CooperVision™

Study Implementation document:

CLINICAL VALIDATION STUDY OF PHOEBE LENSES

Sponsor Study Code:	CV-17-60
Version Number:	1.0
Implementation document Date:	28 September 2017
Sponsor Company:	CooperVision, Inc.
Study Category:	Design Validation
Clinical Sites:	CORL, Indiana University

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DOCUMENT CHANGE HISTORY

Version	Originator	Description of Change(s)	Date
1.0	[redacted]	Original Protocol	28 September 2017

1 Introduction

CooperVision is evaluating the clinical performance of its Phoebe contact lenses (Test) compared to the commercially available MyDay contact lenses (Control) over 3-day of lens wear on a daily wear, daily disposable modality in a randomized, double masked, bilateral, cross-over dispensing study.

2 Study Objective

The purpose of this study is to validate the clinical performance of the Phoebe contact lenses.

The primary variable of interest is:

- Anterior ocular health examination

The secondary variable of interest is:

- Visual acuity and Vision quality

[redacted]

2.1 Study Hypotheses

The primary study hypothesis is that the Phoebe contact lens performs substantially equivalent to the MyDay contact lens for ocular health.

The secondary study hypotheis is that The Phoebe contact lens is not inferior to the MyDay contact lens for vision and visual acuity.

[redacted]

3 Study Design

This will be a double-masked, randomized, bilateral, cross-over, 3-day dispensing study comparing the Phoebe Test lens against the MyDay Control lens. Each subject will be randomized to wear either the Test or Control lenses first as a matched pair. Each lens pair will be worn for 3 days. All lenses will be replaced daily.

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

- Visit 0: Enrolment / Screening / Baseline Visit
- Visit 1: Dispensing of Pair 1
- Visit 2: Follow-up of Pair 1 (+2 days) and Dispensing of Pair 2
- Visit 3: Follow-up of Pair 2 (+2 days) and Exit

4 Ethics Review / Statement of Compliance

4.1 Relevant Standards / Guidelines

This implementation document has been developed in accordance with the following:

- ISO 14155 Clinical Investigation of Medical Devices for Human Subjects, 21CFR 812.2 (b) IDE-abbreviated requirement
- Declaration of Helsinki

4.2 Institutional Review Board

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

The conduct of this study will be approved by an Institutional Review Board prior to commencement.

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

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 and existing approvals from FDA for the MyDay control contact lens. The contact lenses used in this study are intended for daily wear (NOT extended wear) with usage consistent with typical daily wear.

The Phoebe test lens is manufactured with the same material as the MyDay control lens with a modified optical design, and should therefore not present increased risk to the patient.

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.

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.

Non-Invasive clinical procedures including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and [redacted] will be used. [redacted]

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, participants will receive an examination of the front part 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.

7 Materials and Methods

7.1 Clinical sites

The study will take place at Indiana University School of Optometry, Clinical Optics Research Lab.

This site was selected based on the experience of the site investigators and staff in conducting clinical trials, the availability of potential study participants, and the interest of the site in performing the trial. A site investigator agreement and financial disclosure document will be in place prior to commencement of the trial.

7.2 Participants

Up to 80 subjects will be recruited for this study with the goal to have approximately 50 subjects to complete in total. Each subject will be given a unique ID number. 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:

- **Between and 18 and 35 years of age** and has full legal capacity to volunteer
- Has had a self-reported oculo-visual examination in the last two years
- Has read and understood the information consent letter
- Is willing and able to follow instructions and maintain the appointment schedule
- Is correctable to a visual acuity of 20/25 or better (in each eye) with their habitual correction or 20/20 best corrected
- Has a Contact Lens Refraction between -1.00D and -6.00D
- Cylinder power **≤ -0.75DC** in Spherical Cylindrical Refraction
- Currently wears soft contact lenses
- **Is willing to wear lenses for a minimal of 8 hours a day and everyday during the course of the study**
- Has clear corneas and no active ocular disease
- Has not worn lenses for at least 12 hours before the first visit

Exclusion Criteria

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

- Has never worn contact lenses before
- Is wearing Monovision modality
- 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 undergone corneal refractive surgery
- Is participating in any other type of eye related clinical or research study

7.3 Study Materials

7.3.1 Contact lens

Subjects will be randomized to receive either the Test or Control lens as a matched pair at each visit per a predetermined randomization schedule. The lenses used in this study will be provided by the Sponsor.

The Test lens material is approved by the FDA and the Control lens is commercially available. However, both the Test and Control lenses will be labelled with “Investigational” wording on the labels for study masking purpose.

Details of the contact lenses are shown in Table 1.

	Phoebe (Test)	MyDay (Control)
Material	stenfilcon A	stenfilcon A
Manufacture	CooperVision	CooperVision
Base curve (mm)	8.4	8.4
Diameter (mm)	14.2	14.2
Power (D)	-1.00 to -6.00 (0.25D steps)	-1.00 to -6.00 (0.25D steps)

Table 1: Study lenses

7.3.2 Contact Lens care

No contact lens care is required for this study as lenses are to be worn for a single day only. Subjects are allowed to use saline solution for rinsing purpose as needed. The saline solution will be provided to subject by the clinical site. Subject's habitual rewetting drdops may be used if needed.

7.3.3 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).

7.3.4 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 implementation document by subjects who are under the direct supervision of an investigator.

7.3.5 Disposal of Consumables

This study dispenses consumables (lenses) to participants for use during the study. Participants will be instructed to dispose of worn lenses (both test and control lenses) daily. However, participants will be instructed to retain and return "problem" lenses. Study lenses worn by participants on the follow-up visits will be collected and returned to the sponsor at the completion of the study. Worn lenses will be stored in saline solutions. All unworn lenses will also be returned to the sponsor.

7.3.6 Masking and Control of Study Materials

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

7.3.7 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 will be returned to the Sponsor at the end of the study unless the investigator is otherwise directed by the study Sponsor. Worn lenses on the last day of each lens type will be returned to the Sponsor.

7.4 Visit Schedule and Procedures

7.4.1 Visit 0: 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:

1. The patient is expected to attend the baseline visit not wearing their habitual contact lens products.

2. 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 on to the study.

3. Participant demographics (age, sex, medications, allergies) will be recorded.

4. Habitual lens wearing time (average, maximum, average comfortable) will be recorded.

5. [redacted]

6. Auto Refraction/Auto Keratometry: steepest and flattest K readings (mm).

7. Pupil Sizes in High and Low Illumination will be measured using the Neuroptics pupilometer while looking in the distance.

8. Sphero-cylindrical refraction will be conducted

9. Visual Acuity will be assessed with be assessed with Sphero-cylindrical refraction (D)

    a. Distance visual acuity
        i. High Illumination High Contrast (OU)
        ii. High Illumination Low Contrast (OD, OS, OU)
        iii. Low Illumination High Contrast (OD, OS, OU)

    b. Near visual acuity
        i. High Illumination High Contrast (OU)
        ii. Low Illumination High Contrast (OU)

High Illumination: Overhead lights on, Ideal: 60cd/m^2, Range: 120-200cd/m^2

Low Illumination: Overhead lights off, Ideal: Ideal: 3cd/m^2, Range: 1-5cd/m^2

10. Slit lamp biomicroscopy will be assessed according to the guidelines set out in the CVI Grading scales.

11. The investigator will confirm that the patient meets the criteria set out in the inclusion criteria.

7.4.2 Visit 1: Dispensing visit

Dispensing visit may occur on same day as Visit 0. In which case, steps 1,2 &3 are redundant.

1. Entrance distance HIHC VA (OD, OS) with best sphero cylindrical correction.

2. Slit lamp biomicroscopy will be assessed according to the criteria set out in the Appendix 2.
   a. Not required if done in combination with Visit 0.

3. The investigator will confirm that the patient meets the criteria set out in the inclusion criteria.

4. The first pair of lenses will be inserted by the subject according to randomization schedule.

5. Initial contact lens power chosen based on vertexed, spherical equivalent obtained from refraction.

6. The initial lens fit will be assessed for fit acceptance (acceptable or not acceptable). If the fit is acceptable, the subject will be allowed to sit in the waiting area for a minimal of 10 minutes to allow for the lenses to settle.

7. Visual acuity with initial contact lens power will be assessed.

   a. Distance visual acuity
      i. High Illumination High Contrast (OU)
      ii. Low Illumination High Contrast (OU)

   b. Near visual acuity
      iii. High Illumination High Contrast (OU)
      iv. Low Illumination High Contrast (OU)

8. After lens settling a standard distant monocular over-refraction will be performed. The endpoint of this over refraction will be the best objective acuity and subjective acuity improvement.
   a. Up to -0.50D will be given if objective visual acuity is improved.
   b. -0.25D will be given if subjective visual acuity is significantly improved.

9. A lens change will be implemented if over-refraction dictates. The replacement lens will be allowed to settle for 10 minutes.

10. Change lens prescription to that noted by over-refraction, if needed.

11. Visual Acuity will be assessed with the final lens powers.

    c. Distance visual acuity
       v. High Illumination High Contrast (OU)
       vi. High Illumination Low Contrast (OD, OS, OU)

vii. Low Illumination High Contrast (OD, OS, OU)

d. Near visual acuity
   viii. High Illumination High Contrast (OU)
   ix. Low Illumination High Contrast (OU)

High Illumination: Overhead lights on, Ideal: 60cd/m^2, Range: 120-200cd/m^2

Low Illumination: Overhead lights off, Ideal: Ideal: 3cd/m^2, Range: 1-5cd/m^2

[redacted]

14. The subject will be instructed to wear lenses for a minimal of 8 hours/day and every day until the subject come back for the follow-up visit.

15. The subject will be given enough lenses including spares to last them until the next visit.

16. The subject will be discharged and scheduled to come back for the follow-up visit wearing the study lenses for at least two hours within the required visit window.

17. The subject will be instructed to come back for the follow-up visit wearing the study lenses for at least two hours prior to the visit time.

7.4.3 Visit 2: Follow up lens pair 1/Dispensing lens pair 2 (3 days +2 days from Visit 1)

Subjects should attend wearing the study lenses, which should have been in situ for at least two hours. Subjects who attend without lenses in situ for at least two hours will be rescheduled. The following procedures will be performed (any ocular measurement procedures outlined below will be carried out on each eye):

1. Average Wear Time; Wear Time at visit; Problems and Comments will be recorded.

2. Subjects will return any unworn lenses and problem lenses.

[redacted]

5. Visual Acuity will be assessed with the contact lenses.

   a. Distance visual acuity
      i. High Illumination High Contrast (OU)
      ii. High Illumination Low Contrast (OD, OS, OU)
      iii. Low Illumination High Contrast (OD, OS, OU)

b. Near visual acuity
    i. High Illumination High Contrast (OU)
    ii. Low Illumination High Contrast (OU)

High Illumination: Overhead lights on, Ideal: 60cd/m^2, Range: 120-200cd/m^2

Low Illumination: Overhead lights off, Ideal: Ideal: 3cd/m^2, Range: 1-5cd/m^2

6. Monocular over-refraction and High Illumination High Contrast logMAR VA @ 4m (OU) will be performed and recorded.

7. [redacted]

8. Lens removal and lens storage.

9. Slit lamp biomicroscopy will be assessed set out in the CVI grading scales.

10. Eyes will be rinsed.

11. The Randomised Pair 2 lenses will be fitted.

12. Initial contact lens power chosen based on vertexed, spherical equivalent obtained from refraction (i.e. match the initial power of the first pair).

13. The intial lens fit will be assessed for fit acceptance (acceptable or not acceptable). If the fit is acceptable, the subject will be allowed to sit in the waiting area for a mimimal of 10 minutes to allow for the lenses to settle.

14. Visual acuity with initial contact lens power will be assessed.

    a. Distance visual acuity
        i. High Illumination High Contrast (OU)
        ii. Low Illumination High Contrast (OU)

    b. Near visual acuity
        i. High Illumination High Contrast (OU)
        ii. Low Illumination High Contrast (OU)

15. After lens settling a standard monocular over-refraction will be performed. The endpoint of this over refraction will be the best objective acuity and subjective acuity improvement.

    c. Up to -0.50D will be given if objective visual acuity is improved.
    d. -0.25D will be given if subjective visual acuity is significantly improved.

16. A lens change will be implemented if over-refraction dictates. The replacement lens will be allowed to settle for 10 minutes.

17. Change lens prescription to that noted by over-refraction, if needed.

18. Visual Acuity will be assessed with the final lens powers.

    e. Distance visual acuity
        i. High Illumination High Contrast (OU)
        ii. High Illumination Low Contrast (OD, OS, OU)
        iii. Low Illumination High Contrast (OD, OS, OU)

    f. Near visual acuity
        i. High Illumination High Contrast (OU)
        ii. Low Illumination High Contrast (OU)

High Illumination: Overhead lights on, Ideal: 60cd/m^2, Range: 120-200cd/m^2

Low Illumination: Overhead lights off, Ideal: Ideal: 3cd/m^2, Range: 1-5cd/m^2

[redacted]

21. The subject will be instructed to wear lenses for a minimal of 8 hours/day and every day until the subject come back for the follow-up visit.

22. The subject will be given enough lenses including spares to last them until the next visit.

23. The subject will be discharged and scheduled to come back for the follow-up visit wearing the study lenses for at least two hours within the required visit window.

24. The subject will be instructed to come back for the follow-up visit wearing the study lenses for at least two hours prior to the visit time.

7.4.4 Visit 3: Follow-up lens pair 2 and Exit (3 days +2 days from Visit 2)

Subjects should attend wearing the study lenses, which should have been in situ for at least two hours. Subjects who attend without lenses in situ for at least two hours will be rescheduled. The following procedures will be performed (any ocular measurement procedures outlined below will be carried out on each eye):

1. Average Wear Time; Wear Time at visit; Problems and Comments will be recorded.

2. Subjects will return any unworn lenses and problem lenses.

[redacted]

5. Visual Acuity will be assessed with the final lens powers.

    a. Distance visual acuity
        i. High Illumination High Contrast (OU)
        ii. High Illumination Low Contrast (OD, OS, OU)
        iii. Low Illumination High Contrast (OD, OS, OU)

    b. Near visual acuity
        i. High Illumination High Contrast (OU)
        ii. Low Illumination High Contrast (OU)

    High Illumination: Overhead lights on, Ideal: 60cd/m^2, Range: 120-200cd/m^2

    Low Illumination: Overhead lights off, Ideal: Ideal: 3cd/m^2, Range: 1-5cd/m^2

6. Monocular over-refraction and High Illumination High Contrast logMAR VA @ 4m (OU) will be performed and recorded.

[redacted]

8. Lens removal and lens storage.

9. Slit lamp biomicroscopy will be assessed set out in the CVI grading scales.

10. Exit distance HIHC logMAR visual acuity with refraction from baseline visit (OD, OS, OU)

11. Exit statement signed and exit disposition recorded.

7.4.5 Summary of Visits and Procedures for the study.

Table 2 summarizes the visits and procedures for the study.

Table 2: Summary of Visits and Procedures

	Visit 0 *Screening / Baseline*	**Visit 1** *Dispense Pair 1*	**Visit 2** *Follow-up P1 / Dispensing of Pair 2*	**Visit 3** *Follow-up P2 & Exit*
Informed consent	✓	-	-	-
Meet inclusion/exclusion criteria	✓	-	-	-
History at baseline/Demographics	✓	-	-	-
Wearing time	✓	-	✓	✓
Auto-refraction & keratomtery	✓	-	-	-
Pupilometer	✓			
Sphero-cylindrical refraction	✓	-	-	-
LogMAR VAs with spectacle refraction	✓	-	-	-
Slit-lamp biomicroscopy	✓	✓*	✓	✓
Instillation of lens at office	-	✓	✓	-
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Spherical over-refraction (SOR)	-	✓	✓	✓
LogMAR visual acuity	-	✓	✓	✓
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Exit VAs	-	-	-	✓
Study Exit	-	-	-	✓

** Not applicable if Visit 1 occurs on the same day as Visit 0*

Calibration will be done on all applicable instruments (i.e., autorefractor and keratometer) prior to the start of the study and a copy of the calibration document will be kept on file. A copy of the calibration document will be forwarded to the Sponsor.

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)	

22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
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.***

[redacted]

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:

[redacted]

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.

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.

[redacted]

10 Statistical Analysis

10.1 Statistical analysis

Summary statistics will be produced (e.g. mean, standard deviation). Paired t test will be used to compare slit lamp biomicroscopy, [redacted]. 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. Non-inferiory or equivalence testing will be conducted as appropriate.

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, a 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.

Prior to final data freeze, a 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 implementation document 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. 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 Protocol Deviations

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

Major protocol deviations may impact the research protocol, Informed Consent form or other study materials, usually cannot be anticipated ahead of time and are often necessary to ensure the safety and welfare of the subjects.

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

1. Changes in procedures initiated to eliminate immediate risks/hazards to subjects;
2. Enrolment of subjects outside the protocol inclusion/exclusion criteria;
3. Inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design;

4. Informed Consent documentation violations: no documentation of informed consent; incorrect version of, or incomplete, informed consent documentation used.

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

- Logistical or administrative aspects of the study (e.g., study subject missed appointment, change in appointment date or time);
- Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would not impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

11.5.1 Reporting and documenting protocol deviations

Major protocol 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 according to the site's guidelines. All protocol deviations (major and minor) occurring during the study will be documented and included in the final report and data safety monitoring report to the IRB

11.6 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 CooperVision Master Services Research Agreement (dated 20 June 2007), 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.

11.7 Publication

Indiana University may publish the results of this study, subject to the conditions laid out in the CooperVision Master Services Research Agreement, dated 20 June 2007.

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 Appendices

Appendix 1 Randomization Table

Appendix 2 CVI Grading Scales

Appendix 3 Questionnaires

APPENDIX 1

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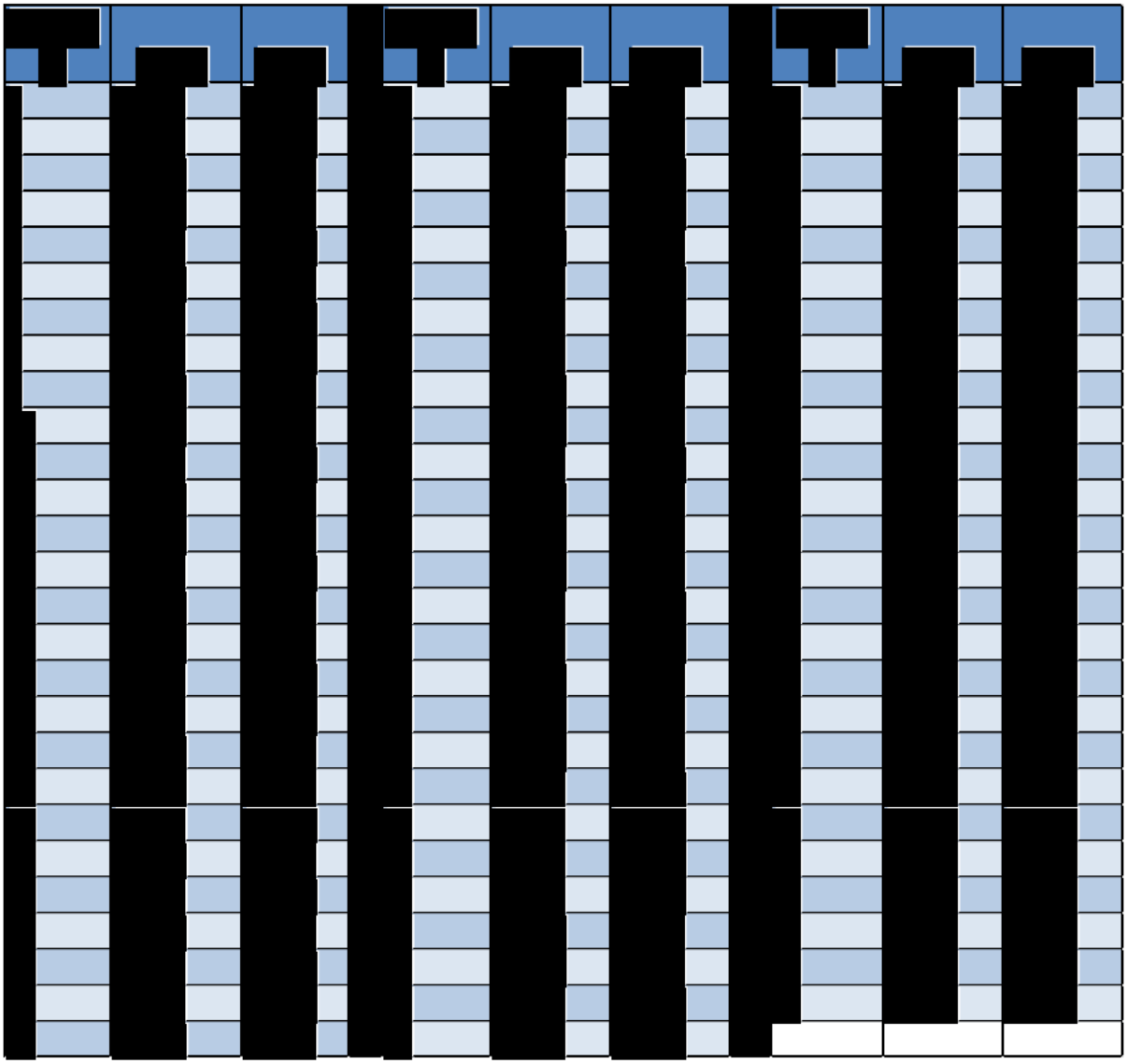

APPENDIX 2

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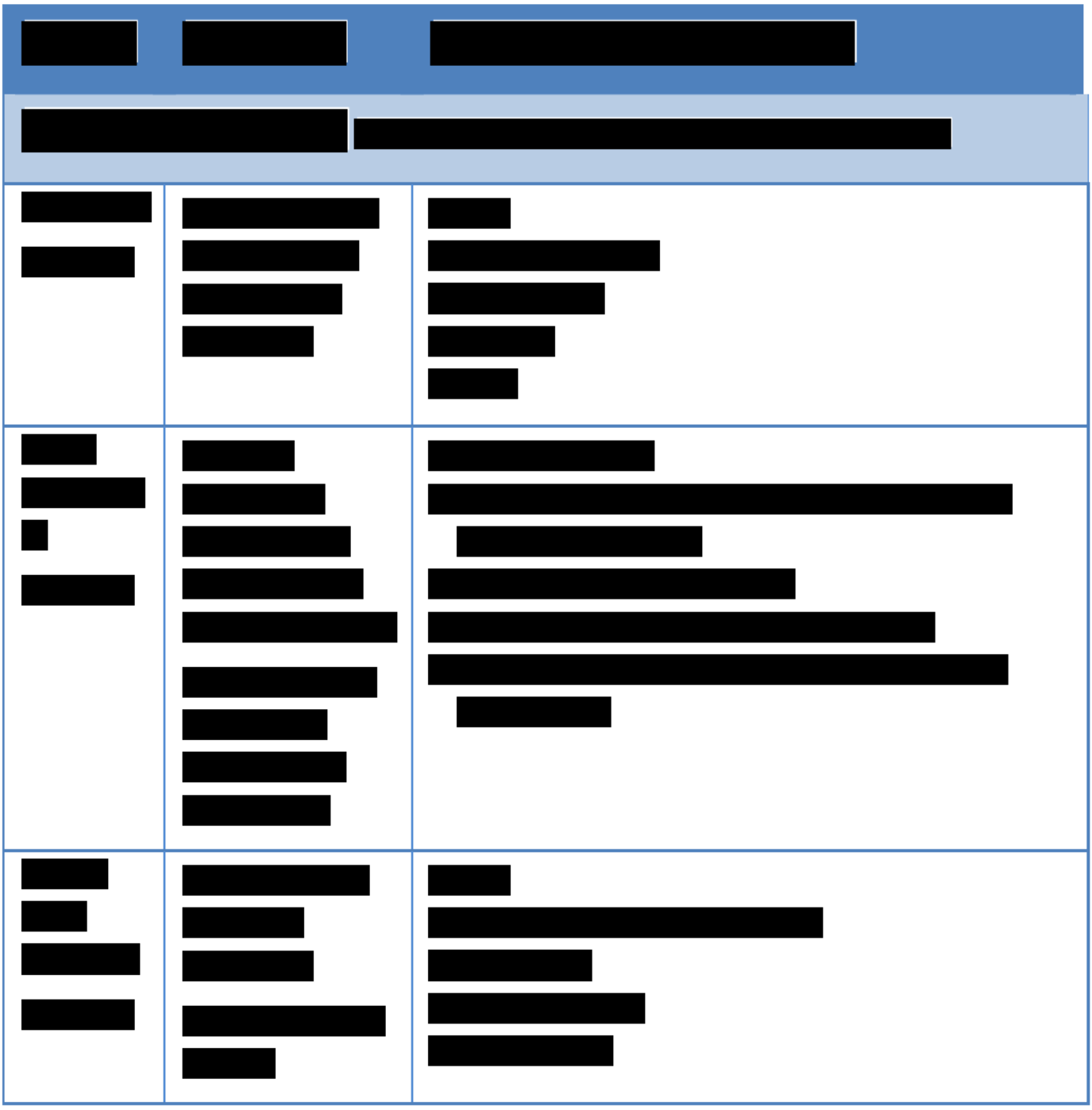

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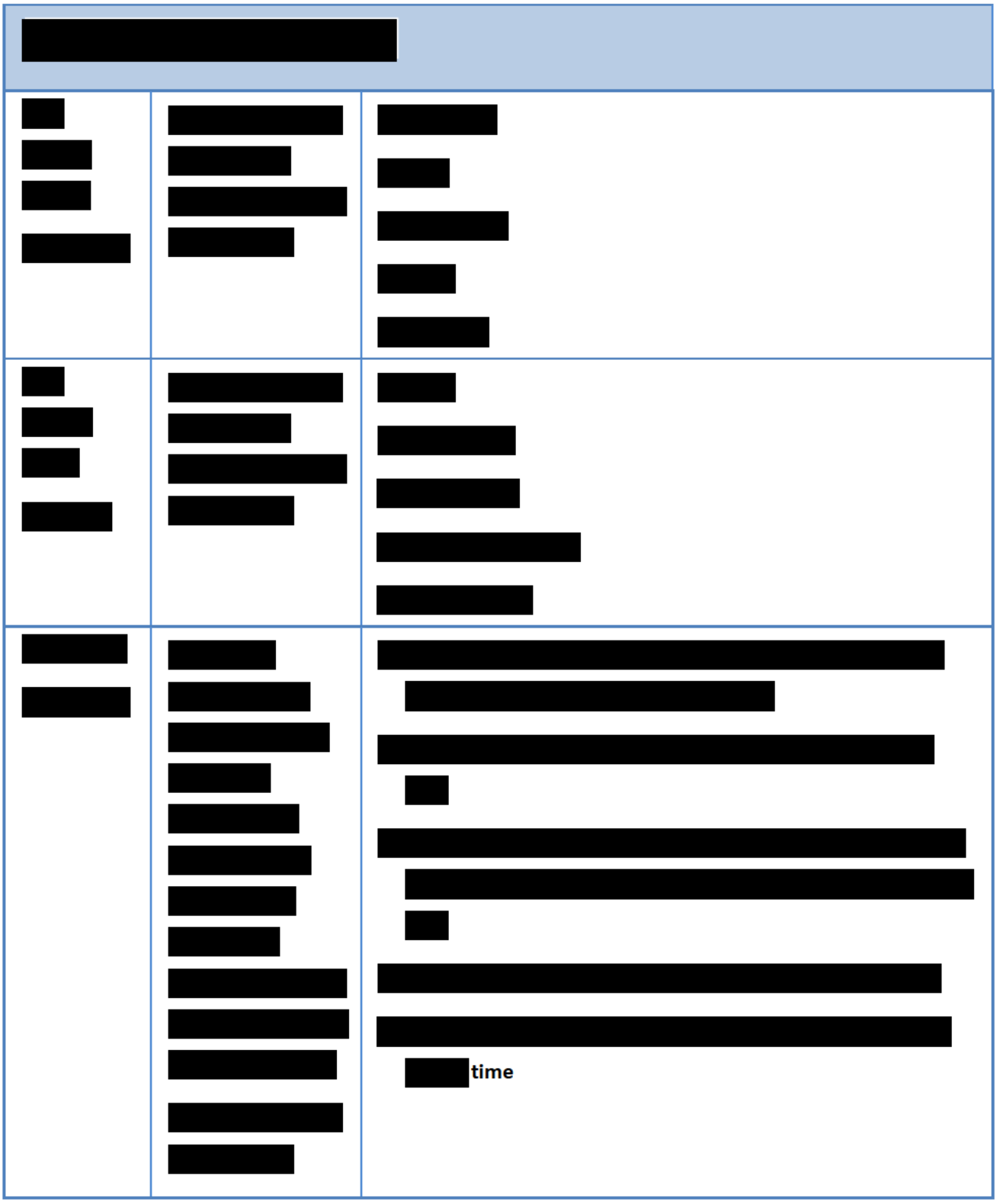

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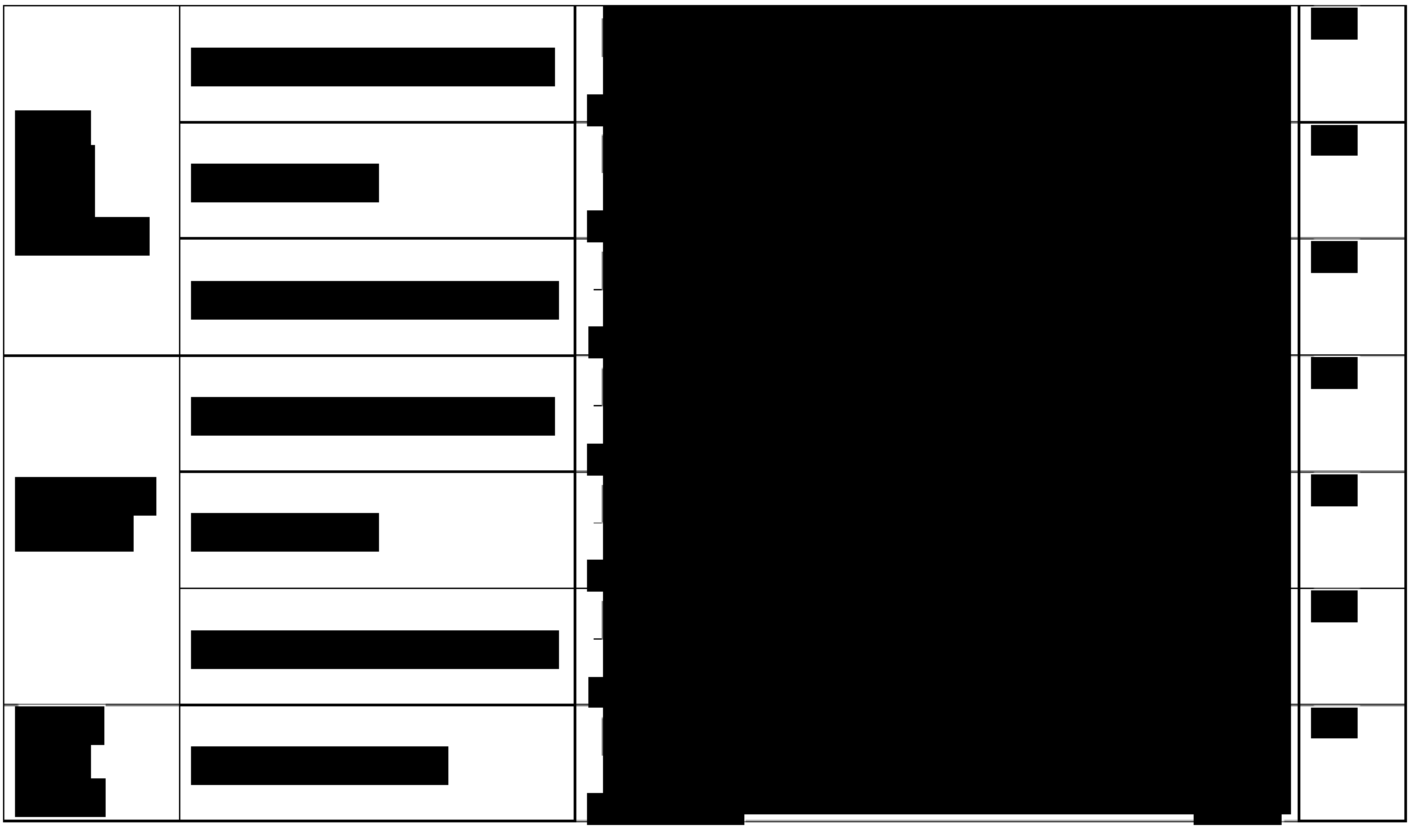

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Based on the STUDY lens performance only, how likely are you to continue wearing the **STUDY** lenses that you are wearing?			
Very Likely	Likely	Unlikely	Very unlikely
☐	☐	☐	☐
Comment/Reason:			

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