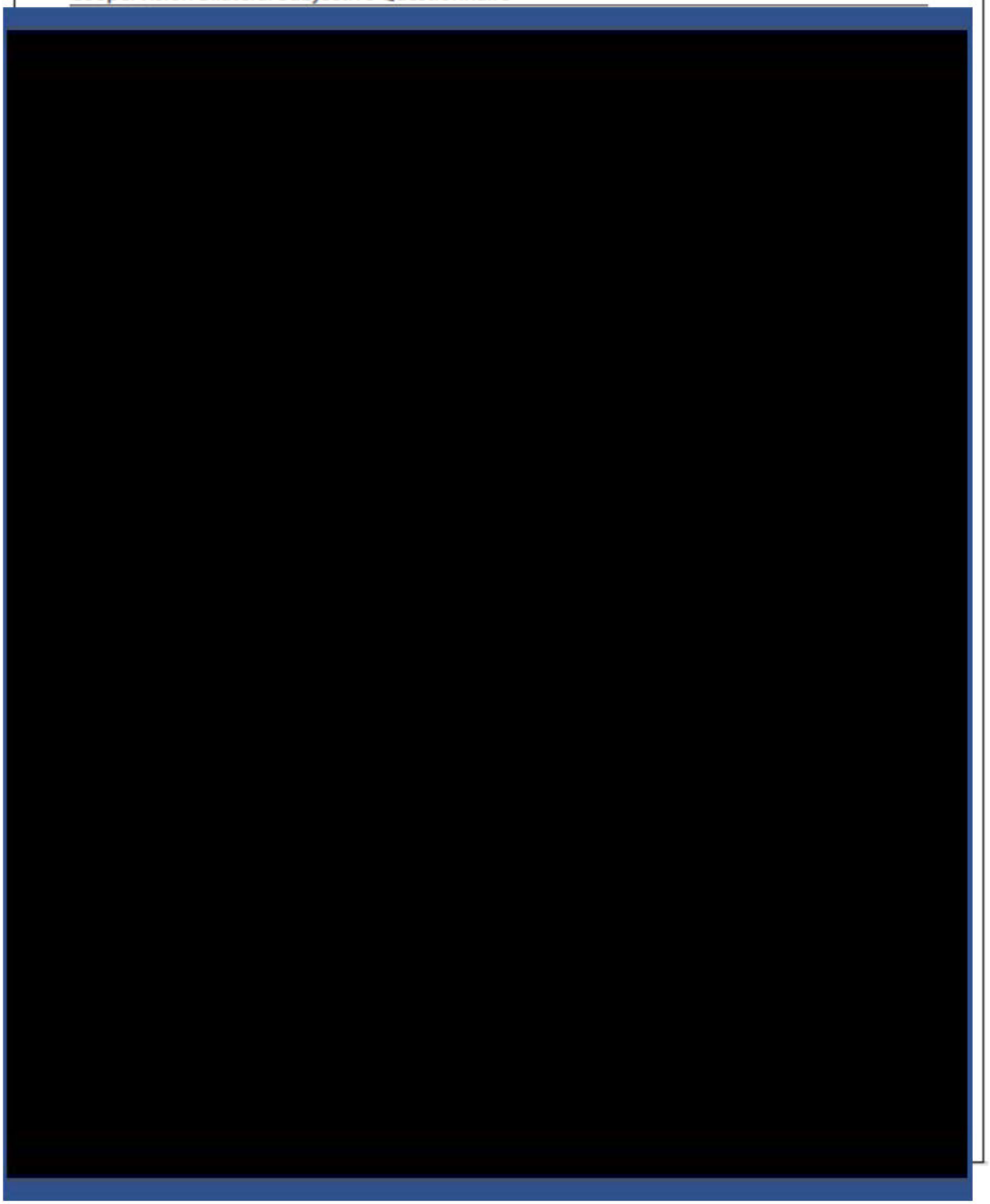
CooperVision Bilateral Subjective Questionnaire

[redacted]

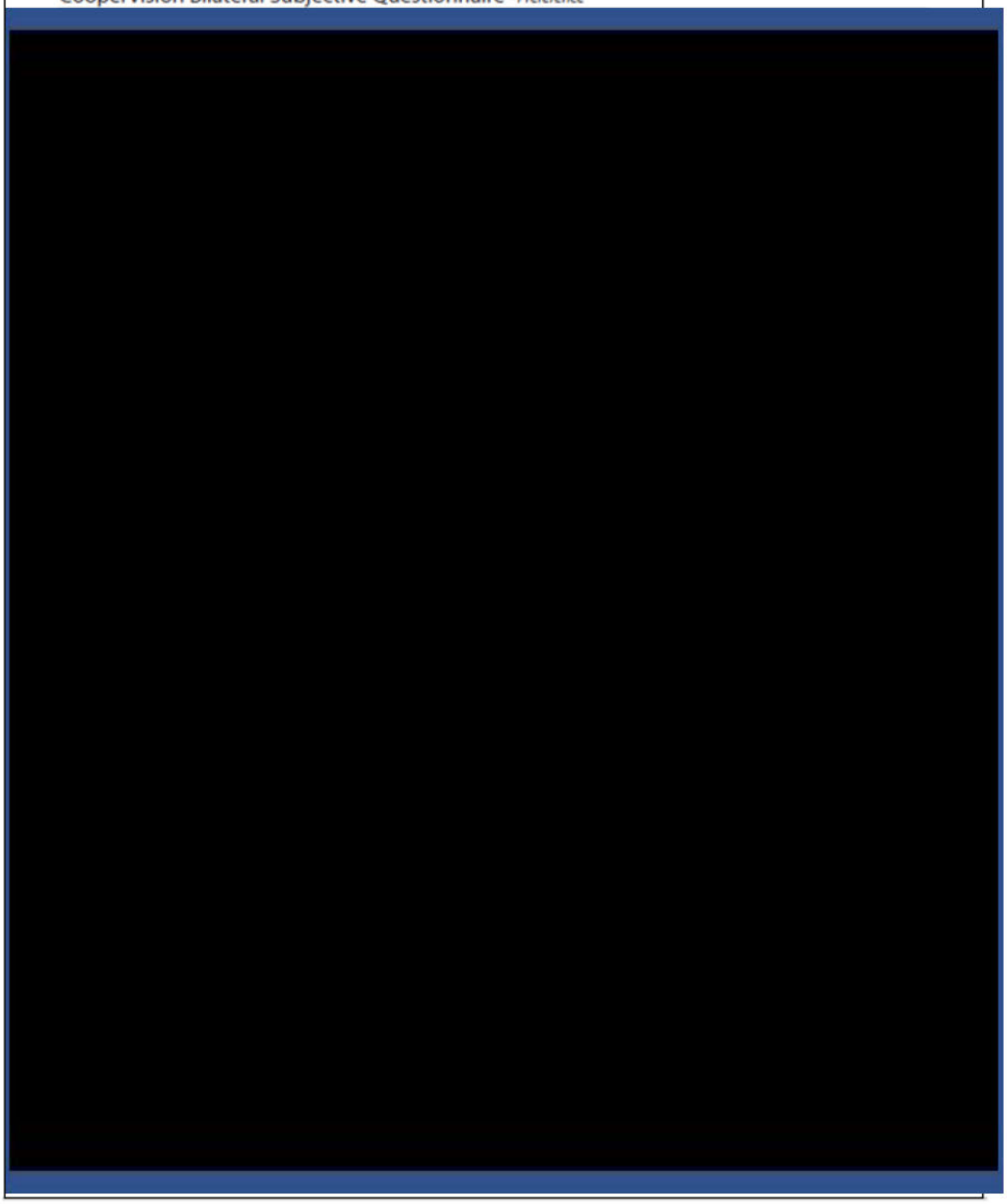
CooperVision Bilateral Subjective Questionnaire



APPENDIX 6

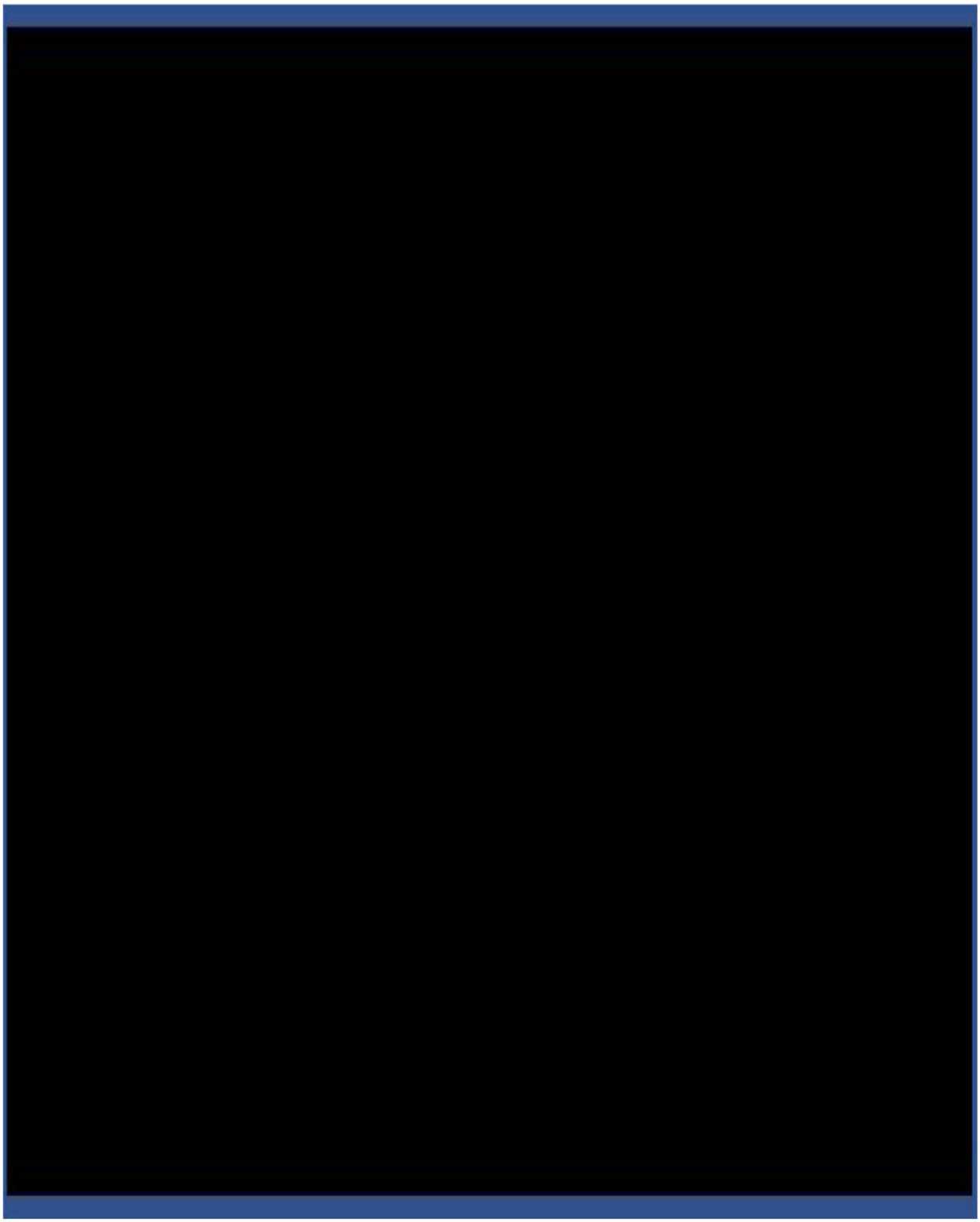
Lens Preference Subjective Questionnaire

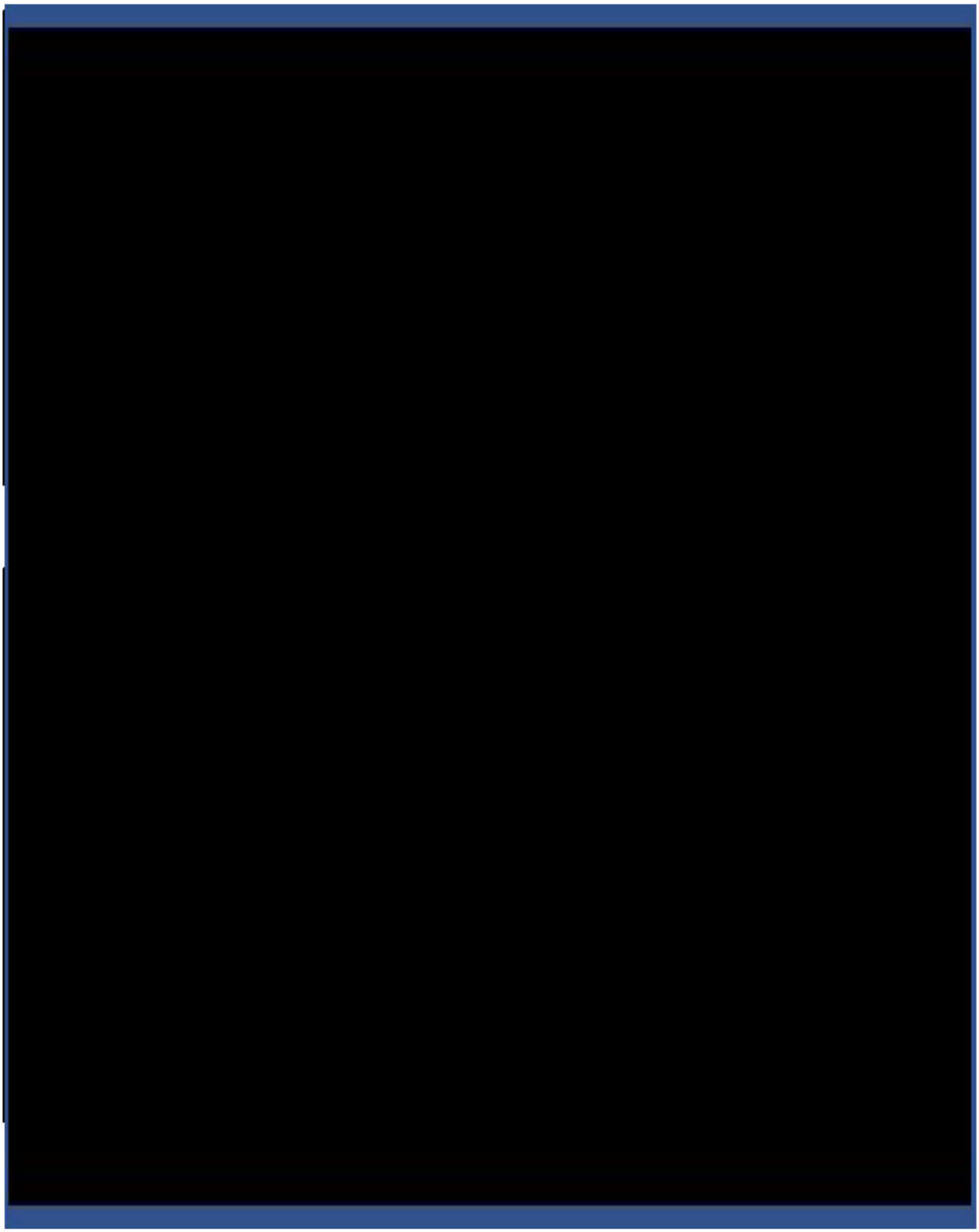
CooperVision Bilateral Subjective Questionnaire - *Preference*



APPENDIX 7

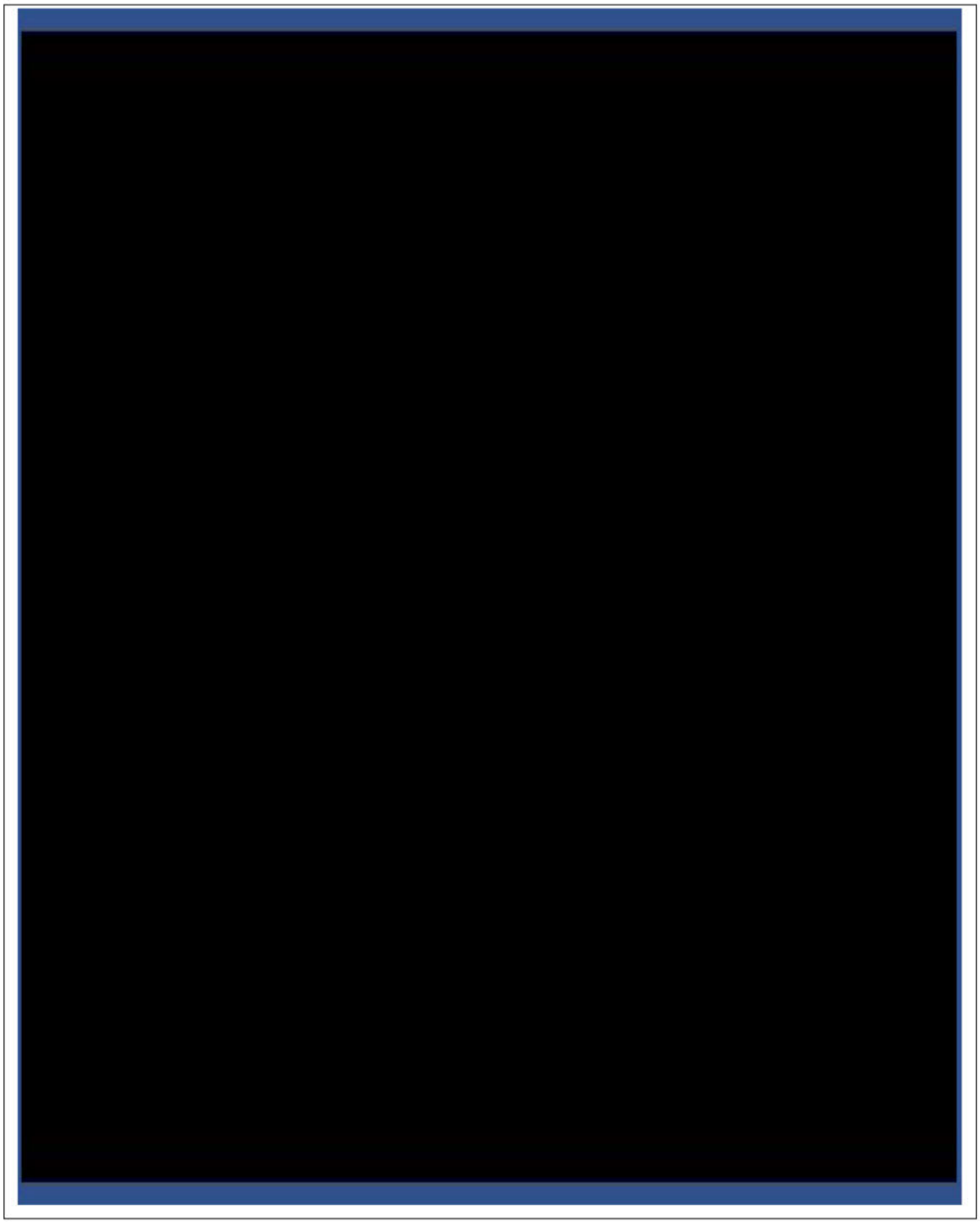
Web-based Comfort throughout the Day Questionnaire





APPENDIX 8

Adverse Event Forms



CVI ADVERSE EVENT OUTCOME FORM