CooperVision™

PROTOCOL

A ONE-WEEK CROSSOVER DISPENSING EVALUATION OF [redacted] DAILY WEAR SOFT CONTACT LENSES

Sponsor Study Code:	CV-17-29
Sponsor Company:	CooperVision, Inc.
Version Number:	1.1
Protocol Issue Date:	14 July 2017
Sponsor Company:	CooperVision, Inc.
Study Category:	[redacted]
Clinical Sites:	CORL, Indiana University
Sponsor:	**CooperVision, Inc.** 5870 Stoneridge Drive, Suite 1 Pleasanton, CA, USA 94588

Study Sponsor Representative: [redacted] Date: 14 July 2017

[redacted]

CooperVision Sponsor Management: [redacted] Date: 14 July 2017

[redacted]

Site Principal Investigator: [redacted] Date: 17 July 2017

[redacted]

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DOCUMENT CHANGE HISTORY

Version	Originator	Description of Change(s)	Date
1.0	[redacted]	Original Protocol	30 May 2017
1.1	[redacted]	[redacted] - Additional variable added (lens fit parameters) - Reference to ISO 14155 updated - Clinical trial registration amended - Addition, ID number will not be reused in event of screen failure or discontinuation [redacted] - Minor modifications to, and errors corrected in, procedures - Early read of data with subsequent report added to Statistical Analysis section - Modification of publication & confidentiality sections	14 July 2017

1 Introduction

CooperVision is evaluating the clinical performance of [redacted] riofilcon A lens (test) compared to Alcon Focus Dailies All Day Comfort lens (control) when worn on a daily wear, daily disposable modality in a randomized, bilateral crossover dispensing study.

2 Study Objective

This pilot study seeks to compare the performance of [redacted] design lenses against Alcon Focus Dailies All Day Comfort lenses and will be used to provide additional performance information to add business confidence prior to a larger post market study.

The primary variables of interest are:

- Lens fit acceptability

Additional variables are:

- [redacted]

2.1 Study Hypothesis

The study hypothesis is that there will be no difference in clinical performance between the [redacted] test lens and the Alcon Focus Dailies control.

3 Study Design

This will be a double-masked, randomized, bilateral, 1-week crossover, dispensing study, comparing the [redacted] test lens against Focus Dailies All Day Comfort control lens, such that each lens type will be worn for a week each. Each subject will be randomized to wear either the test lenses or the control lenses as a matched pair, according to a predetermined randomization

schedule. All lenses will be replaced daily. [redacted]

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

- Visit 0: Enrolment / Screening / Baseline Visit (Day 0)
- Visit 1: Dispensing of Pair 1 (Day 0)
- Visit 2: One-week follow-up of Pair 1 (-1/+4 days) and Dispensing of Pair 2
- Visit 3: One-week follow-up of Pair 2 (-1/+4 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
- ICH Harmonized Tripartite Guideline for Good Clinical Practice
- 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.

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 previous cytoxicity 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 45 subjects will be enrolled and dispensed in order for approximately 40 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. 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 20/25 in each eye.
- Wears CLs in both eyes (monvision 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 Sites

The study will be take place at a single site: CORL, Indiana University.

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.

7.3 Study Materials

7.3.1 Contact lens

The test lens is an investigational product. The control lens is approved by the FDA and is commercially available in the USA.

Subjects will be randomized to receive either the test or control lens as a matched pair at each visit, per a predetermined randomization schedule (Appendix 2). The test 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 [redacted]	**Control Focus Dailies All Day Comfort**
Manufacturer	CooperVision, Inc.	Alcon
Material	riofilcon A	nelfilcon A
Base curve (mm)	8.60	8.60
Diameter (mm)	14.00	13.80
Power (D)	-1.00 to -6.00D	-1.00 to -6.00D

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.

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. All study lenses worn between study visits will be discarded by the participant, although subjects will be asked to retain the study lens foils. Lenses worn to the follow-up visits will be collected and stored in unpreserved saline for return to the Sponsor. Unworn test 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. If standard labelling does not sufficiently mask the study material then over-labelling will be performed.

7.3.7 Ordering and Accountability of Study Materials

The test will be provided by the sponsor and the control lenses sourced by the site. 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.

7.3.8 Rewetting Drops

Subjects will be allowed use of habitual rewetting drops if required during the study, except for on the days of the study visits. Type of drop and frequency of use will be recorded, if any.

7.4 Visit Schedule and Procedures

The investigator should confirm with the subject that they are able to attend the follow-up visits within the visit window before enrolling them in the study. Visits that fall outside of the specified visit windows will be counted as unscheduled visits for analysis purposes.

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:

- 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 to be enrolled on to the study.
- Habitual lens wearing time (average, maximum, average comfortable). Also habitual type of comfort/re-wetting drop 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 (Appendix 1).
- The investigator will confirm that the patient meets the criteria set out in the inclusion criteria.

7.4.2 Visit 1: Dispensing Pair 1 (Day 0)

Dispensing visit may occur on same day as Visit 0. If Visit 1 is conducted on a different day to Visit 0, slit lamp biomicroscopy should be conducted again to confrm eligibility.

- Baseline auto-keratometry if not done within the previous 6 months.
- HVID (mm) and palpebral aperture size (mm) measurements using slit lamp oculars.
- The first study pair of contact lenses will be selected according to the randomization table (Appendix 2).
- The contact lenses will be provided by a study coordinator/technician to maintain masking of the investigator. The lenses will be inserted by the subject from the blister pack after the label is removed by the study coordinator/technician.
- [redacted]
- An initial fit assessment will be made to ensure lens fit is acceptable. The subject should be discontinued and exited if the lens fit is found unacceptable and the primary reason for poor fit recorded.
- Monocular spherical over-refraction (SOR) will be conducted to determine if a different lens power is required.
- Final lenses will be inserted and allowed to settle for 15 minutes, if applicable.
- [redacted]
- [redacted]

[redacted]

- Lens fit (OD/OS) will be assessed and graded according to the CVI grading scales (Appendix 1):

  - Overall lens fit acceptance (0-4 scale) and investigator reason, if unacceptable.
- 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.

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

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

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  - [redacted]
- Lens fit (OD/OS) will then be assessed and graded according to the CVI grading scales (Appendix 1):
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - Overall lens fit acceptance (0-4 scale) and investigator reason, if unacceptable

[redacted]

- The lenses will be removed and retained for return to the Sponsor.
- Slit lamp biomicroscopy will be assessed according to the CVI approved study biomicroscopy CRF.

Dispense Pair 2

- The second study pair of contact lenses will be selected according to the randomization table (Appendix 2).
- The contact lenses will be provided by a study coordinator/technician to maintain masking of the investigator. The lenses will be inserted by the subject from the blister pack after the label is removed by the study coordinator/technician.
- [redacted]
- An initial fit assessment will be made to ensure lens fit is acceptable. The subject should be discontinued and exited if the lens fit is found unacceptable and the primary reason for poor fit recorded
- Monocular spherical over-refraction (SOR) will be conducted to determine if a different lens power is required.
- Final lenses will be inserted and allowed to settle, if applicable.
- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- Lens surface (OD/OS) will be assessed and graded according to the CVI grading scales (Appendix 1):
  - [redacted]
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  - [redacted]
  - [redacted]
  - [redacted]
  - Overall lens fit acceptance (0-4 scale) and investigator reason, if unacceptable
- The subject will be instructed to wear the study lenses for a minimum of 8 hours per day / 5 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.

7.4.4 Visit 3: One-Week Follow-up Pair 2 (Day 7 +4/-1 days) and Exit

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

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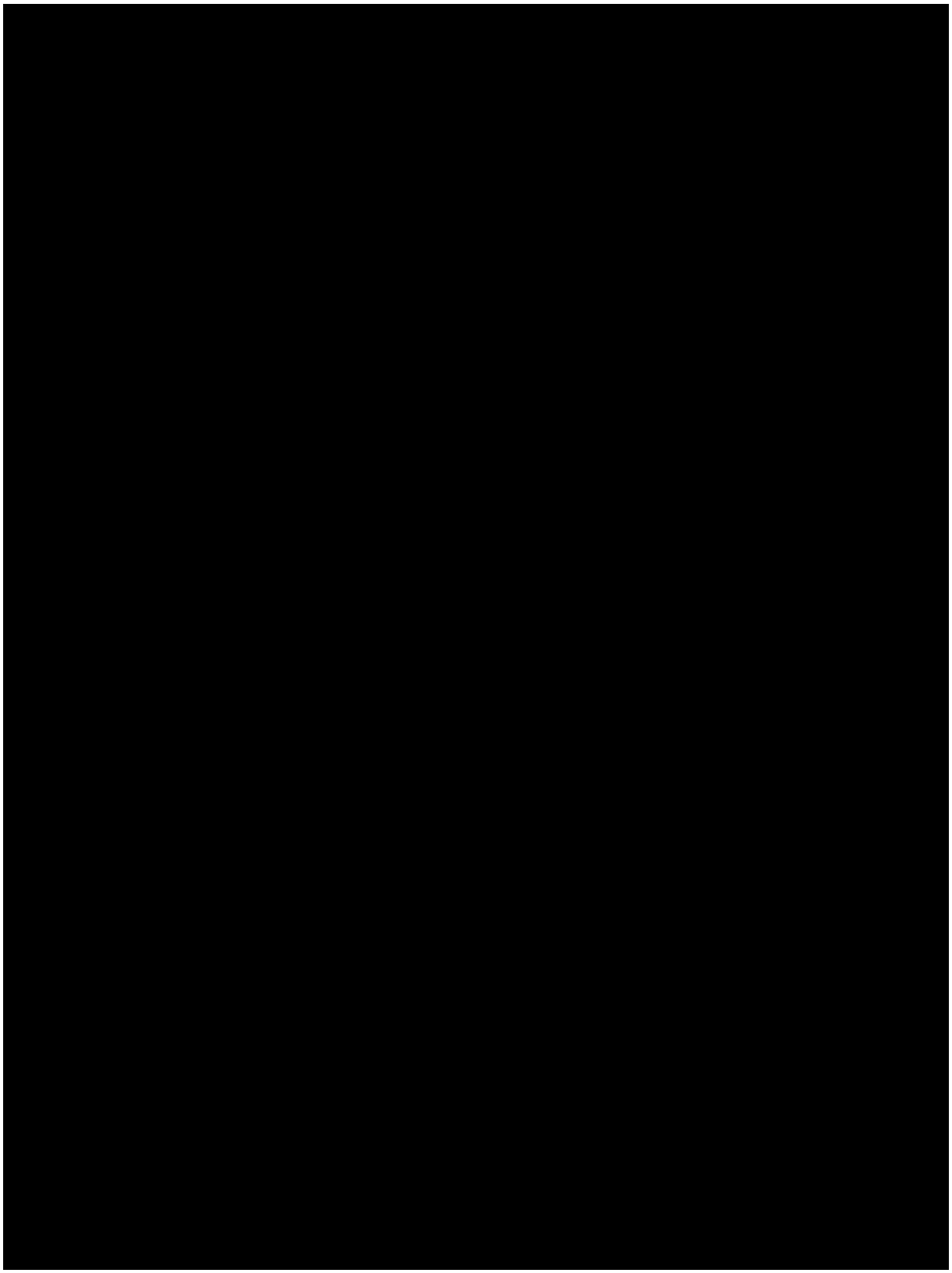
- Lens fit (OD/OS) will then be assessed and graded according to the CVI grading scales (Apprendix 1):
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - Overall lens fit acceptance (0-4 scale) and investigator reason, if unacceptable
- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- The lenses will be removed and retained for return to the Sponsor.
- [redacted]
- Exit HIHC logMAR visual acuities will be recorded (OD/OS)
- The subject will be discharged and will sign the exit statement.

7.4.5 Comfort Throughout the Day Questionnaire



7.4.6 Summary of Visits and Procedures

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** *1-week follow-up Pair 1 / Dispensing of Pair 2*	**Visit 3** *1 week follow-up Pair 2 & Exit*
Informed consent	✓	-	-	-
Meet inclusion/exclusion criteria	✓	-	-	-
History at baseline	✓	-	-	-
Demographics	✓	-	-	-
Wearing time	✓	-	✓	✓
HVID / palpebral aperture size	✓	-	-	-
Auto-refraction & keratomtery	✓	-	-	-
Sphero-cylindrical refraction	✓	-	-	-
HIHC & HILC VAs with spectacle refraction	✓	-	-	-
[redacted]	✓	✓*	✓	✓
Instillation of lens at office	-	✓	✓	-
[redacted]	-	✓	✓	✓
[redacted]	-	✓	✓	✓
Lens fit assessments	-	✓	✓	✓
[redacted]	-	✓	✓	-
[redacted]	-	✓	✓	✓
[redacted]	-	-	-	✓
Exit VAs	-	-	-	✓
Study Exit	-	-	-	✓

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

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.

The subject will be asked to score their subjective response as detailed in CVI Grading scales

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**
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)	**days**; IRB reporting as per requirements
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: [redacted]
Phone: [redacted]
Address: [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.

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 Malfunctions.

10 Statistical Analysis

10.1 Statistical analysis

Summary statistics will be produced (e.g. mean, standard deviation). Paired t-test or two sample 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 timepoints. The critical alpha level for statistical significance will be set at $p \leq 0.05$, with adjustment for multiple comparisons.

An early read of performance variables (interim data) will be taken prior and a report produced prior to completion of the study.

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. Copies of all original raw data forms and completed CRF's will be forwarded to the sponsor at completion of the final report at the Sponsor's request.

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 the web-delivered comfort 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. [redacted]

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

11.6 Publication

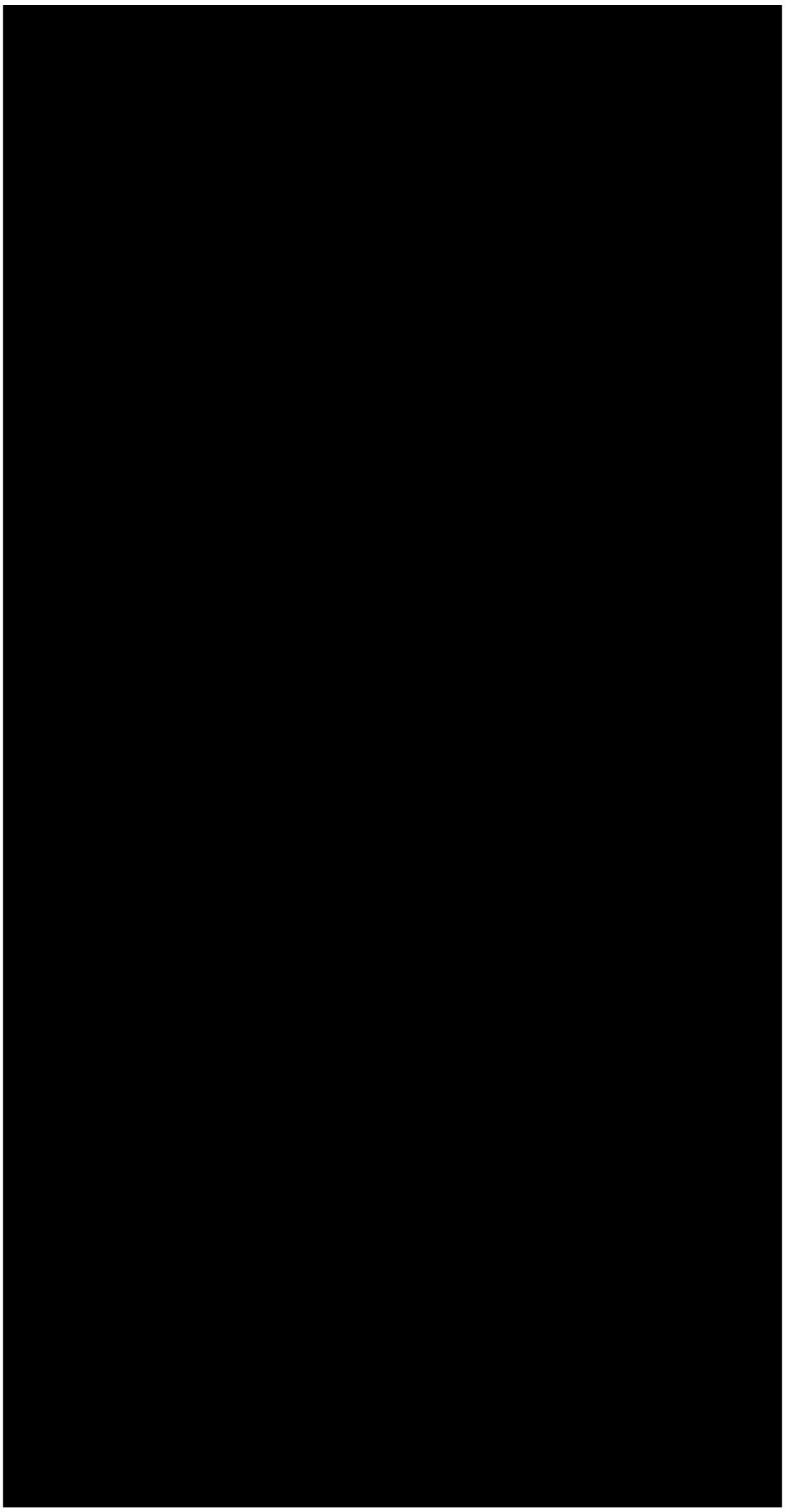
Indiana University may publish the results of this study, subject to the conditions laid out in the [redacted]

12 Study Costs

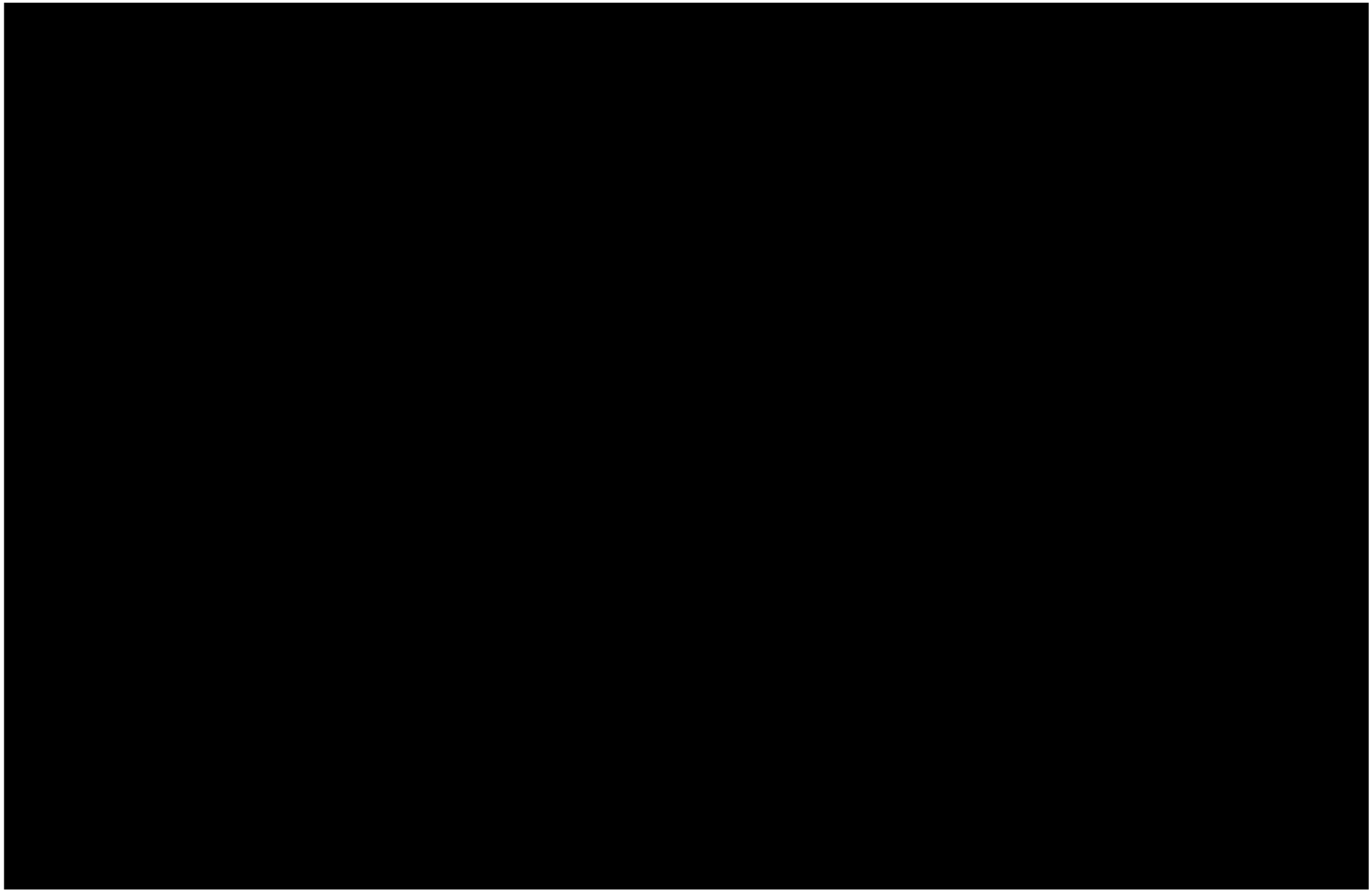
The sponsor will compensate the clinical site and the subjects for their time and participation in this voluntary study.

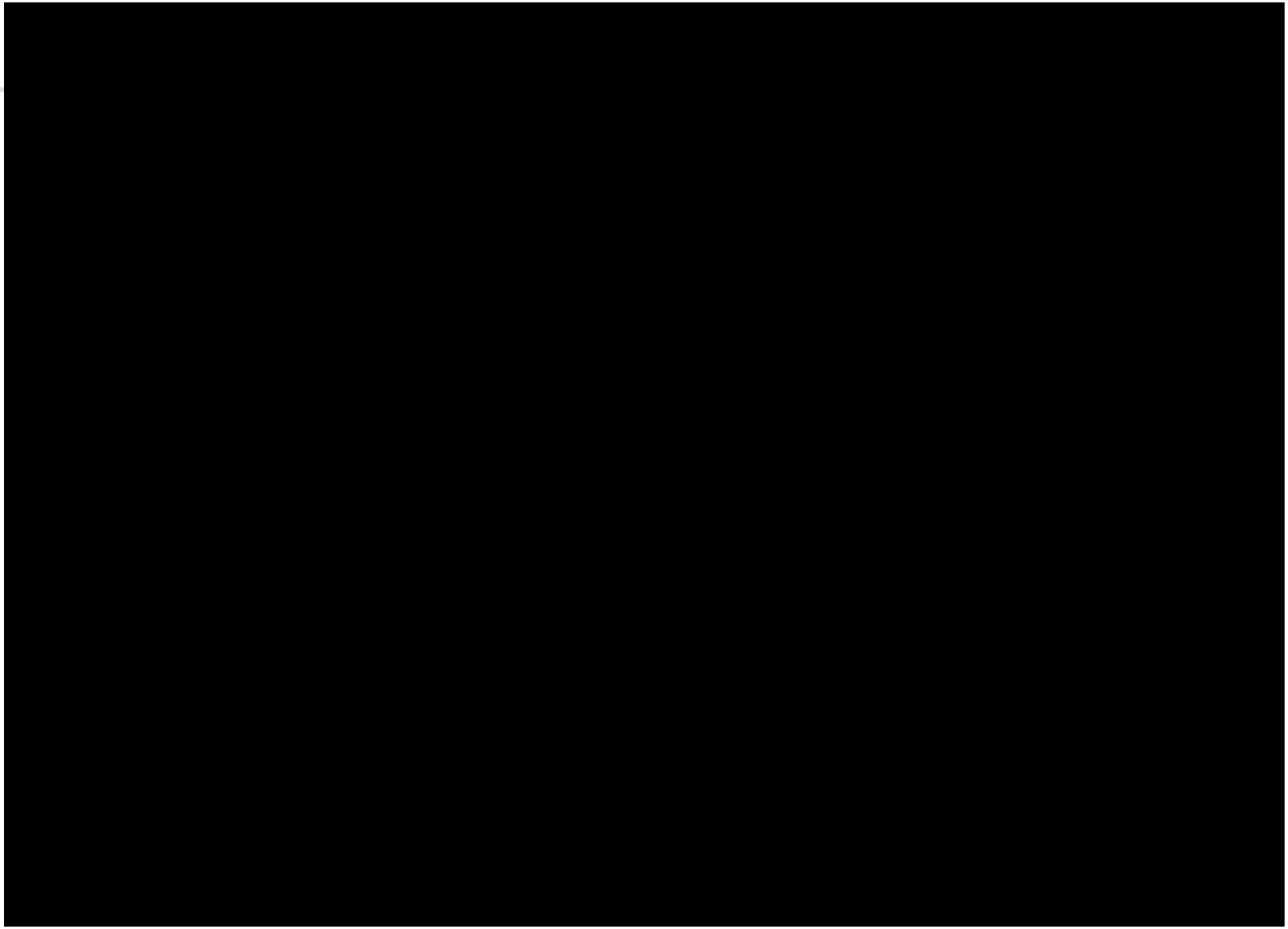
Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The participant must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

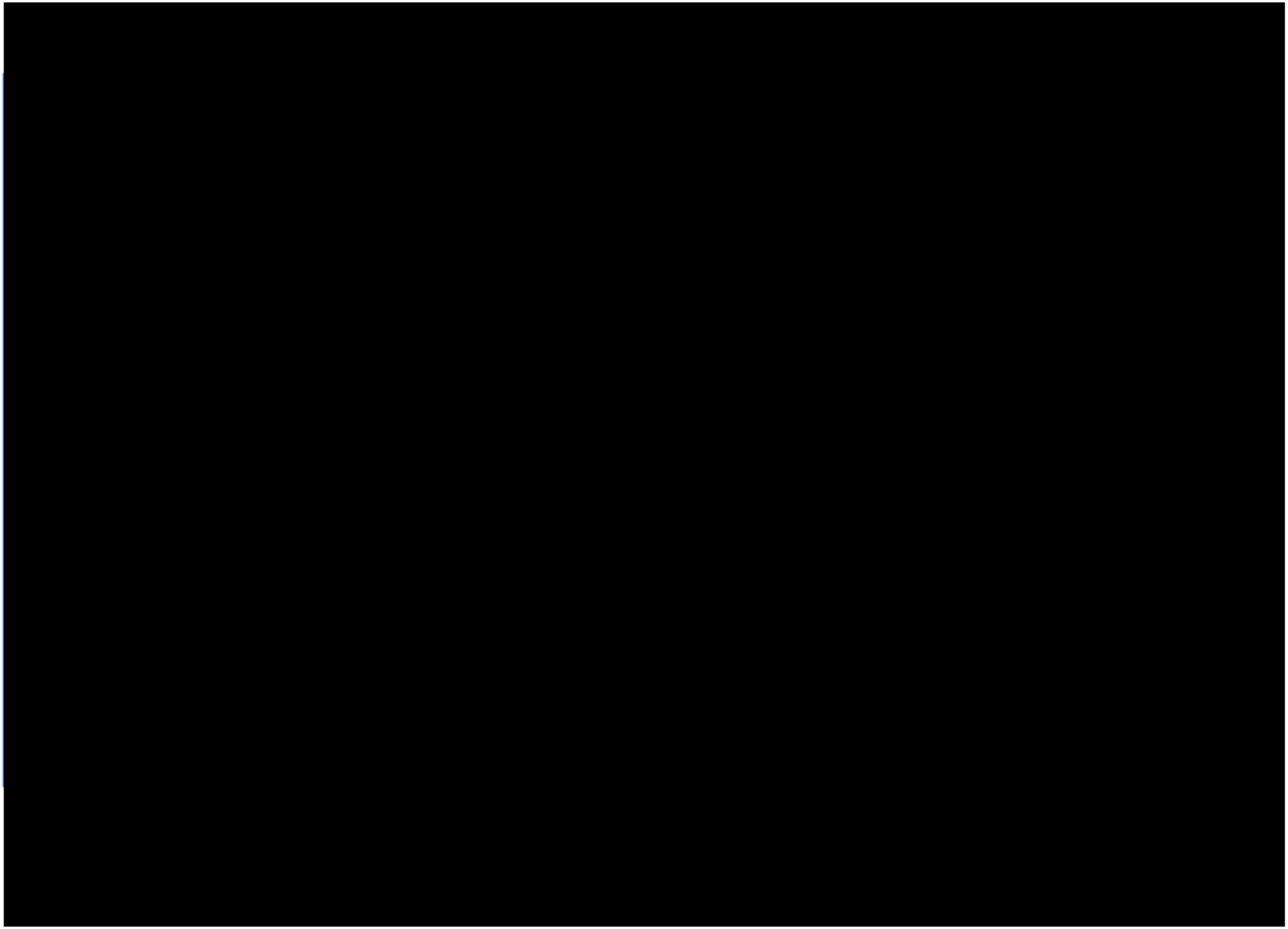
APPENDIX 1

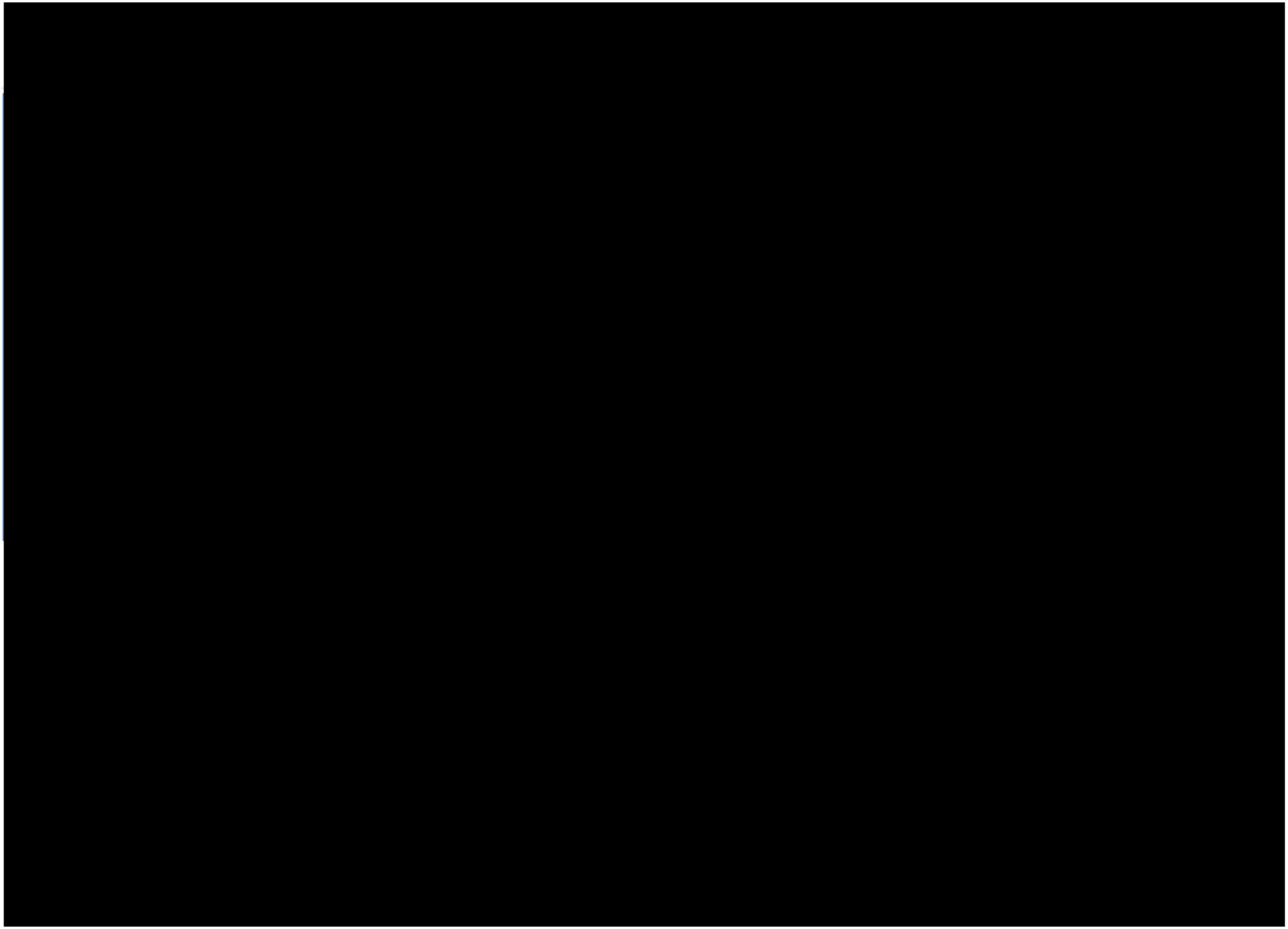


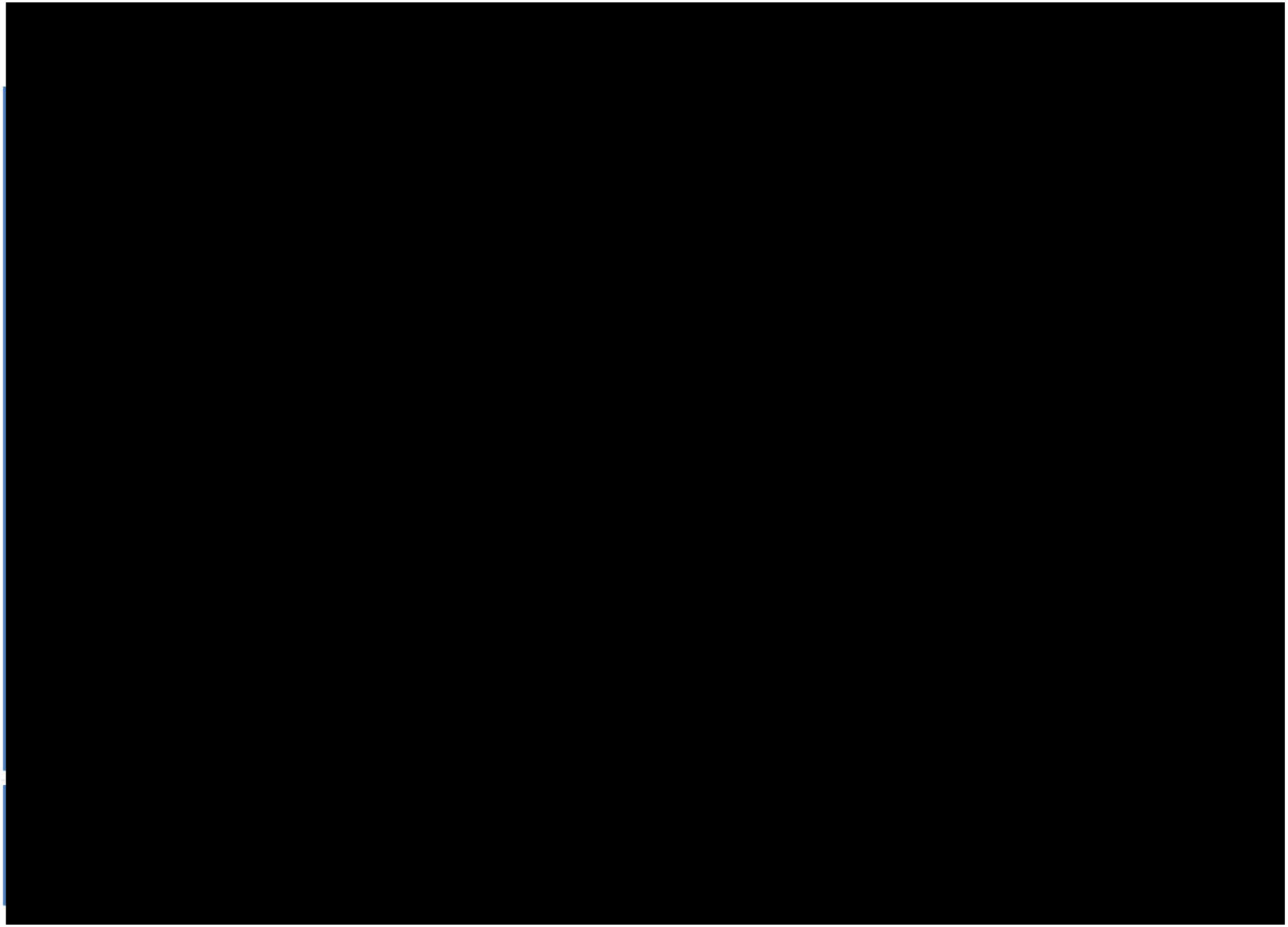
APPENDIX 2











APPENDIX 3