CooperVision™

PROTOCOL TITLE:

CLINICAL VALIDATION OF THE [redacted] DAILY DISPOSABLE SOFT CONTACT LENS

Sponsor Study Code:	CV-20-63
Version Number:	1.0
Date:	21 MAY 2021
Sponsor Company:	COOPERVISION, INC.
Clinical Site:	CORL, Indiana University
Study Stage:	Design Validation

Sponsor Representative: [redacted] Date: 25-May-2021

[redacted]

Sponsor Management: [redacted] Date: 24-May-2021

[redacted]

Document Change History

Version	Originator	Description of Change(s)	Date
1.0	[redacted]	Original Protocol	21-May-2021

Protocol Signature Page – Principal Investigator

Protocol: CV-20-63

Study Title: Clinical Validation of the [redacted] Daily Disposable Soft Contact Lens

Protocol Version: 1.0, Date: 21 May, 2021

I have received and read this protocol and agree to adhere to the requirements. I am aware that my adherence to the above protocol is mandatory and that any changes in the protocol or informed consent form must first be approved by CVI, Inc. and the Institutional Review Board, except those changes necessary to eliminate apparent immediate hazards to subjects. I will provide copies of this protocol and all pertinent information to the study personnel under my supervision. I will discuss this material with them and ensure they are fully informed regarding their role in the study. I will ensure that the study is conducted in compliance with the protocol, Good Clinical Practice (GCP), and all applicable regulatory requirements, and with the reviewing Institutional Review Board (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

[redacted]

Signature

26-MAY-2021

Date

[redacted]

Printed Name

Overall Synopsis of the Clinical Investigation Plan (Protocol)

Sponsor Address:	CooperVision, Inc 5780 Stoneridge Drive Pleasanton CA 95788
Funding Source:	CooperVision, Inc
Investigation Site:	Clinical Optics Research Lab (CORL) Indiana University School of Optometry 800 E. Atwater Avenue Indiana 47405
Principal Investigator:	[redacted] [redacted] Indiana University School of Optometry 800 East Atwater Avenue Bloomington, IN. 47405 [redacted] [redacted]
Protocol Synopsis:	This protocol outlines the procedures that will be executed in this study
Planned Start Date	Anticipated June-July 2021
Estimated Duration	Approx 2 months
Primary Study Objective	To validate the clinical performance of the [redacted] daily disposable (DD) soft contact lens against the [redacted] DD lens
Overview of Study Design	This will be a prospective, double-masked (investigator and subject), randomized, two day crossover study comparing the Test lens against an appropriate comparator (Control) lens. Each subject will wear the [redacted] Test and [redacted] Control lenses bilaterally for two days each in random order.
Primary Outcome(s)	Comfort
Secondary Outcome(s)	Vision Lens fit Lens handling Anterior ocular health
Visit Schedule	Visit 1 - Baseline/Dispensing Pair 1 Visit 2 - Assessment of Pair 1 and Dispensing Pair 2 Visit 3 - Assessment of Pair 2 & Exit
Study Products	[redacted](Test) and [redacted] (Control)
Subject Population	**# of subjects**: Maximum 50 subjects (45 to complete)
Inclusion/Exclusion	**Main Inclusion criteria:** As per section 7.3.1 below **Main Exclusion criteria:** As per section 7.3.2 below

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1 Study Objective

This is a confirmatory Design Validation study to provide supportive evidence to demonstrate that the [redacted] lens meets the clinical performance requirements specified in the User Requirements Design Inputs per D28298, DHF0122.

Specifically, the User Requirements to be evaluated in this clinical study are:

- Vision of [redacted] is equivalent to [redacted]
- Comfort of [redacted] is equivalent (or better) to [redacted]
- Lens fit of [redacted] is equivalent to [redacted]
- Lens handling of [redacted] is equivalent to [redacted]
- Ocular health of [redacted] is equivalent to [redacted]

Details of the statistical hypothesis that are required to be met in fulfilment of Validation can be found in Section 9.1 below.

2 Study Design

This will be a prospective, two-day, double-masked (investigator and subject), randomized, bilateral crossover study comparing the Test lens against an appropriate comparator (Control) lens. Each subject will wear either the [redacted] lens or the [redacted] comparator lens (Control) in a bilateral fashion for two days followed by the alternate lens for two days. The [redacted] lens is a currently marketed product that is representative of the state-of-the art of contact lenses.

There will be a total of three visits in the study as described in 7.5 below

3 Study Devices and Comparator Products

3.1 Contact lenses

A summary description of the Test and Control lenses to be used in the clinical study are shown in Table 1. The Test lens is an investigational silicone hydrogel lens, with a slight modification to a contact lens material and design currently approved / cleared in the EU only [riofilcon A/[redacted]. The Control lens is also an investigational lens, currently approved / cleared in the EU only.

Further details regarding the investigational lens is described in the Investigator Brochure.

Table 1: Study lenses

	Test Lens	Control Lens
Device Name	[redacted]	[redacted]
Regulatory status	Investigational	Investigational
Manufacturer	CooperVision, Inc	CooperVision, Inc
Material	riofilcon A (+ DAB)	riofilcon A
Water Content (%)	58	58
Base curve (mm)	8.60	8.60
Diameter (mm)	14.10	14.00
Power range (D)	-1.00 to -6.00	-1.00 to -6.00
Label	Investigational [Masked]	Investigational [Masked]

3.1.1 Intended Use

In this clinical investigation, the study lenses are intended to be used as a single use soft contact lens. Single use lenses will be used for a maximum of one day of lens wear.

3.1.2 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).

3.2 Adjunct Products

3.2.1 Contact Lens Care Products

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

3.2.2 Other

No other medical devices will be used in this study.

4 Justification for the Study Design

The Apollo lens has successfully passed the preclinical biocompatibility tests as identified in the risk assessment document. Preliminary safety and clinical performance of of the [redacted] lens have been evaluated in one feasibility clinical study. This study is summarized in the Investigator Brochure (IB).

A two-day crossover study is sufficient to validate the clinical performance of the lens against the User Requirements. A crossover design has been chosen since it minimizes the impact of potential sympathetic effects between the two eyes (e.g. an uncomfortable lens in one eye may impact the subjective rating of the fellow eye). The study contact lenses do not alter the physiology of the eye and hence there is no carryover effect requiring a washout period. The order effect will be tested.

The choice of comparator product was made in order to assess the clinical performance against a currently marketed product representative of generally accepted state of the art.

The choice of study design was made to to demonstrate statistical equivalence to the comparator (Control) lens over two days of lens wear. A sample size determination was made of sufficient magnitude so as to be able to adequately test the primary statistical hypothesis, and is shown in Section 9.2.

5 Benefits/Risks of Study Device(s) and Study Procedures

5.1 Anticipated Clinical Benefits

There might not be direct benefits to the subjects in this study, however participation in a new 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 of their eyes and may have the opportunity to try a different type of soft contact lens and/or different lens care products at no cost to them.

5.2 Anticipated Adverse Device Effects

Ocular complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The incidence of infection due to daily-wear soft lenses is 0.035%.[1] Almost always an infection will occur only in one eye. This risk is assumed by 35-million Americans who currently wear contact lenses.

5.3 Risks Associated with Participation in the Clinical Investigation

This is considered 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 associated with the investigational contact lenses have been estimated in accordance with ISO 14971. A synopsis of pre-clinical and prior clinical testing results are included in the Investigator's Brochure. Risk controls to reduce the risk as far as possible have been implemented and any residual risks will be further mitigated through close evaluation by the investigators under this clinical protocol and communicated via informed consent.

5.4 Risks of Clinical Procedures to be Utilized in the Study

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

5.5 Possible Interactions with Concomitant Medical Treatments

The use of contact lenses can interact with concomitant topical, ocular and/or systemic medical treatments, therefore only healthy subjects who are not currently taking concomitant medical treatments will be included in this study. Only those products approved for the use with contact lenses can be used according to their indication under this protocol.

5.6 Steps That will be Taken to Control or Mitigate the Risks

The following Information for Safety for contact lens wear during the clinical study will be reviewed with each subject:

Hands should be washed and dried prior to touching the lenses for insertion or removal. If inserting the lenses yourself, they should be checked for tears and/or whether they are inside out prior to insertion. Eye rubbing should be avoided. Contact lenses should never be worn while swimming or in any other hazardous environment. The contact lenses are not to be slept in during the study or worn overnight and are to be replaced with a new pair according to the study lens wear schedule.

5.7 Rationale for Benefit-Risk Ratio

The knowledge gained from this confirmatory Validation study may lead to important conclusions regarding the ocular response and performance of new contact lens materials and designs. The potential risks for participating in this study are minimal, therefore the benefit-risk ratio is acceptable.

6 Ethics Review / Statement of Compliance

6.1 Relevant Standards / Guidelines

This study was developed in accordance with 21 CFR Part 812 Investigational Device Exemptions [or local regulations] and the good clinical practice (GCP) principles and ethical considerations of ISO 14155 Clinical Investigation of Medical Devices for Human Subjects and Declaration of Helsinki. The detailed descriptions of ocular Adverse Events details and the biomicroscopy grading scales are adapted from ISO 11980 Ophthalmic Optics – Contact lenses and lens care products – Guidelines for clinical investigations.

6.2 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.

This study will adhere to a protocol and informed consent document approved by the Institutional Review Board at Sterling IRB.

Address:
Sterling Institutional Review Board
6300 Powers Ferry Rd Suite 600-351
Atlanta GA 30339
Tel: 1-888-636-1062

6.3 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.

6.4 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.

7 Design of the Clinical Investigation

7.1 Study Endpoints

The primary endpoint is:

- Comfort

The secondary endpoints are:

- Vision
- Lens fit
- Lens handling
- Anterior ocular health

7.2 Clinical Site

The clinical site was selected based on the availability of representative population of subjects and Investigator's clinical research experience.

The Investigators will be required to fulfill the following criteria:

- Trained and experienced in the conduct of clinical research
- Willingness to follow the study protocol
- Trained in Good Clinical Practice (GCP) and the study protocol prior to commencing the study.

7.3 Subjects

A maximum of 50 subjects will be enrolled in this study in order for approximately 45 to complete the study. Each subject will be given a unique ID number. ID numbers will not be re-used. All subjects must meet the study inclusion and exclusion criteria listed below.

7.3.1 Inclusion criteria

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

- Has had a self-reported oculo-visual examination in the last two years.
- 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.
- Is an adapted soft contact lens wearer, having worn contact lenses for a minimum 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 on at least two consecutive days for each study pair.

7.3.2 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 concomitant 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 undergone corneal refractive surgery.
- Is participating in any other type of eye-related clinical or research study.

7.4 Procedures to Minimize Bias

7.4.1 Labelling and Masking

The Test and Control lenses will be labelled with investigational labels, according to local regulations where the clinical study is being conducted. The investigational labels will also include lens coding in order to facilitate investigator masking.

Decoding/Masking Procedures:

The Principal Investigator will be provided, prior to commencing the study, with the masking codes in a sealed envelope and decoding/demasking procedures for use in a medical emergency or where Serious Adverse Events are considered to be related to the Investigative or Control devices.

In order to mask the investigators, where possible, the investigator who is involved with lens insertion will be different than the investigator involved with the lens assessments.

7.4.2 Randomization procedures

In this crossover study design, each subject will wear the Test lens or the Control lens first in a bilateral fashion followed by the alternate lens. The order of lenses will be determined by a predetermined randomization schedule.

7.5 Visit Procedures

7.5.1 Visit 1a - Baseline 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 subject 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 to be enrolled in to the study.
- Auto-Refraction and Auto-Keratometry

- 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 (Appendix 2).
- HVID (mm) and palpebral aperture size (mm) measurements using slit lamp oculars.
- The investigator will confirm that the subject satisfies the criteria set out in the inclusion/exclusion criteria.

7.5.2 Visit 1b: Pair 1 Dispensing Visit

Dispensing visit should occur on same day as Visit 1a. In the event of unacceptable short-term slit-lamp fings, e.g. excessive corneal staining, Visit 1b may be conducted on a different day to Visit 1a, where slit lamp biomicroscopy should be conducted again to confirm eligibility.

- The first study pair of contact lenses will be selected by the investigator according to the randomization table (Appendix 3) for insertion by the subjects. Subjects will be dispensed the lens power nearest to their vertex corrected refractive error requirement. The lens powers of Pair 1 and Pair 2 will be matched.
- 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 (Appendix 4), including:
    - Lens insertion
    - Comfort satisfaction & comfort rating (6-point Likert & 100-point scales)
- A gross assessment of lens surface will be made:
    - Overall lens surface quality/wettability (acceptable / unacceptable)
    - Comments, if applicable

- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales (see Appendix 2).
    - Lens centration (0.1mm steps)
    - Corneal coverage (Yes / No / Borderline)
    - 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.
- Information for Safety for contact lens wear during the clinical study as described in the section 5.6 will be reviewed with each subject.
- The subject must have a minimum of 8 hours of exposure in the lens on at least 2 days before their next study visit.
- 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.

7.5.3 Visit 2: Pair 1 Follow-up Visit 2 days (+2 days) & Pair 2 Dispensing

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

- The following information will be collected from the subject by the investigator:
    - Wear time at visit (hours).
    - Time of insertion and removal daily since last visit, (to calculate average time and maximum wear time (hours).
    - Time of day lenses become uncomfortable, if at all, i.e. average comfortable wear time (hours).
- Subjective responses will be collected per the Follow-up Questionnaire (Appendix 5), including:
    - Overall satisfaction (6-point Likert & 100-point scales)
    - Comfort & comfort rating (6-point Likert & 100-point scales)
    - Comfort (insertion) (6-point Likert & 100-point scales)
    - Comfort (end of day) (6-point Likert & 100-point scales)
    - Dryness (freq/severity/bothersomeness) (5-point Likert scales)
    - Stinging/burning (freq/severity/bothersomeness) (5-point Likert scales)
    - Itchiness (freq/severity/bothersomeness) (5-point Likert scales)
    - Scratchy/gritty (freq/severity/bothersomeness) (5-point Likert scales)
    - Lens movement/awareness (freq/severity/bothersomeness) (5-point Likert scales)
    - Handling (6-point Likert & 100-point scales)

        - Insertion (freq/severity/bothersomeness) (5-point Likert scales)
        - Removal (freq/severity/bothersomeness) (5-point Likert scales)
        - Lens holding/handling (freq/severity/bothersomeness) (5-point Likert scales)
    - Vision (6-point Likert & 100-point scales)
        - Driving at night (6-point Likert & 100-point scales)

- Monocular and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (SOR will be used if the subject is wearing monovision).
- A gross assessment of lens surface will be made:
    - Overall lens surface quality/wettability (acceptable / unacceptable)
    - Comments, if applicable
- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales (see Appendix 2).
    - Lens centration (0.1mm steps)
    - Corneal coverage (Yes / No / Borderline)
    - 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 remove the study lenses which will be retained for return to the Sponsor.
- Slit lamp biomicroscopy will be assessed according to the guidelines set out in the CVI Grading scales (Appendix 2)
- Subjects will undergo washout with saline solution.

Pair 2 Dispensing

- The second study pair of contact lenses will be selected by the investigator according to the randomization table (Appendix 3) for insertion by the subjects. Subjects will be dispensed the lens power matching that of Pair 1.
- 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 and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (SOR will be used if the subject is wearing monovision).
- Subjective responses will be collected per the Post-Settling Questionnaire (Appendix 4), including:

- Lens insertion
- Comfort satisfaction & comfort rating (6-point Likert & 100-point scales)

- A gross assessment of lens surface will be made:
  - Overall lens surface quality/wettability (acceptable / unacceptable)
  - Comments, if applicable

- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales (see Appendix 2).
  - Lens centration (0.1mm steps)
  - Corneal coverage (Yes / No / Borderline)
  - 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.

- Information for Safety for contact lens wear during the clinical study as described in the section 5.6 will be reviewed with each subject.

- The subject must have a minimum of 8 hours of exposure in the lens on at least 2 days before their next study visit.
- 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.

7.5.4 Visit 3 – Pair 2 Follow-up Visit 2 days(+2 days) & Exit

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

- The following information will be collected from the subject by the investigator:
  - Wear time at visit (hours).
  - Time of insertion and removal daily since last visit, (to calculateaverage time and maximum wear time(hours).
  - Time of day lenses become uncomfortable, if at all, i.e. average comfortable wear time (hours).
- Subjective responses will be collected per the Bilateral Follow-up Questionnaire (Appendix 5), including:
  - Overall satisfaction (6-point Likert & 100-point scales)
  - Comfort & comfort rating (6-point Likert & 100-point scales)
  - Comfort (insertion) (6-point Likert & 100-point scales)

    - Comfort (end of day) (6-point Likert & 100-point scales)
    - Dryness (freq/severity/bothersomeness) (5-point Likert scales)
    - Stinging/burning (freq/severity/bothersomeness) (5-point Likert scales)
    - Itchiness (freq/severity/bothersomeness) (5-point Likert scales)
    - Scratchy/gritty (freq/severity/bothersomeness) (5-point Likert scales)
    - Lens movement/awareness (freq/severity/bothersomeness) (5-point Likert scales)
    - Handling (6-point Likert & 100-point scales)
        - Insertion (freq/severity/bothersomeness) (5-point Likert scales)
        - Removal (freq/severity/bothersomeness) (5-point Likert scales)
        - Lens holding/handling (freq/severity/bothersomeness) (5-point Likert scales)
    - Vision (6-point Likert & 100-point scales)
        - Driving at night (6-point Likert & 100-point scales)

- Monocular and binocular **HIHC** and **HILC** distance logMAR visual acuities will be recorded (SOR will be used if the subject is wearing monovision).
- A gross assessment of lens surface will be made:
    - Overall lens surface quality/wettability (acceptable / unacceptable)
    - Comments, if applicable
- Lens fit will then be assessed and graded according to the guidelines detailed in CVI Grading scales (see Appendix 2).
    - Lens centration (0.1mm steps)
    - Corneal coverage (Yes / No / Borderline)
    - 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 remove the study lenses which will be retained for return to the Sponsor.
- Slit lamp biomicroscopy will be assessed according to the guidelines set out in the CVI Grading scales (Appendix 2)
- Subjects will complete the Preference Questionnaire (Appendix 6)
    - Comfort Preference
    - Vision Preference
    - Handling Preference
- Exit visual acuities (logMAR) with baseline sphero-cylindrical refraction.
- The subject will be discharged and will sign the exit statement.

7.5.5 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** *Pair 1 Dispense*	**Visit 2** *Pair 1 Follow-up & Pair 2 Dispense*	**Visit 3** *Pair 2 Follow-up & 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 sph-cyl refraction	✓	-	-	-
Slit lamp biomicroscopy	✓	✓*	✓	✓
Instillation of lens at office	-	✓	✓	-
Subjective Questionnaire	-	✓	✓	✓
Lens surface assessment	-	✓	✓	✓
Lens fit assessments	-	✓	✓	✓
Spherical over-refraction (SOR)	-	✓	-	-
HIHC & HILC Distance VAs (with CLs)	-	✓	✓	✓
Lens Preference Questionnaire	-	-	-	✓
Exit VAs	-	-	-	✓
Study Exit	-	-	-	✓

** Slit lamp biomicroscopy to be repeated to re-confirm eligibility in the event Visit 1b does not occur on the same day as Visit 1a*

8 Adverse Events and Device Deficiencies

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 11980 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 (Appendix 1) will be completed for each adverse event. 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 an Adverse Event Outcome Form (Appendix 1) completed indicating the course of 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:	[redacted]
Phone:	[redacted]
Address:	5870 Stoneridge Dr. Suite 1 Pleasanton, CA 94588

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 a discontinuation/exit form will be completed.

8.5 Device Deficiencies

A device deficiency means the inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance. *Any device deficiency that will 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 deficiency.*

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

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 complaints or Device Deficiencies.

9 Statistical Design and Analysis

9.1 Statistical Hypothesis

The primary statistical hypothesis is that the comfort performance with the Test lens will demonstrate statistical equivalence to the comparator (Control) lens over two days of lens wear.

The secondary statistical hypothesis is that the vision performance with the Test lens will demonstrate statistical equivalence to the comparator (Control) lens over two days of lens wear.

Other hypotheses:

The lens fit performance with the Test lens will demonstrate statistical equivalence to the comparator (Control) lens over two days of lens wear.

The lens handling performance with the Test lens will demonstrate statistical equivalence to the comparator (Control) lens over two days of lens wear.

Corneal staining performance with the Test lens will demonstrate statistical equivalence to the comparator (Control) lens over two days of lens wear.

9.2 Sample Size Calculations

This is a confirmatory Design Validation clinical investigation where the calculated sample size is sufficient to test the primary and secondary hypotheses described in Section 9.1.

9.2.1 Primary Hypothesis

Table 3 below shows the sample size estimations for a paired t-test (alpha = 0.05) in order to detect differences in mean ocular comfort scores between Test vs. Control conditions. Assuming a standard deviation of a paired difference of 13 points, a sample size of 44 subjects provides adequate power to detect a potential paired difference of 7 points on a 0-100 point scale.

Table 3: Sample size estimation (0-100 numerical scale)

n=20		Paired Difference		
		5	7.5	10
S.D. (Paired difference)	8	76%	98%	99%
	10	56%	89%	99%
	12	42%	76%	94%
	15	29%	56%	81%

9.2.2 Secondary Hypothesis

Assuming a standard deviation of a paired difference of 0.1 logMAR, a sample size of 27 subjects provides adequate power to detect a potential paired difference of 0.05 logMAR in mean vision scores between Test vs. Control conditions for a paired t-test (alpha = 0.05).

Therefore, a sample size of approximately 45 completing subjects is sufficient for this study.

9.3 Statistical Analysis

Summary statistics [may/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. Where applicable, 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.

Equivalence testing will be undertaken to first determine statistical non-inferiority and then equivalence (if applicable) to the comparator (Control) lens, to confirm the primary and secondary hypotheses.

9.4 Data Entry / Data Management

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the clinical site Principal Investigator. The Principal Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

The clinical data for this study may be entered by designated study site personnel onto paper or electronic case report forms (CRFs). Case history and symptoms questionnaires may be given to subjects to complete in paper or electronic form.

Unless otherwise documented, the CRFs will be considered the source document.

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.

If study information is collected using an automated piece of equipment, the information may be recorded directly from the instrument display, captured electronically as output, or printed and entered into the CRF. The CRF will become the source document if there is no printout.

9.5 Data Quality Assurance

The CRFs will be completed at the time of the visit. All clinical data generated in the study will be submitted to the Sponsor for quality assurance review and analysis. All forms will be reviewed for completeness and evident recording errors will be rectified by contacting the appropriate clinical site. Computerized editing routines will be used to identify missing, invalid, inconsistent, or questionable data entries for verification prior to data analysis. These data issues will be resolved by contacting the relevant clinical site.

10 General Study Management

10.1 Monitoring Plan

The Sponsor will ensure site qualification of the investigative site has been completed prior to conducting the clinical study in order to ensure that the site facility is adequate, personnel are qualified and resources are satisfactory.

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, a remote site visit may be conducted to verify that written informed consent was obtained using the IRB approved ICF prior to each subject's participation in the study.

Findings of non-compliance shall be reviewed with the Investigator and disclosed in a written monitoring report. The Monitor will report to the Sponsor any non-compliance with signed agreements, conditions imposed by the IRB/EC and the requirements of the study protocol. The Sponsor shall then either secure compliance or discontinue shipments of the lenses to the Investigator and may terminate the Investigator's participation in the investigation, if required.

Prior to final data freeze, a remote close-out visit/discussion will be conducted 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.

10.2 Amendments

Amendments to this Protocol that may affect the rights, safety, or well-being of subjects will require review and approval from IRB before the changes are implemented in the study. Investigators at the site will be provided with the revised protocol version, the site trained and the Protocol Signature Page of the amended protocol completed prior to enacting the amendments.

10.3 Protocol Deviations

A Protocol Deviation is an instance of failure to follow, intentionally or unintentionally, the requirements of the protocol. Investigators will not deviate from the pprotocol except to protect the rights, safety and well-being of human subjects. Under emergency circumstances deviations may proceed without prior approval of the Sponsor and the IRB/EC. Deviations shall be reported to the Sponsor, IRB/EC and the regulatory bodies, as required.

Significant deviations which require changes to the research protocol or informed consent process/document or other corrective actions to protect the safety, welfare, or rights of patients or others must be reported to the IRB/EC within ten business days of the deviation occurring (or its discovery). All deviations shall be reported to the Sponsor within two working days.

All deviations occurring during the study will be documented on a protocol deviation form and documented in the final Clinical Study Report (CSR).

10.4 Suspension or Premature Termination of the Clinical Investigation

The study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the

suspending or terminating party to the Investigator, the Sponsor and the Institutional Review Board (IRB), as appropriate. If the study is prematurely terminated or suspended, the Investigator will promptly inform the IRB and will provide the reasons for the termination or suspension. In terminating the clinical investigation, CooperVision and the Principal investigator will assure that adequate consideration is given to the protection of the subject's interests.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

The blinding/masking code may be broken and communicated to the Principal Investigator only in the case of an emergency, such as an Adverse Event that requires knowledge of the identity of the investigational product in order to manage the subjects' condition.

The study may resume once concerns about safety, protocol compliance or data quality are addressed and satisfy the Sponsor and IRB/EC.

Subjects will continue to receive follow-up care until they are able to be exited from the study (in the case of study termination) or are able to resume participation in the study (in the case of temporary study suspension), whereupon they will also be followed to exit.

10.5 Record Retention

Following study completion, data will be available in electronic and/or paper format for audit, Sponsor use, or subsequent analysis.

Documents will be retained in a manner which allows for timely retrieval. Where documents are maintained in an electronic system, the system will be required to be maintained for the life of the document or the documents migrated to a system allowing for the continued retrieval of the document until the retention period has been completed.

Access to the Network, eQMS or other electronic storage is secured to minimize potential loss or unauthorized changes. Documents will be stored in a manner to prevent loss and damage.

Applicable hard copy documents will be secured as appropriate and maintained in a manner to prevent loss or damage.

If hard copy records are retained in an archive store, a log of the content of each pallet and box in the archive should be kept in order to enable swift record retrieval. This log should contain the pallet and box owning department, record type and date range covered.

The content of archives should be reviewed periodically. The storage of the records in the archive must be appropriate and in good condition to ensure that records inside are not damaged.

Certain Quality/Regulatory Documented Information is noted as having permanent retention periods due to complex regulatory requirements. Permanent records should be held securely. A fireproof room or safe may be used.

Permanent records may be considered for destruction. Consideration will be based on a documented request forwarded to the site Quality Assurance leader, or a member of the Global Quality Systems team. The request must be reviewed and approved prior to any destruction.

The request and approval will include:

- the requestors name and title,
- date of the request,
- approvers name and title,
- date of approval,
- list of the Documented Information to be destroyed.

In the event that this Protocol document is indicated for Design Validation purposes, as indicated on the title page, copies of all original raw source data forms and completed CRF's will be forwarded to the Sponsor at completion of the final report.

10.6 Confidentiality and Privacy

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 be handled in accordance with HIPAA (1996) standards. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data.

Confidentiality of data shall be observed by all parties involved at all times throughout the clinical investigation. All data shall be secured against unauthorized access. The principal investigator or investigation site shall provide direct access to source data during and after the clinical investigation for monitoring, audits, IRB review and regulatory authority inspections.

11 Device Accountability

11.1 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 study protocol by subjects who are under the direct supervision of an investigator.

11.2 Disposal of Consumables

This study dispenses consumables (lenses) to participants for use during the study. Study solutions used and/or study lenses worn by participants will be collected at the completion of the study.

11.3 Ordering and Accountability of Study Materials

The Test and the Control lenses lenses will be provided by the Sponsor. The investigator must complete an accurate accounting of the study product at the completion of the study. 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.

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.

13 Publication Policy

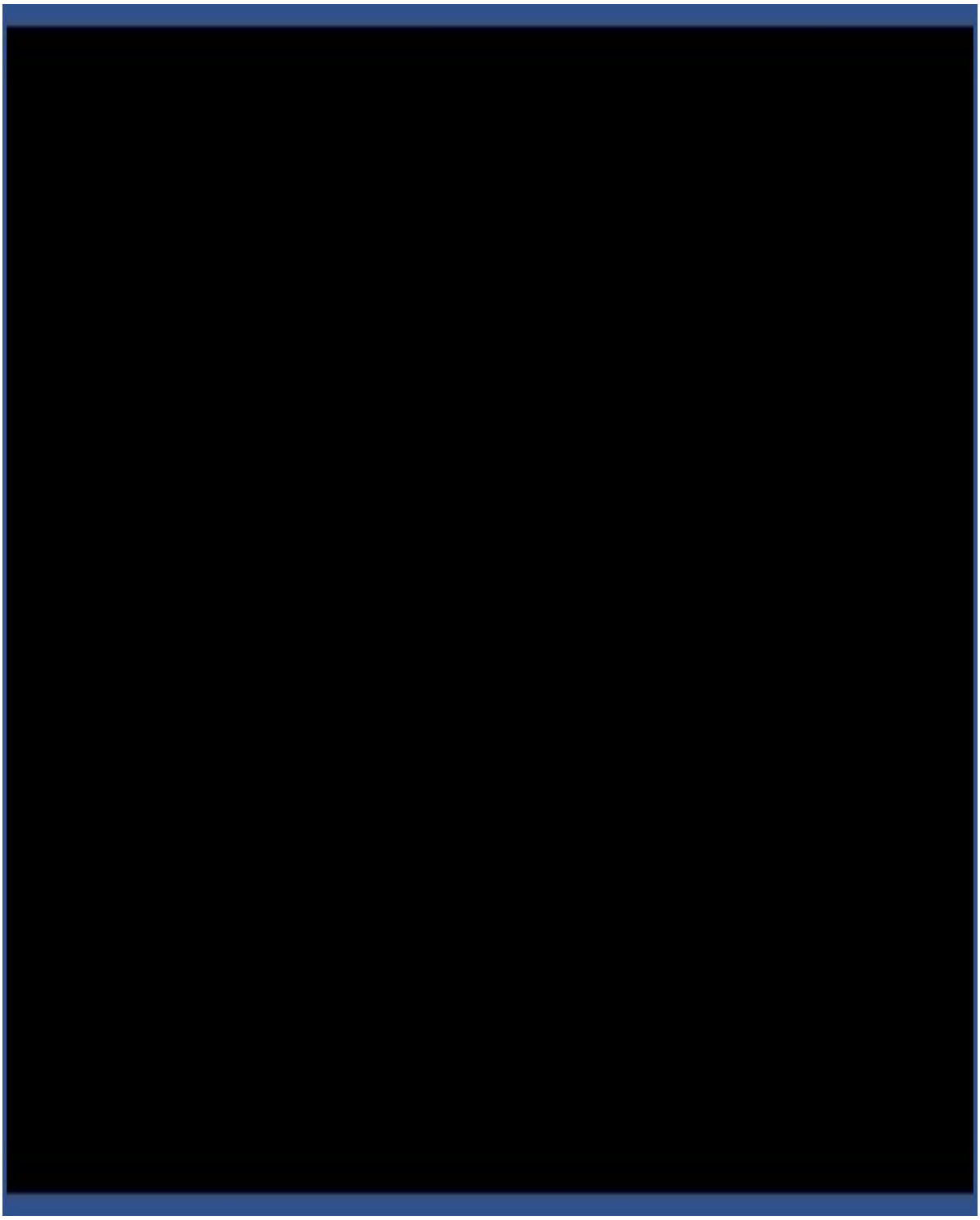
Indiana University may publish the results of this study, subject to the conditions laid out in the [redacted] Agreement, [redacted]

14 References

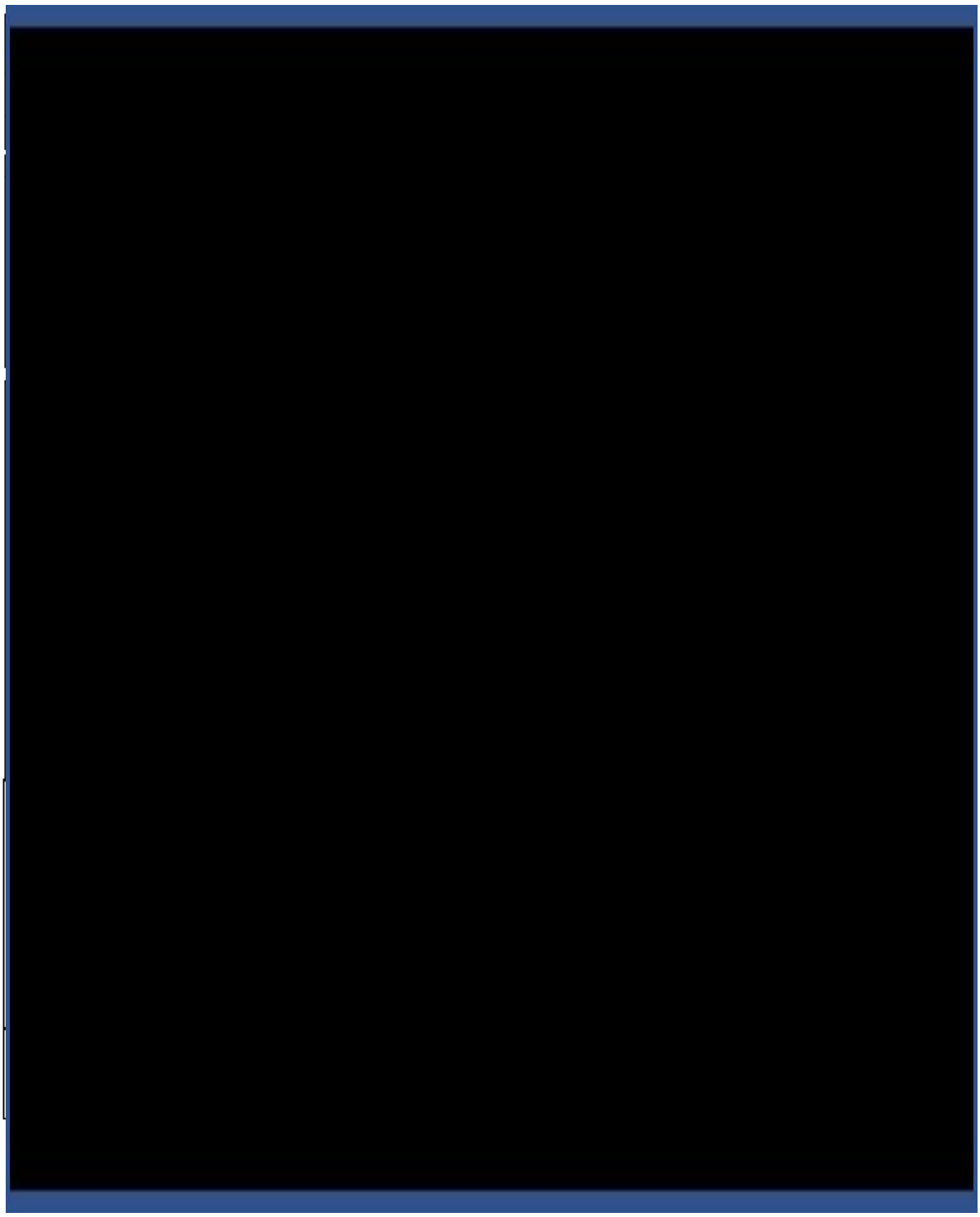
Cheng K, Leung S, Hoekman H, Beekhuis W, Mulder P, Geerards A, Kijlstra A. Incidence of contact-lens-associated microbial keratitisand its related morbidity. The Lancet 1999; 354:181-185.

15 Appendix 1 – Adverse Event Case Report Forms

CVI ADVERSE EVENT NOTIFICATION FORM

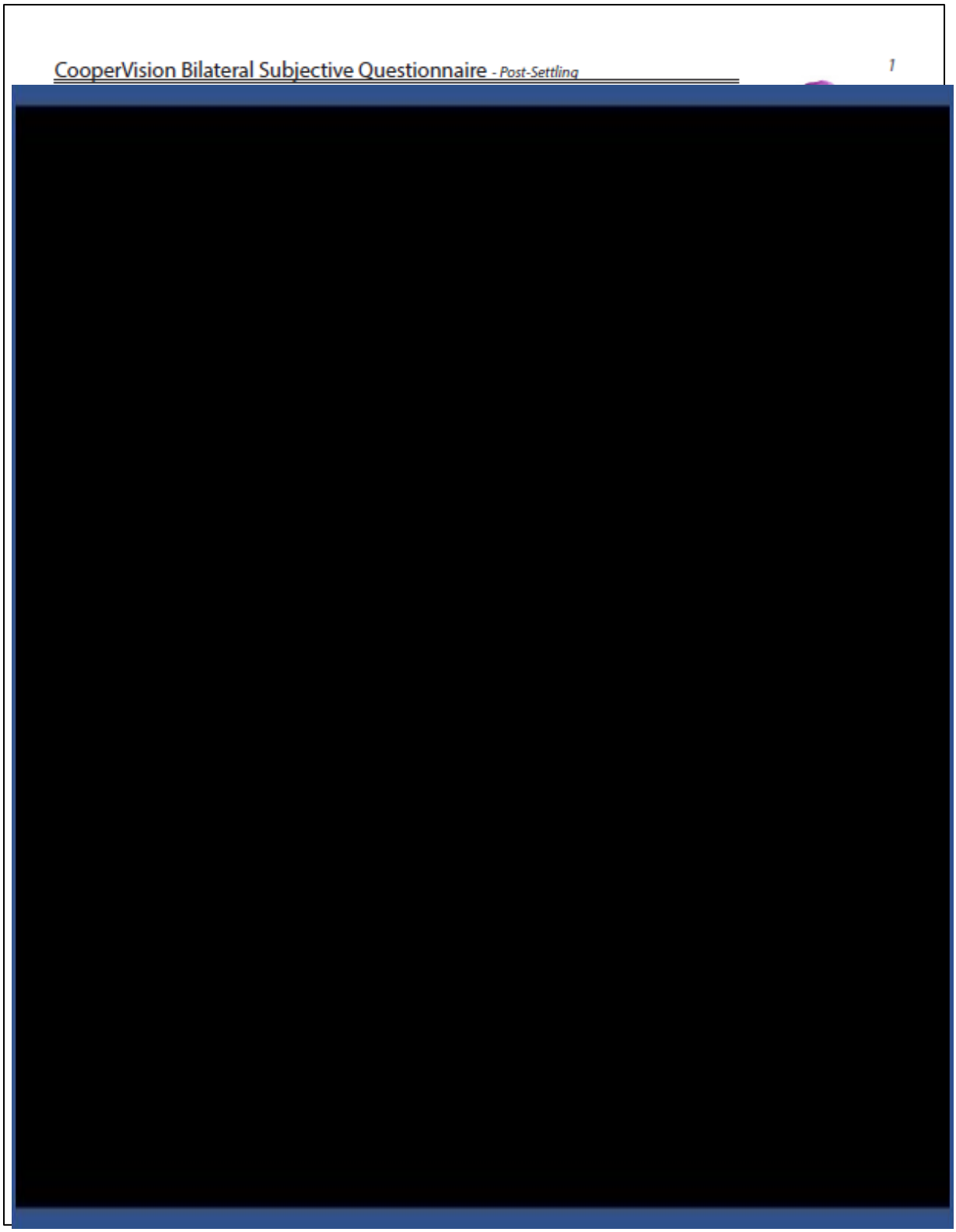


CVI ADVERSE EVENT OUTCOME FORM

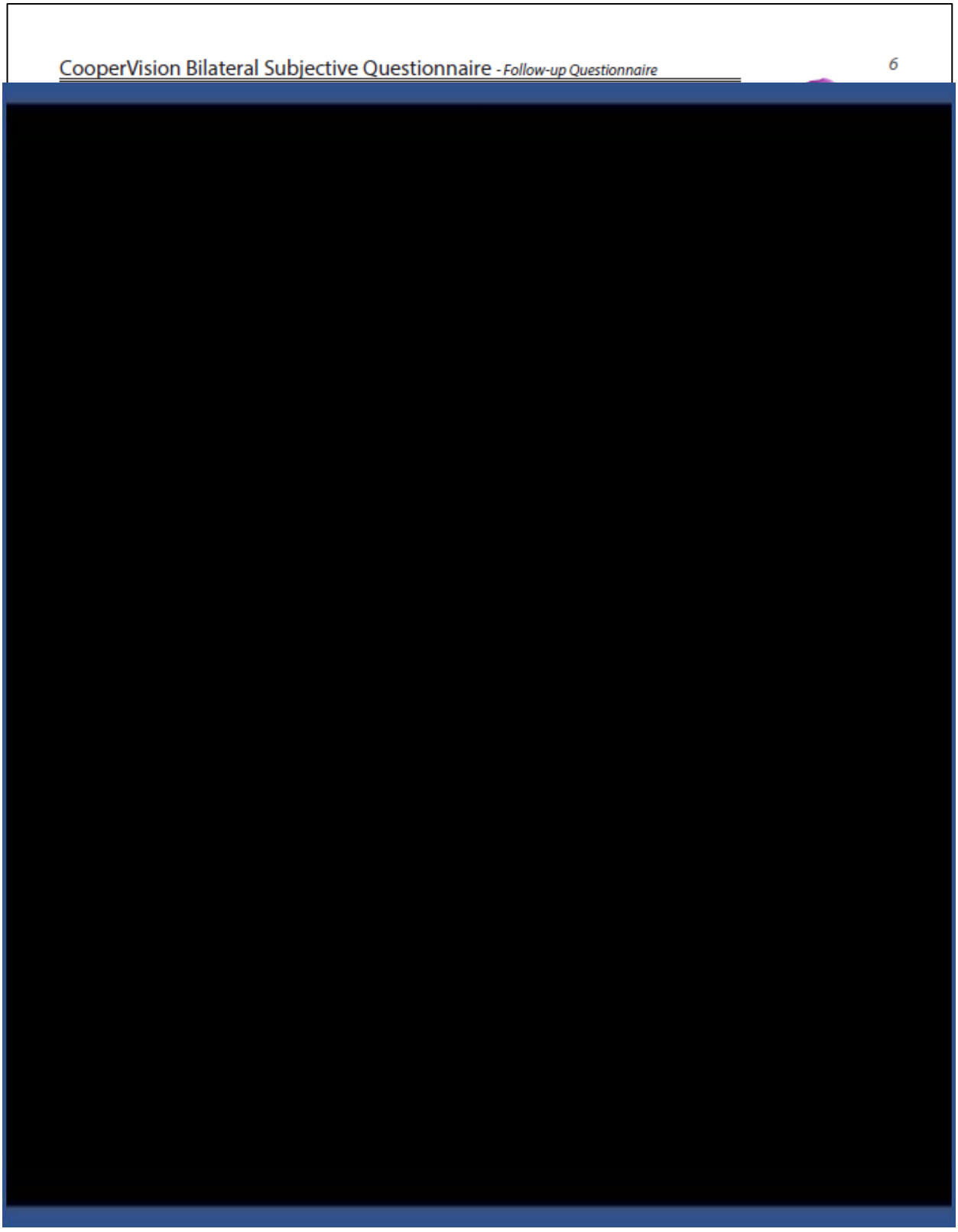


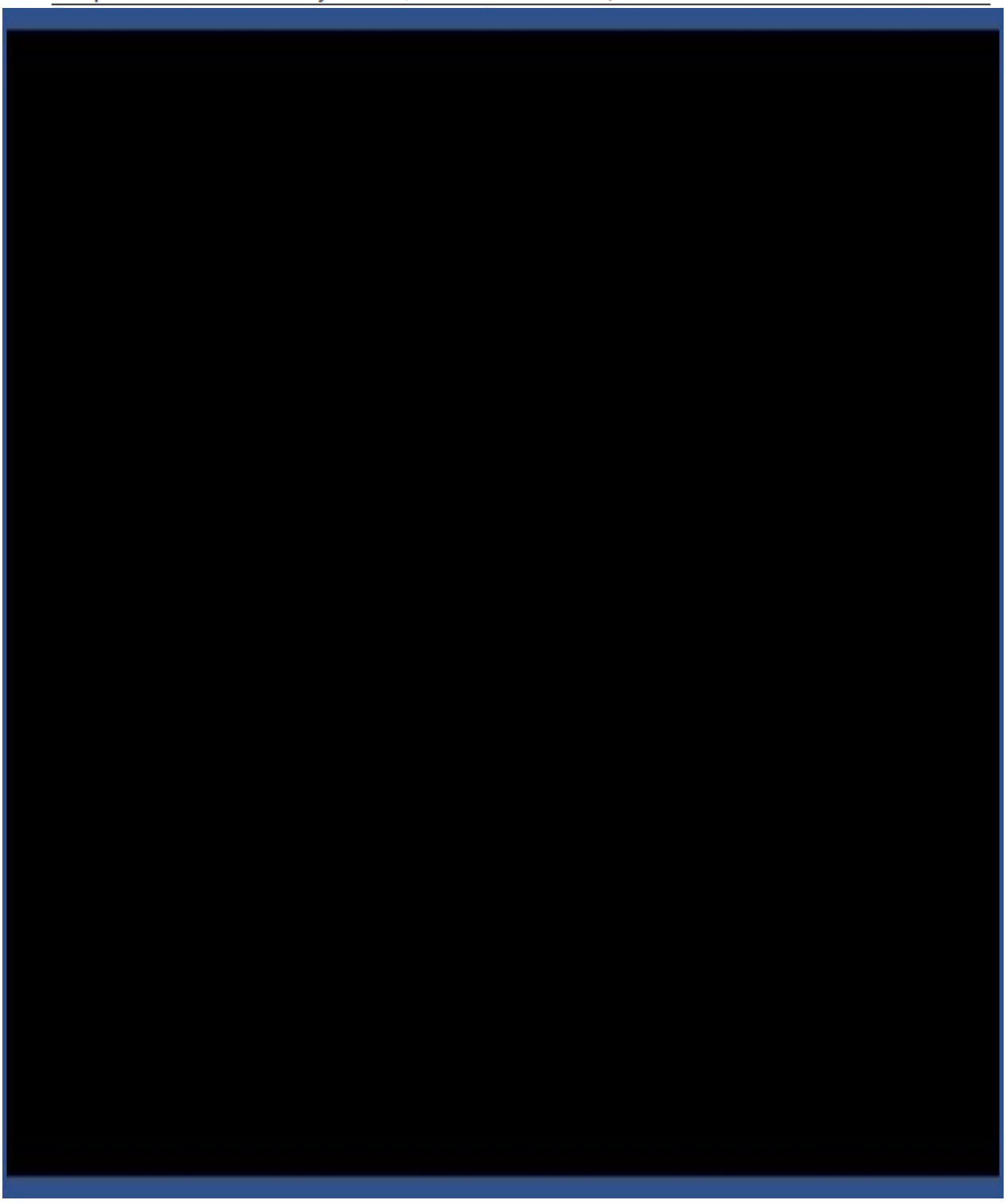
16 Appendix 2 – Slit Lamp Biomcroscopy Grading Scales

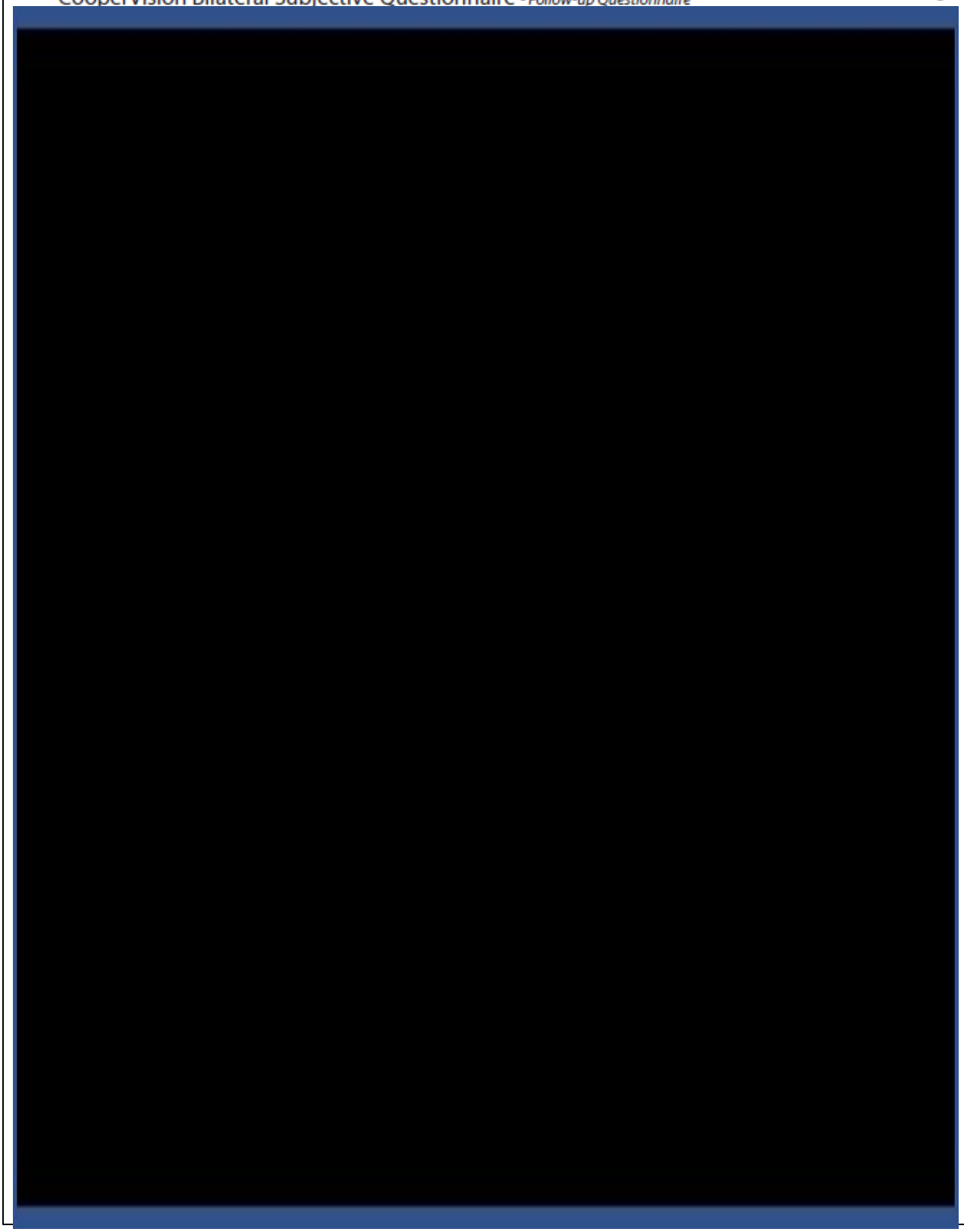
17 Appendix 3 – Post-Settling Questionnaire



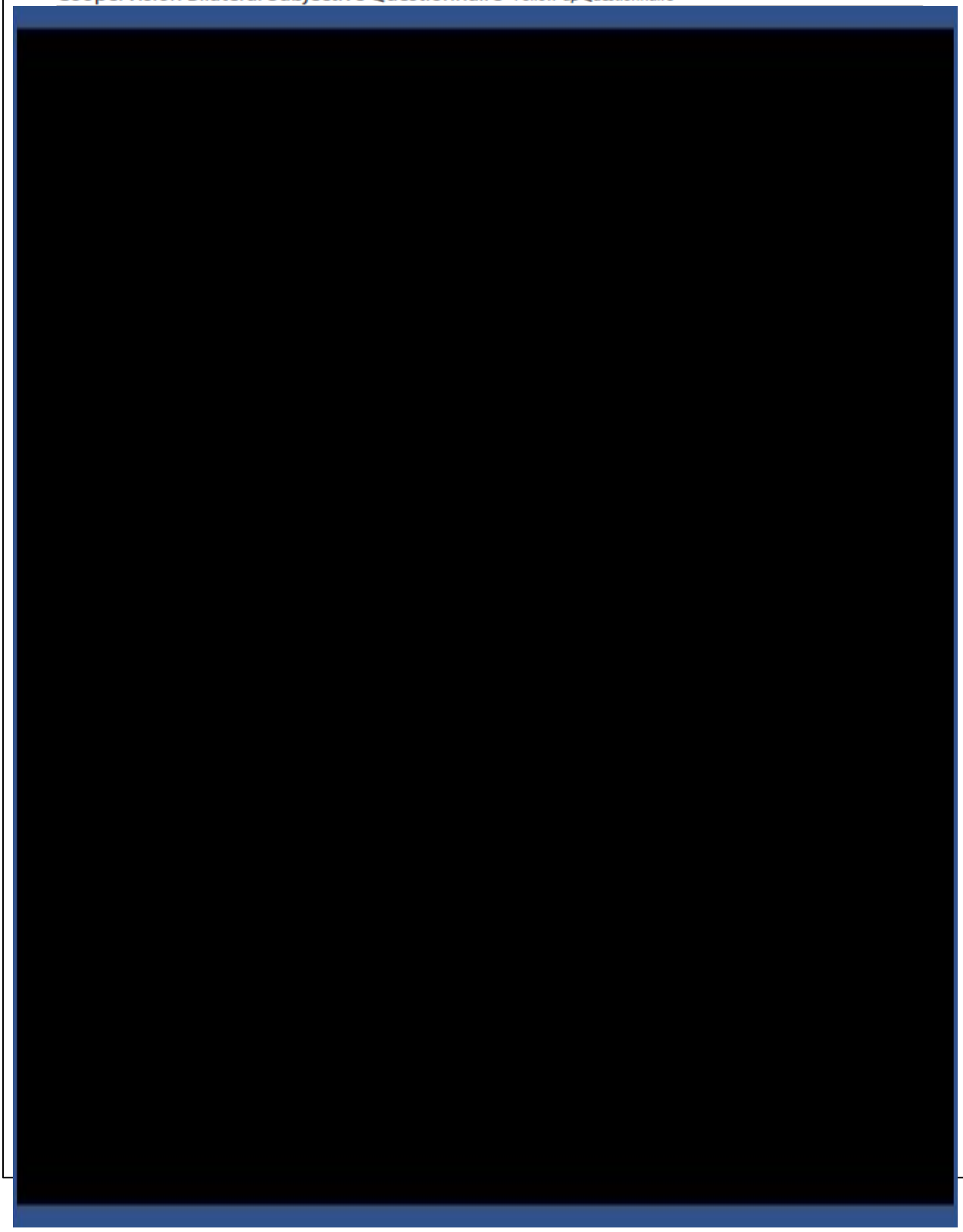
18 Appendix 4 – Follow-up Questionnaire (Pairs 1&2)



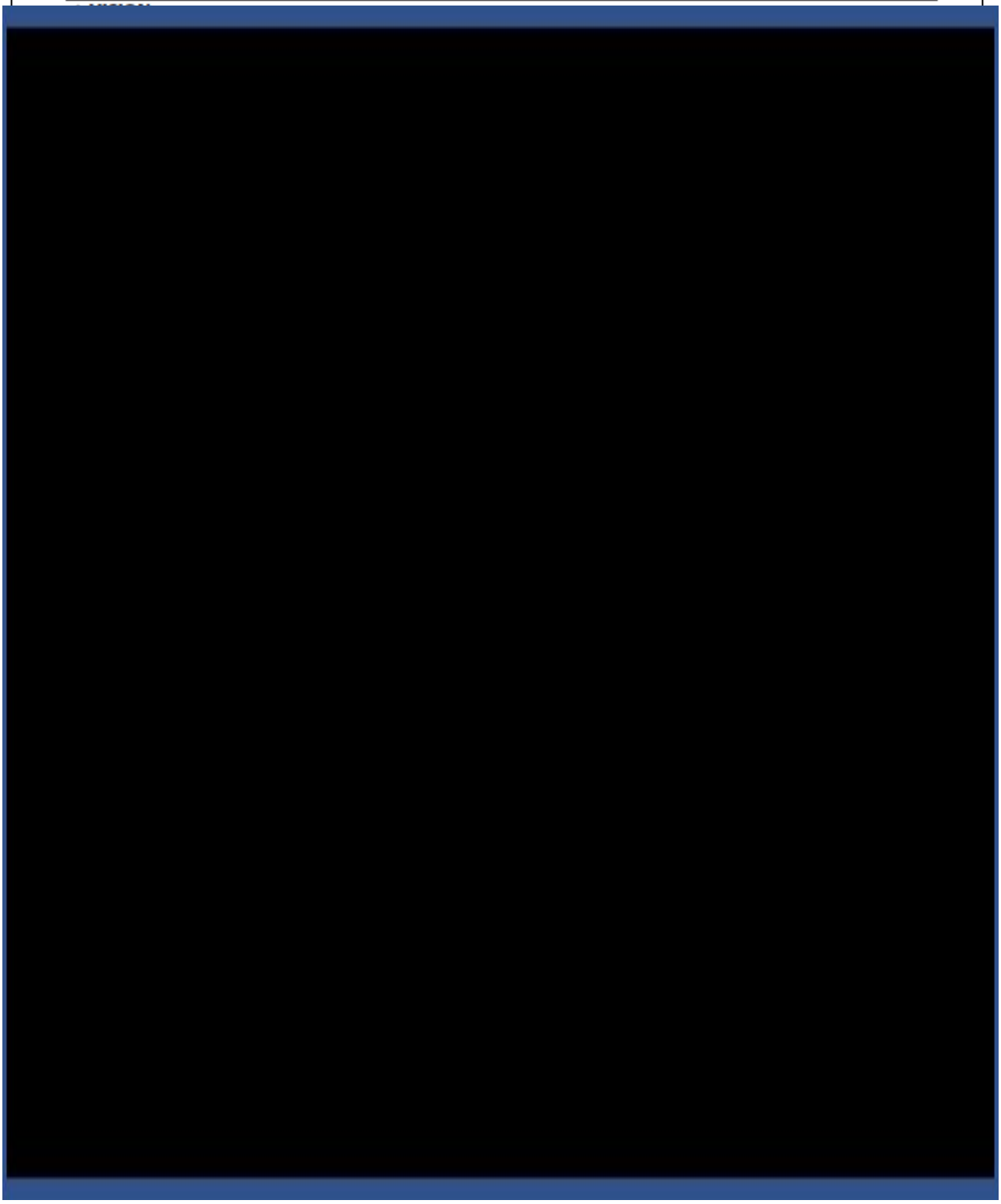




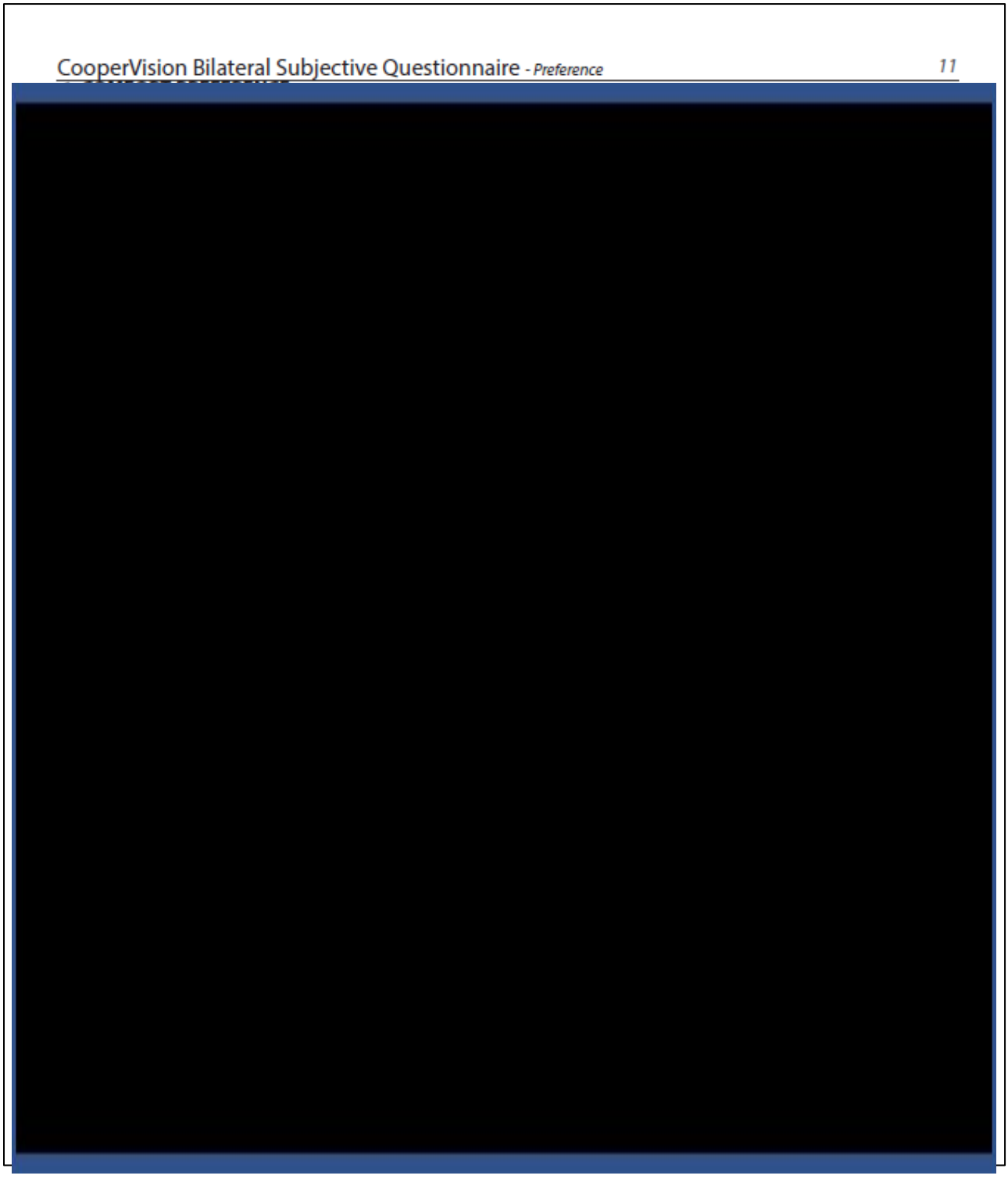
CooperVision Bilateral Subjective Questionnaire - *Follow-up Questionnaire* 9



CooperVision Bilateral Subjective Questionnaire - *Exit Questionnaire* 10



19 Appendix 5 – Final Preference Questionnaire



20 Appendix 6 – Lighting Specifications

Lighting Condition	Distance	Plane of Face
High – chart luminance (cd/m2)	120-200	N/a
High – room illuminance (Lux)	300-600	300-600
Low – chart luminance (cd/m2)	1-5	n/a
Low – room illuminance (Lux)	1-5	1-5