PROTOCOL TITLE:

CLINICAL EVALUATION OF COMFILCON A CONTACT LENSES

Sponsor Study Code:	CV-23-86
Site Study Code: (if applicable)	N/A
Version Number:	1.1
Date:	02 NOV 2023
Sponsor Company:	COOPERVISION INTL LTD.
Clinical Sites:	Multi-Site Trial, see Appendix 13
Study Stage:	Confirmatory

Protocol Author:	[redacted]
Sponsor Management:	[redacted]
Data Management/Statistician:	[redacted]
CVI Operations Lead:	[redacted]

Document Change History

Version	Originator	Description of Change(s)	Date
1.0	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

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Overall Synopsis of the Clinical Investigation Plan (Protocol)

Sponsor Address:	[redacted]
Funding Source:	CooperVision Intl Ltd – For more details, see Study Agreements
Investigation Sites:	See Appendix 13
Principal Investigators:	See Appendix 13
Protocol Synopsis:	The objective of this study is to confirm the clinical performance of two different manufacturing processes for comfilcon A contact lenses.
Planned Start Date	Nov 2023
Estimated Duration	4 months
Primary Study Objective	To assess the clinical performance of comfilcon A lenses
Overview of Study Design	30 day refit, parallel arm of comfilcon A with a novel process (Test) vs comfilcon A with the current process (Control)
Primary Outcome(s)	logMAR visual acuity
Secondary Outcome(s)	None
Visit Schedule	Baseline & Dispensing, 1-week, 4-weeks
Study Products	Supplied by the Sponsor
Subject Population	**# of subjects**: A maximum of 79 subjects will be enrolled in order to achieve a minimum of 72 completed subjects **Adults (mix of symptomatic and asymptomatic)**
Inclusion/Exclusion	**Main Inclusion criteria: Standard inclusion criteria** **Main Exclusion criteria: Standard exclusion criteria**

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1 Study Objective

In an effort to continually improve our products, the objective of this study is to confirm the clinical performance of a novel manufacturing process for comfilcon A contact lenses. The lenses in the study are approved for commercial use, but the Test lenses have yet to be released for commercial distribution. The Control lenses will represent our current manufacturing process. This study seeks to confirm the performance of comfilcon A lenses over one month of wear.

The primary endpoint is:

- logMAR distance (4m) high illumination high contrast visual acuity at the 4 week timepoint

2 Study Design

This will be a prospective, multiple day, double (investigator and subject)-masked, randomized, bilateral re-fit parallel arm study comparing a Test lens against an appropriate Control lens. Subjects will be randomized to wear the Test or Control lens for 30±2 days. There will be an interim visit after 7±1 days of lens wear. Subjective questionnaires will also be collected over the duration of lens wear.

There will be a total of 3 visits in the study as described in Section 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 and Control lenses are both currently marketed contact lenses. Test lenses will be dispensed at a ratio of two for every one Control lens. To maintain masking, Test lenses will be randomized as two of the three groups used in the study.

Further details regarding the study lenses are described in the Package Insert.

Table 1: Study lenses

	Test Lens	Control Lens
Device Name	comfilcon A with novel process	comfilcon A with current process
Regulatory status	Commercial, FDA approved	Commercial, FDA approved
Manufacturer	CooperVision	CooperVision
Material	comfilcon A	comfilcon A

Water Content	48%	48%
Base curve (mm)	8.6	8.6
Diameter (mm)	14.0	14.0
Power range (D)	-0.50 to -6.00 in 0.25D steps	-0.50 to -6.00 in 0.25D steps
Label	Investigational for randomization purposes, to two of Lens A, B, C	Investigational for randomization purposes, to one of Lens A, B, C

3.1.1 Intended Use

In this clinical investigation, the study lenses are intended to be used as a reusable soft contact lens. Reusable lenses will be worn as a daily wear lens, cleaned and stored in a commercially-available lens care solution. Subjects will be asked for their current contact lens regimen and the site will be responsible to provide the lens care solution to the subjects.

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

Study lenses used for more than one day will be cleaned and stored using commercially available lens care product and stored in commercially available lens cases, according to manufacturer recommendations. Contact lens re-wetting drops may be used during this study, as needed by the subject.

The site will be responsible for providing contact lens solutions to match the subjects habitual lens care regiment.

3.2.2 Other

No other medical devices will be used in this study.

4 Justification for the Study Design

Nonclinical testing methods are not adequate to provide the information needed to advance the development of the comfilcon A Contact Lens. A biocompatibility assessment has been completed and the benefit/risk assessment (see Section 5 below) supports the use of the device in this study.

A parallel-group study design has been chosen given the length of the study and to minimize recall bias in determining subjective preference.

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.

5 Benefits/Risks of Study Device 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.

5.2 Anticipated Adverse Device Effects

Ocular complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, burning, grittiness, 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 States Food and Drug Administration (FDA) 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 risks associated with this device are discussed within the Package Insert. 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. Artificial tears, re-wetting drops, and lubricating agents are not considered medical treatments. 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. Contact lens care solution will be provided by the Investigator and should be used according to manufacturer instructions.

Additionally, the contact lens should not be used if there is an active ocular inflammation, any eye disease or systemic disease that may affect contact lens wear, or if there is any known allergic reaction to a known ingredient in the lens or lens care solution.

The risks associated with contact lens wear are known to increase with the following and will be communicated to the subject in the safety instruction pamphlet.

- Overnight wear/sleeping with lenses
- Exposure of lenses or lens case to water
- Smoking
- Exposure to aerosols or noxious stimuli
- Unclean hands for insertion/removal
- Exposure to water (such as using water to rinse a lens)
- Swimming
- Use of lens care solution with daily disposable lens wear
- Cosmetic use
- Eye rubbing
- Insertion of an inverted lens
- Insertion of the wrong lens into the wrong eye
- Use of tools to either remove the lens from the blister pack or to insert the lens onto the eye
- Sharing contact lenses with others
- Improper storage
- Use of a lens from a damaged blister pack

5.7 Rationale for Benefit-Risk Ratio

The knowledge gained from this 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 and the Good Clinical Practice (GCP) principles and ethical considerations of ISO 14155 Clinical Investigation of Medical Devices for Human Subjects, Declaration of Helsinki, and 21 CFR Part 50 Protection of Human Subjects. 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). Copies of all IRB correspondence with the investigator/Sponsor will be kept on file.

This study adheres 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

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law.

7 Design of the Clinical Investigation

7.1 Study Endpoints

The primary endpoint is:

- logMAR distance (4m) high illumination high contrast visual acuity at the 4-week timepoint

7.2 Clinical Sites

The clinical sites were 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 79 subjects will be enrolled in this study in order for approximately 72 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 they:

- Have had a self-reported oculo-visual examination in the last year.
- Are at least 18 years of age and has full legal capacity to give their informed consent.
- Have read and understood the informed consent form.
- Are willing and able to follow instructions and maintain the appointment schedule.
- Have a contact lens spherical prescription between -0.50 D to -6.00 D (inclusive)
- Are correctable to a visual acuity of 20/40 or better (in each eye) with their habitual vision correction or 20/20 best-corrected.
- Have spectacle cylinder of ≤ 0.75 D in both eyes.
- Is a habitual comfilcon A wearer and worn a comfilcon A lens for at least one month (minimum of 8 hours a day, 5 days per week)
- Currently employ the use of a peroxide or multipurpose solution cleaning and disinfecting regimen in one of the following brand names:

- Bausch and Lomb BioTrue Multi-Purpose Solution
- Bausch and Lomb BioTrue Hydration Plus Multi-Purpose Solution
- Bausch and Lomb ReNu Advanced Formulation Multi-Purpose Solution
- Alcon Opti-Free Puremoist with Hydraglyde Multi-Purpose Solution
- Alcon Opti-Free Replenish Multi-Purpose Solution
- Alcon Clear Care Plus Hydrogen Peroxide Solution
- Acuvue RevitaLens Multi-Purpose Solution

- Have clear corneas and no active ocular disease.
- Have not worn habitual lenses for at least 12 hours before the baseline/screening examination
- Are willing to wear the study contact lenses for at least 8 hours per day, 5 days per week

7.3.2 Exclusion Criteria

A person will be excluded from the study if they:

- Have never worn contact lenses before.
- Are currently wearing daily disposable contact lenses.
- Have any systemic disease affecting ocular health.
- Are using any systemic or topical medications that will affect ocular health.
- Have any ocular pathology or abnormality that would affect the wearing of contact lenses.
- Have any clinically significant lid or conjunctival abnormalities, active neovascularization or any central corneal scars.
- Are aphakic.
- Have undergone corneal refractive surgery.
- Are participating in any other type of eye related clinical or research study.
- Require a change in lens power from more than 1 diopter as dictated by over-refraction with their habitual lens prescription.

7.4 Procedures to Minimize Bias

7.4.1 Labelling and Masking

Although approved for use in the country where the clinical study is taking place, the Test and Control lenses will all be overlabelled with an investigational label to facilitate investigator and subject 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 surface assessments.

7.4.2 Randomization Procedures

In this parallel group study design, subjects will be randomized to wear either the Test or the Control lens in a bilateral fashion according to a predetermined randomization schedule. Test lenses will be dispensed at a ratio of two for every one Control lens. To maintain masking, Test lenses will be randomized as two of the three groups used in the study. The randomization will be performed using a randomization algorithm using REDCap Cloud.

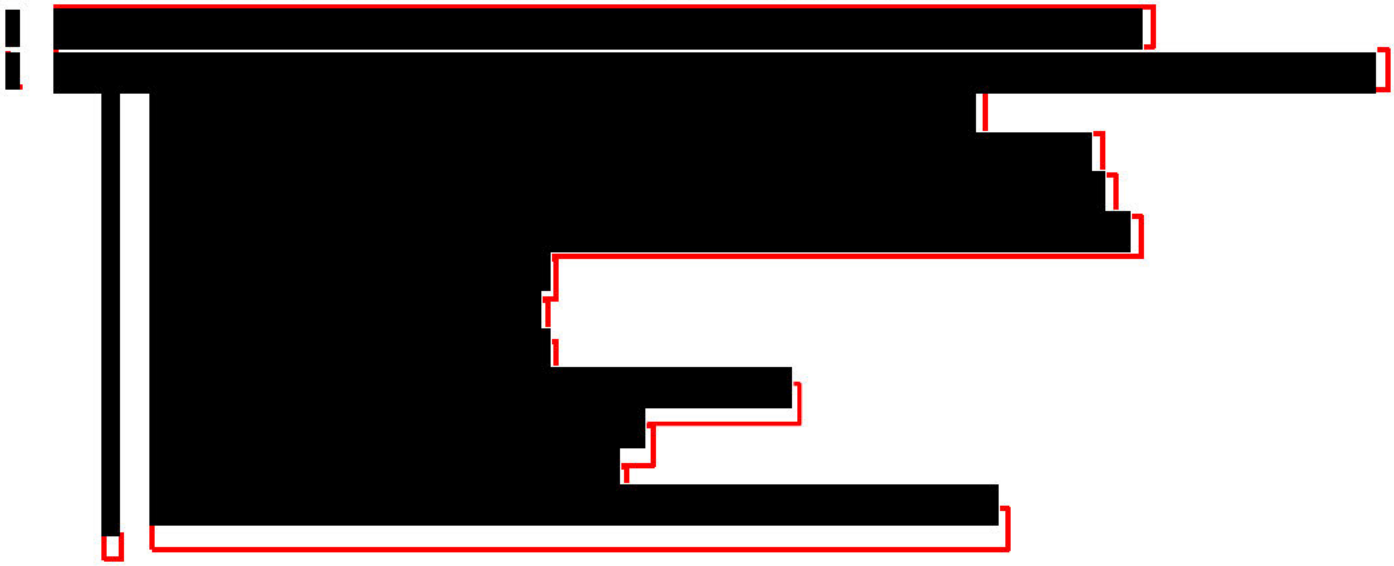
7.5 Visit Procedures

7.5.1 Visit 1- Baseline & Dispensing 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 wearing their habitual spectacles (if they have a pair), but not wearing any contact lens products.
- The subject will be required to read and sign an Informed Consent Form prior to enrollment. When the subject has signed the consent form, the subject will be considered to be enrolled into the study.
- Subject demographics and medical history (age, sex, race and ethnicity, medical conditions, allergies)
- Contact lens wearing history including:
    - Habitual lenses, modality, solution, average wear time and comfortable wear time, re-wetting drop use
- Baseline logMAR distance (4m) visual acuity high illumination high contrast with spectacles or spectacle refraction.
- Slit lamp biomicroscopy (including bulbar and limbal hyperaemia) will be assessed using sodium fluorescein according to the guidelines set out in the CVI Grading scales (Appendix 3).
- The subject's eyes will be rinsed with saline, if requested by the subject.



- [redacted]
- The investigator will confirm that the subject satisfies the criteria set out in the inclusion and exclusion criteria.
- The study contact lenses will be dispensed based on the habitual contact lens prescription.
- Lenses will be dispensed according to the randomization table and allowed to settle for at least five minutes.
- Monocular over spherical refraction will be carried out. If over-refraction dictates a lens change of greater than 1 diopter, the subject will be excluded from the study.
- Monocular logMAR distance (4m) visual acuity high illumination high contrast with final prescription.
- [redacted]
- A Subject Instruction Guide will be provided to the study subjects.
- Contact lens solution and storage cases will be dispensed to the subject.
- The subject will be asked to wear the study lenses for at least 8 hours per day and 5 days per week while in the study.
- The subject will be asked to complete the daily interim questionnaire twice a week during their lens wear period (Appendix 9 and 10).
- The subject will be discharged and reminded of their instructions for the next visit.

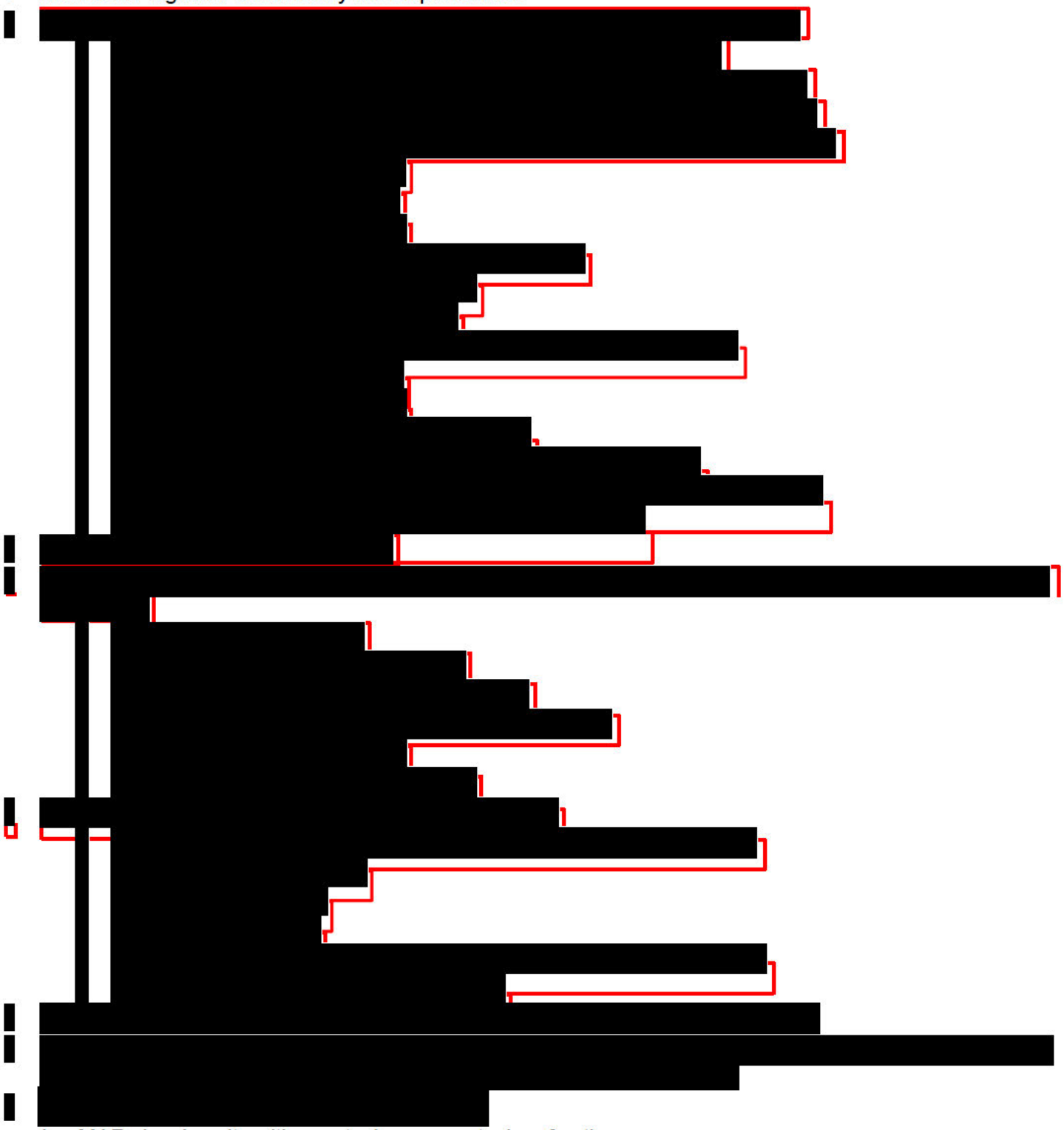
7.5.2 Visit 2 – 1 Week Visit (Day 7±1)

- Subject will arrive after wearing lenses for at least 5 hours.
- Monocular logMAR visual acuity will be performed.
- [redacted]

- Lenses will be removed and retained.
- Slit lamp biomicroscopy (including bulbar and limbal hyperaemia) will be assessed using sodium fluorescein according to the guidelines set out in the CVI Grading scales (Appendix 3).
- The subject's eyes will be rinsed with saline, if requested by the subject.
- The subject may choose to wear their study lenses or habitual spectacles at the completion of the visit.
- The subject will be reminded to complete their remote questionnaires and will be reminded of the date for their next visit.

7.5.3 Visit 3 – 4 Week Visit (Day 30±2)

- Subject will arrive after wearing the lenses for at least 5 hours.
- Monocular logMAR visual acuity will be performed.



- LogMAR visual acuity with spectacles or spectacle refraction.
- The subject will be discharged and will sign the exit statement.

7.5.4 Interim Questionnaires

Subjects will be asked to complete subjective questionnaires (Appendix 9 and 10) at regular intervals throughout the study. Questionnaires will be delivered at no more than two times per week and will be administered using an electronic data capture system.

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 1 *Baseline*	**Visit 2** *One week*	**Visit 3** *Four weeks*	**Interim subjective q'aire***
Informed Consent	✓			
Meet inclusion/exclusion criteria	✓			
History at baseline	✓			
Demographics	✓			
VA with spectacles or refraction	✓			
Instillation of lens at office	✓			
Subjective assessments	✓	✓	✓	✓
Lens surface and fit assessments	✓	✓	✓	
VA with contact lenses	✓	✓	✓	
Slit lamp findings	✓	✓	✓	
Exit study			✓	

* Between each visit at regular intervals

8 Adverse Events

8.1 Adverse Event Definitions

An 'adverse event' refers to any undesirable clinical occurrence in a subject, 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
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11980 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)	reporting as per requirements
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 Adverse Events Management

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.

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

An Adverse Event Notification Form (Appendix 1) will be completed for each adverse event. Whenever possible, the adverse event will be photo-documented.

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 per the IRB's reporting requirements. 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 days after the occurrence.

Sponsor contact details **for adverse events** are:

Contact: Clinical Operations, CooperVision
Email: adverse.events@coopervision.com
Phone: (925) 730-6766 or (925) 251-6684 / Fax: (925) 251-6641
Address: 5870 Stoneridge Drive, 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.

9 Device Deficiency Reporting

9.1 Product Defect Reporting (Investigator Responsibility)

Product Defect is the terminology typically used in contact lens products for an *unexpected* observation related to the identity, quality, durability, reliability, or usability of the product under investigation.

NOTE: Observations on study products that are anticipated as a part of the device development process are not considered to be Product Defects or Device Deficiencies.

If the Product Defect is associated with an adverse event, the investigator shall report the Product defect via the Adverse Event Notification Form (Appendix 1).

If the Product Defect is not associated with an adverse event, the investigator shall report the Product Defect via the Clinical Product Defect Notification Case Report Form (Appendix 2).

If the investigator judges that the Product Defect could have led to a Serious Adverse Event if no preventative action was taken, the Product Defect should be reported to the Sponsor via the Product Defect Notification Case Report Form within 24 hours of becoming aware of the defect. The investigator should report to the IRB per their reporting requirements.

All other Product Defects should be reported to CVI as soon as possible, but no later than 5 working days after occurrence.

Sponsor contact details **for Product Defect Notifications** are:

Contact:	Clinical Operations, CooperVision
Email:	clinical.operations@coopervision.com
Address:	5870 Stoneridge Drive, Suite 1
	Pleasanton, CA 94588

9.2 Device Deficiency Reporting (Sponsor Responsibility)

Device Deficiency is defined as the inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance.

The Sponsor will review the Product Defect Notification Case Report Form, gather additional information if needed from the Investigator and determine whether the notification represents a Device Deficiency. Device Deficiencies will be reported as per Internal CVI procedures.

A summary of Device Deficiencies will be documented in the clinical study report. If no Device Deficiencies are observed in a study, then a statement stating as such will be included in the clinical study report.

10 Statistical Design and Analysis

10.1 Statistical Hypothesis

In this confirmatory study, the primary statistical hypothesis is that the logMAR visual acuity performance with the Test lens will demonstrate there is no statistical difference comparing to the Control lens over one month of lens wear.

The null and alternative hypotheses are:

H_0: $\mu_t = \mu_c$

H_1: $\mu_t \neq \mu_c$

Where μ_t refers to the LogMAR of Test lenses and μ_c refers to LogMAR of Control lenses.

10.2 Sample Size Calculations

The number of subjects that has been chosen in this study is to provide sufficient evidence to demonstrate the study hypothesis of “there is no difference between the Test and Control” versus “there is a difference between the Test and Control” on visual acuity (LogMAR) measurement. With assumed standard deviation is equal to 0.06, a sample size of 24 subjects per group will provide adequate power (92%) to detect a visual acuity difference of 0.06 (3 letters) at α=0.05 level.

Therefore, for this parallel arm study design with 2:1 ratio, minimum 72 subjects (48 in test arm and 24 in control arm) to complete is required. To account for subject attrition of 10%, up to 79 subjects will be enrolled in this study.

10.3 Statistical Analysis

Statistical analysis will be undertaken by the study biostatistician. Data for all subjects who have completed the trial will be included in the analysis.

Descriptive statistics (e.g., mean, standard deviation) and/ or frequency of counts for categorical data may be produced for primary and/or second interests. Paired t-test may 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 may 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.

10.4 Interim Analysis

An interim analysis is planned to be completed once 30 subjects have completed all visits or on Dec 18, 2023, whichever comes first. The Sponsor may stop enrollement for this study if there are obvious signs that the Test and Control lenses are not performing similarly.

10.5 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 and 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.

10.6 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.

11 General Study Management

11.1 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 Principal 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.

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

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 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.

11.3 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 protocol except to protect the rights, safety and well-being of human subjects or if otherwise pre-approved by the Sponsor in writing for non-emergency circumstances. Under emergency circumstances deviations may proceed without prior approval of the Sponsor and the IRB. Deviations shall be reported to the Sponsor, IRB 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 within ten business days of the deviation occurring (or its discovery). All deviations shall be reported to the Sponsor within five working days.

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

Sponsor contact details **for Protocol Deviations** are:

Contact:	Clinical Operations, CooperVision
Email:	clinical.operations@coopervision.com
Address:	5870 Stoneridge Drive, Suite 1
	Pleasanton, CA 94588

11.4 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 Investigators will assure that adequate consideration is given to the protection of the subjects interests.

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

- Determination of unexpected, significant, or unacceptable risk to subjects
- 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.

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.

11.5 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 by the Sponsor 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.

11.6 Confidentiality and Privacy

This study is confidential in nature. All information gathered during this study is proprietary and should be made available only to those directly involved in the study. Information and reports arising from this project are the property of the Sponsor.

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. Documentation containing personal and/or confidential identifying information for clinical trial subjects participating in studies will be maintained in a secured locked location. 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.

Details on publishing rights are contained in each site's master clinical services agreement with the Sponsor.

12 Device Accountability

12.1 Clinical Supply Inventory

The Principal 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.

12.2 Disposal of Consumables

This study dispenses consumables (lenses) to subjects for use during the study. All study lenses, including study lenses worn by subjects will be collected at the completion of the study. Unopened contact lens care solutions will be returned to the Sponsor; any opened solutions may be discarded or kept by the sites.

12.3 Ordering and Accountability of Study Materials

The Test and Control lenses will be provided by the Sponsor. The Principal 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 site is otherwise directed by the study Sponsor.

13 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 subject must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

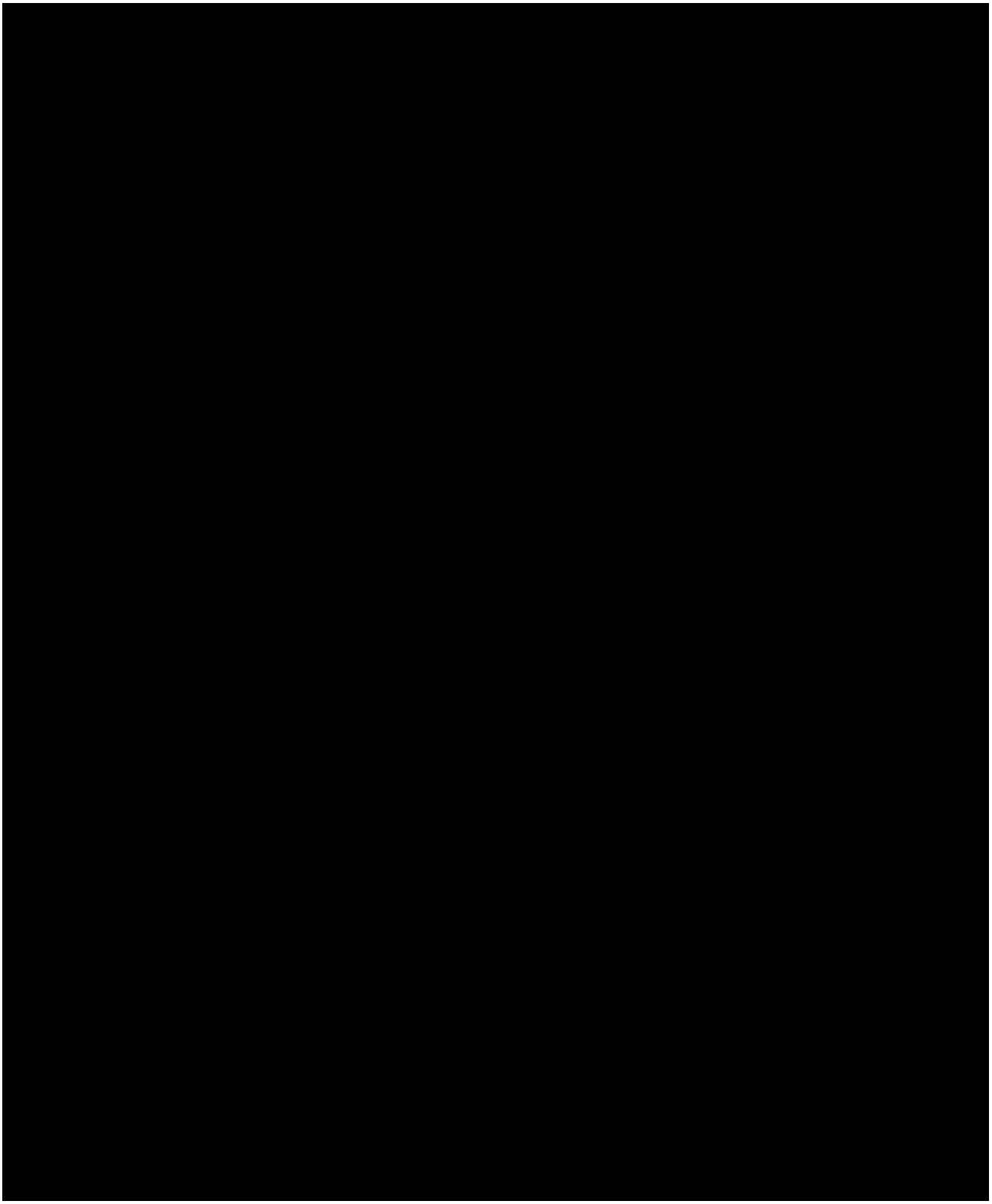
14 Publication Policy

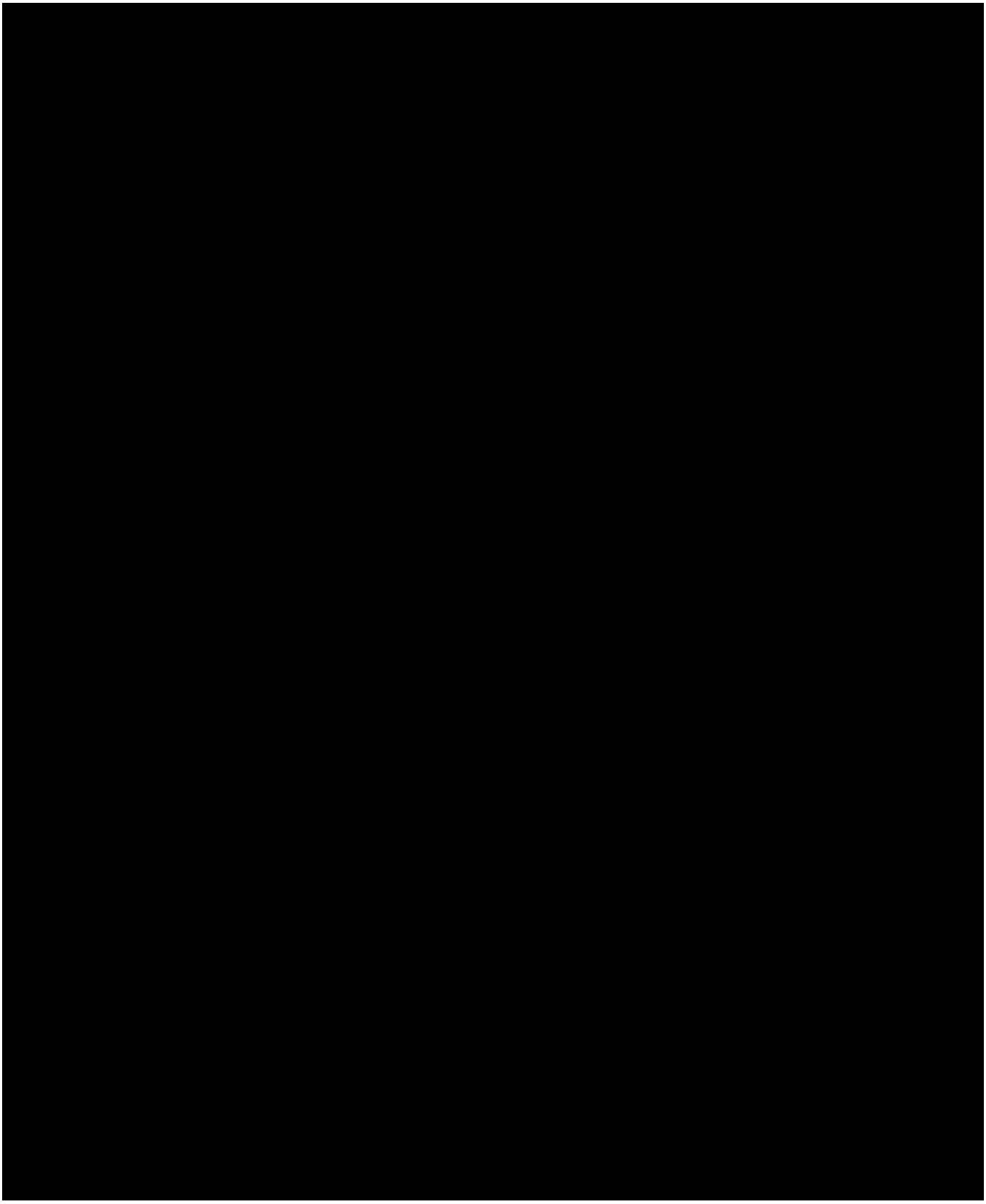
Due to the confidential and proprietary nature of the clinical study, any presentation and/or publication including but not limited to those made at scientific meetings, in-house, in peer-review journals, professional publications, etc. cannot be published without the written consent of the Sponsor. Details of the publication procedures are in the clinical study agreement or within the master clinical services agreements.

15 References

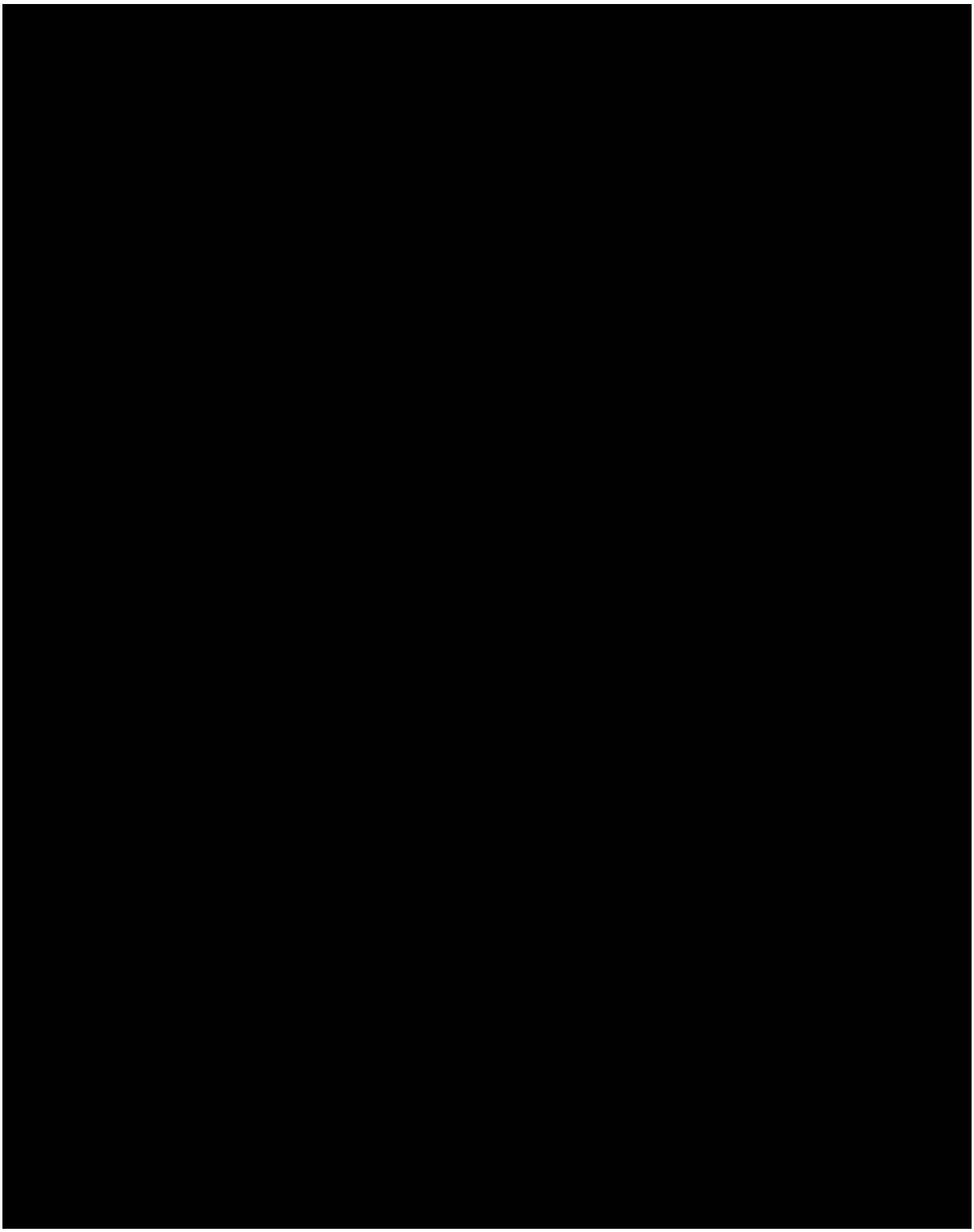
[1] Cheng K, Leung S, Hoekman H, Beekhuis W, Mulder P, Geerards A, Kijlstra A. Incidence of contact-lens-associated microbial keratitisand its related morbidity. The Lancet 1999; 354:181-185.

16 Appendix 1 – Adverse Event Case Report Forms

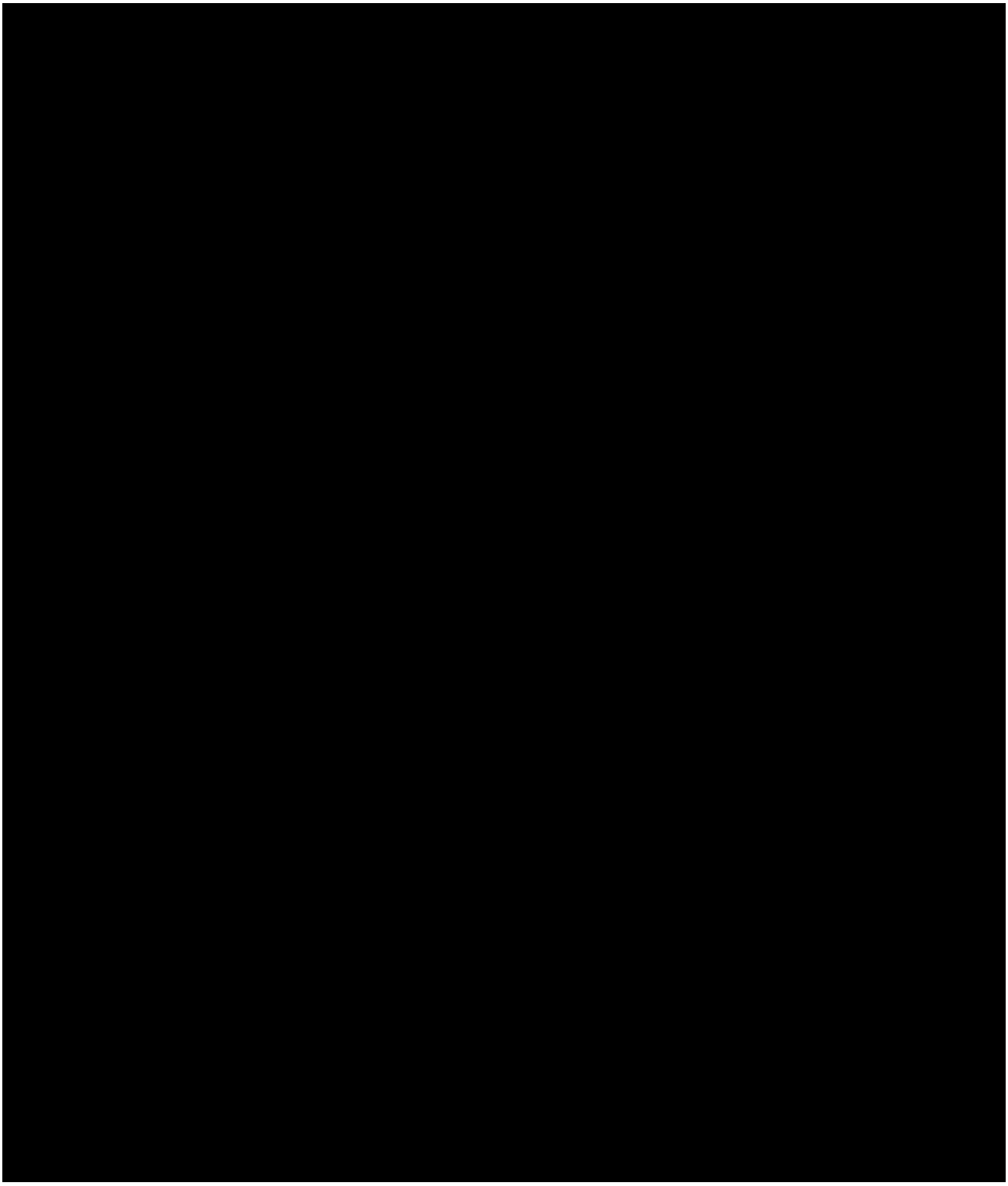




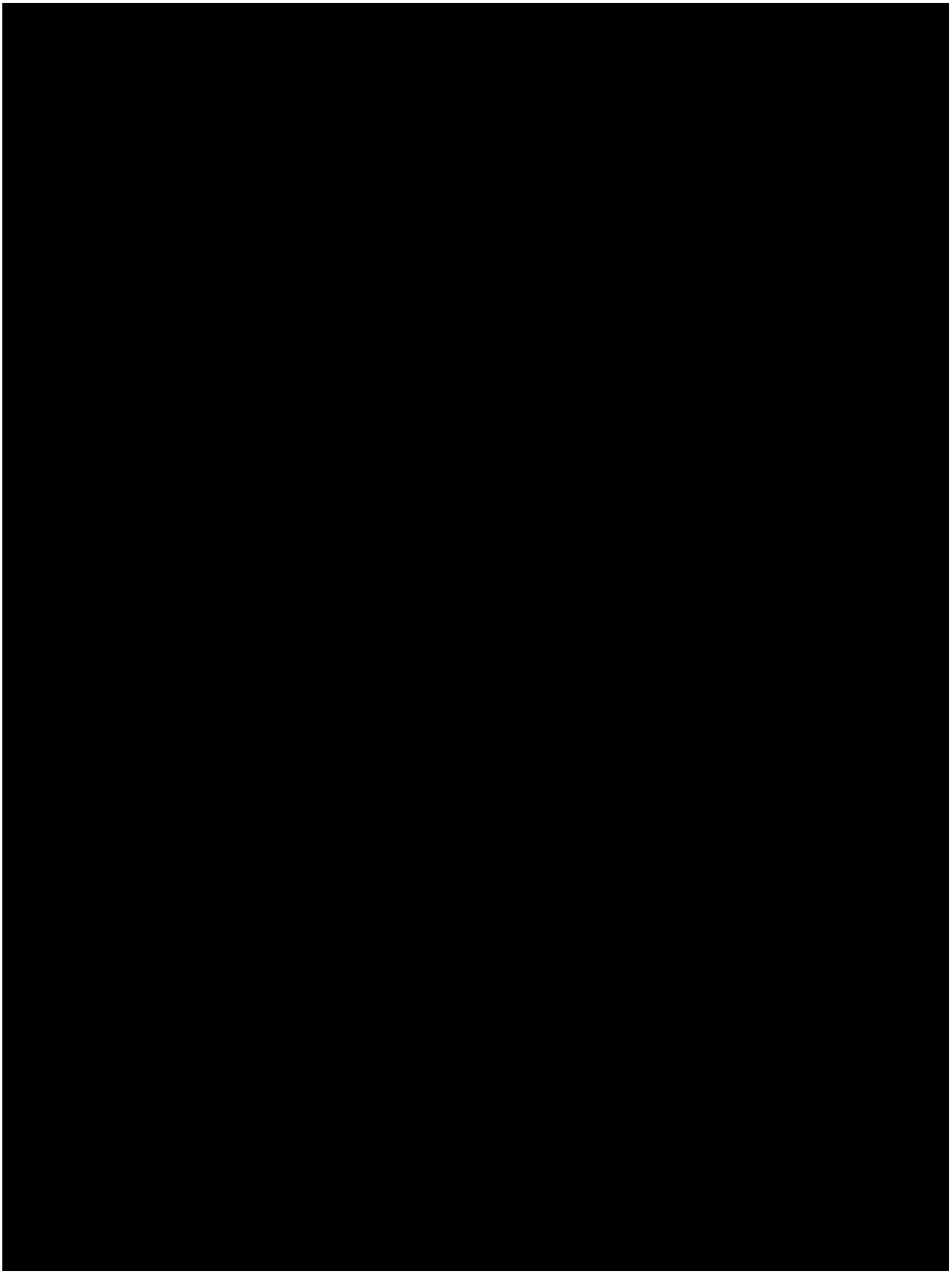
17 Appendix 2 – Clinical Trial Product Defect Notification Form

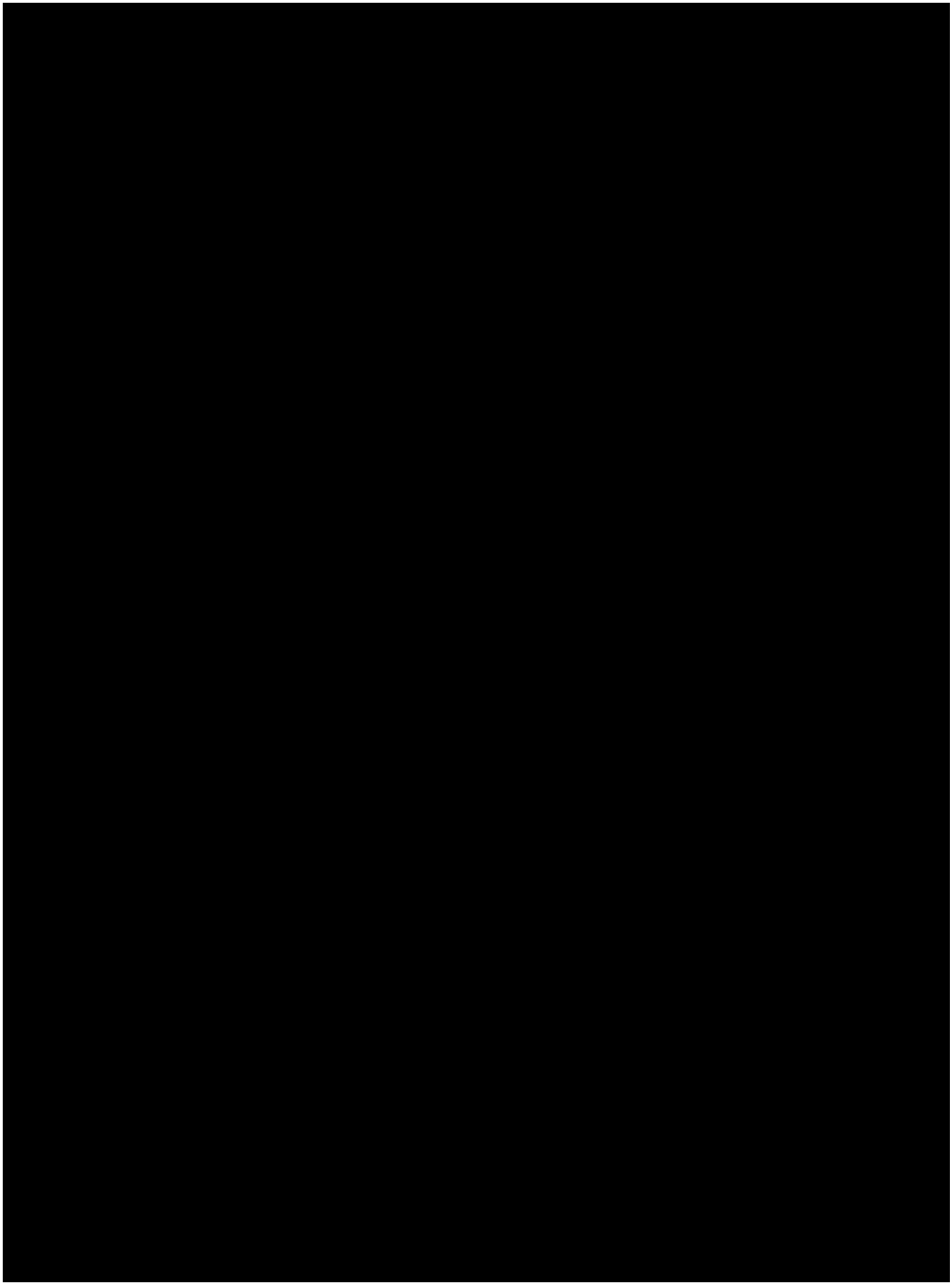


18 Appendix 3 – Slit Lamp Biomicroscopy Scales



19 Appendix 4 – CLDEQ8 and DEQ5





20 Appendix 5 – Habitual Questionnaire

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CooperVision™

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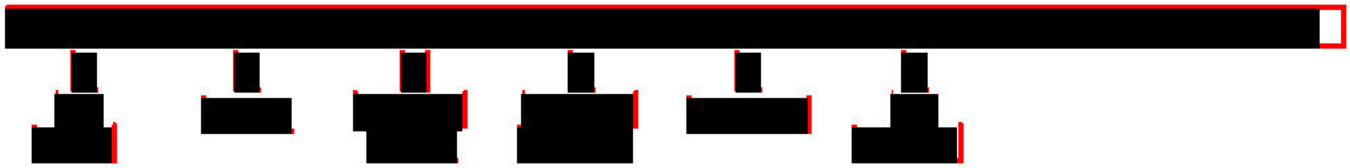

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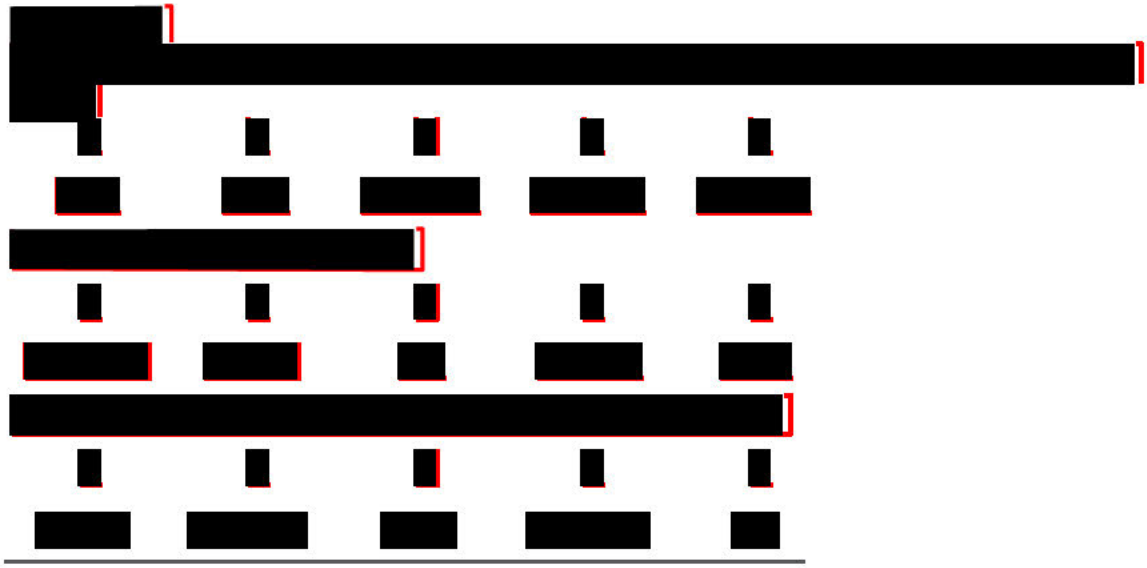

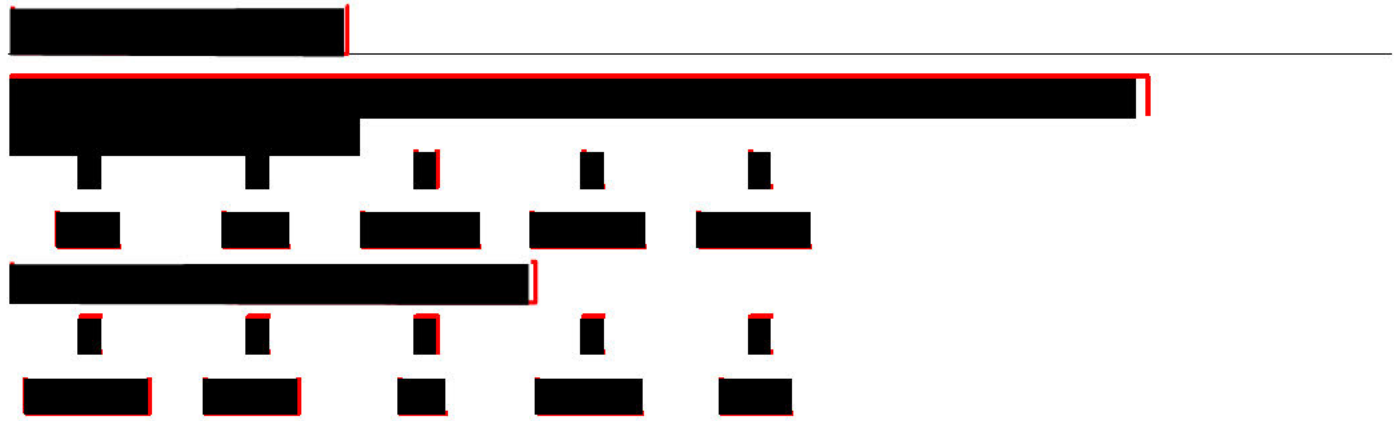

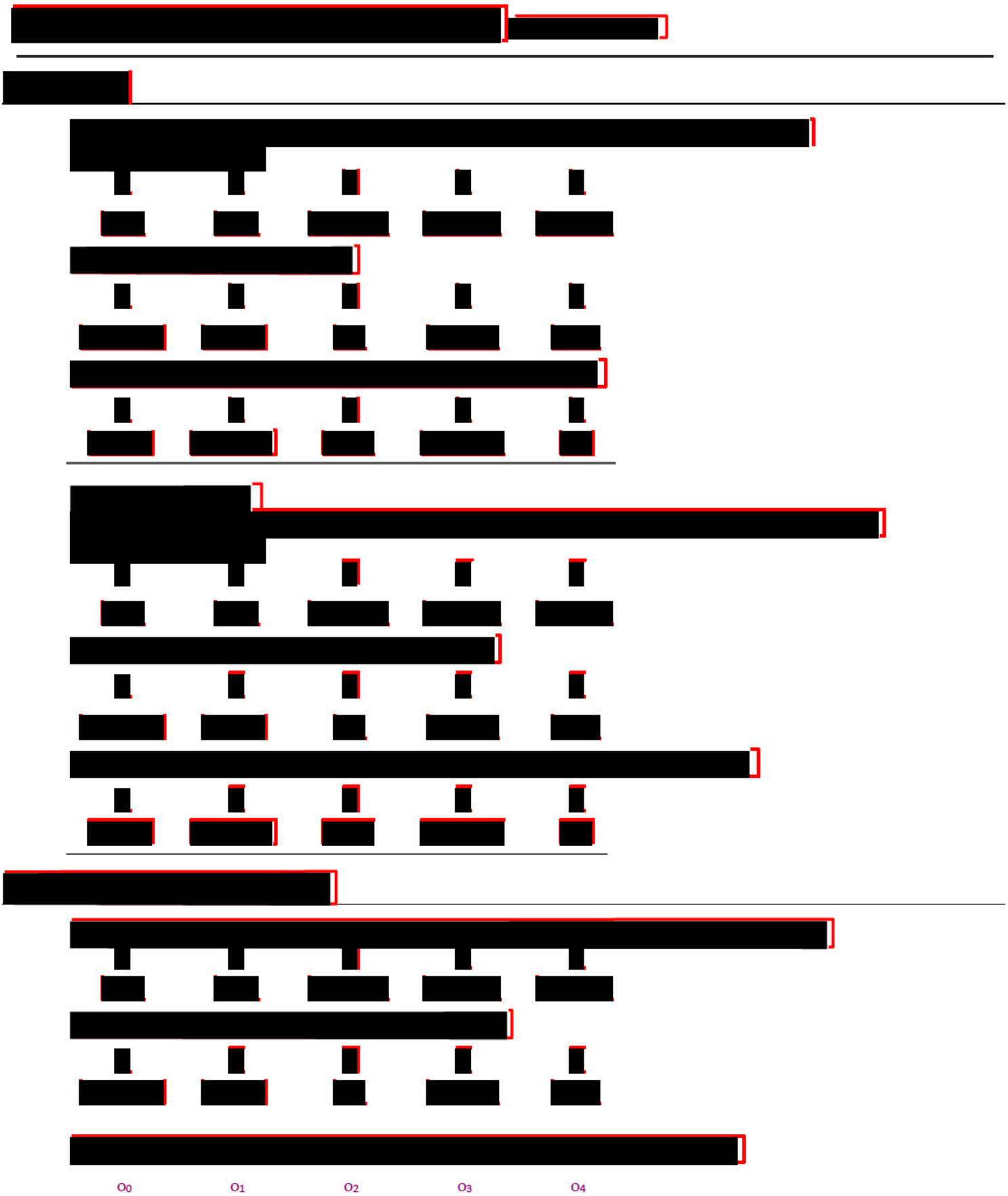
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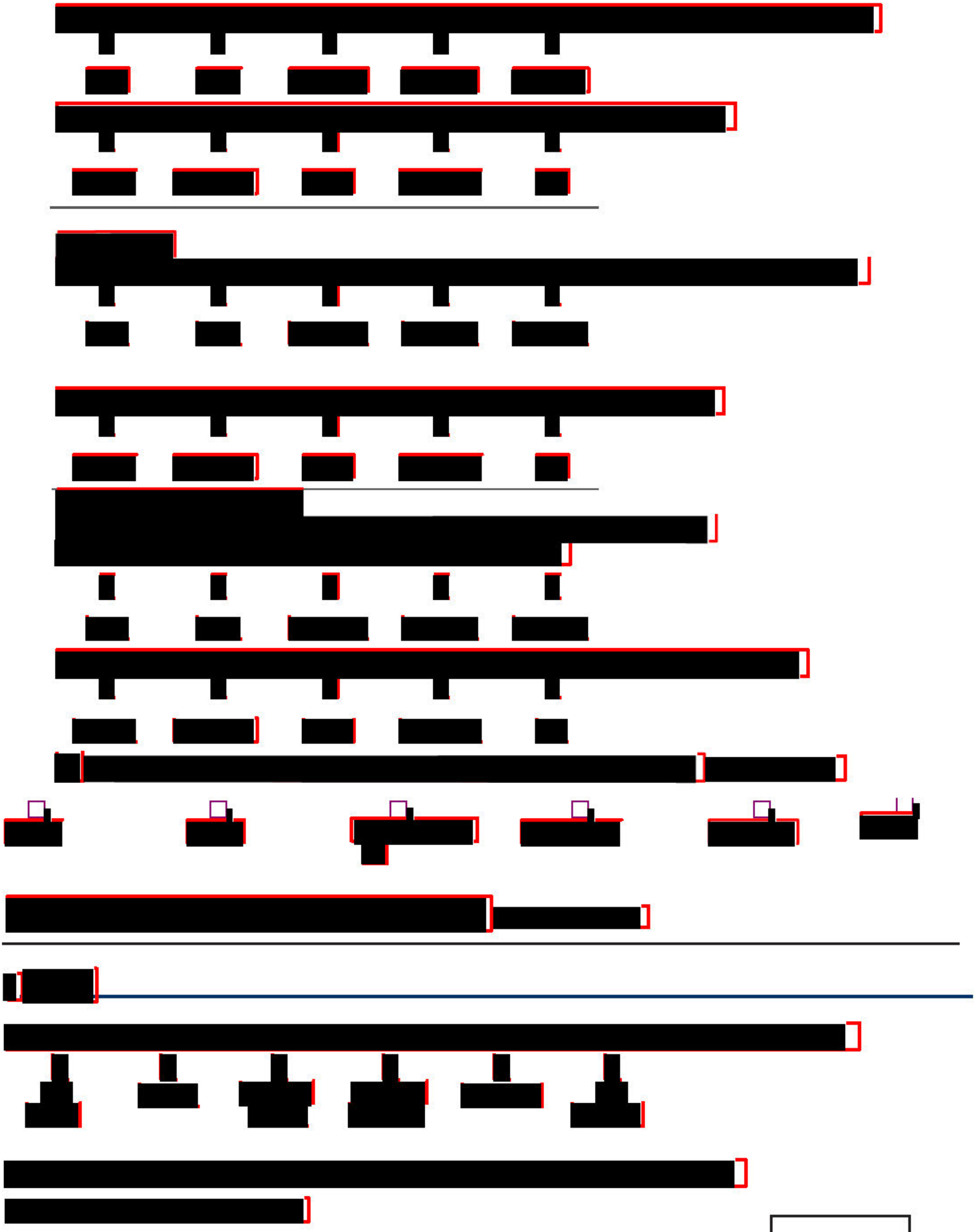
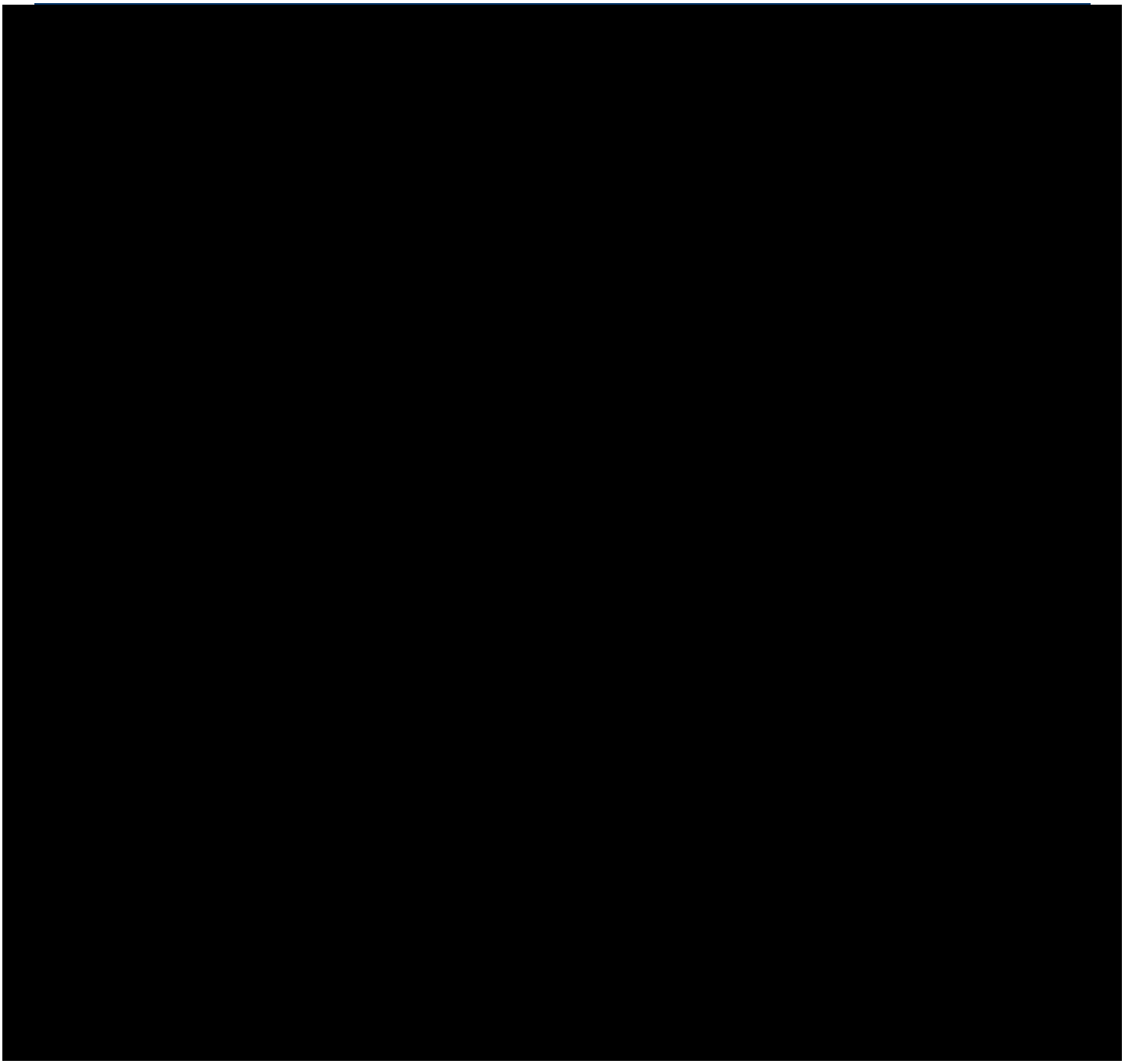
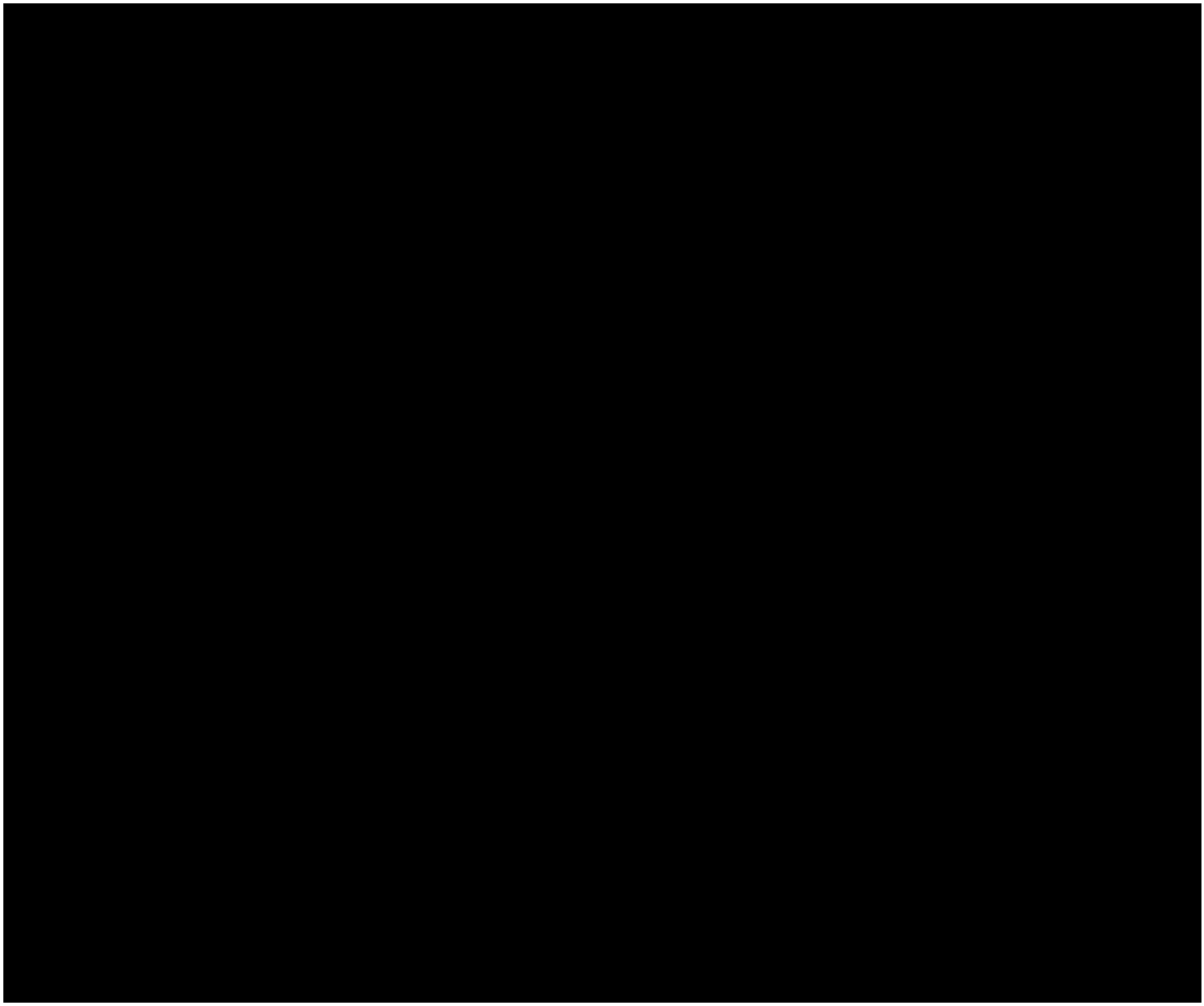
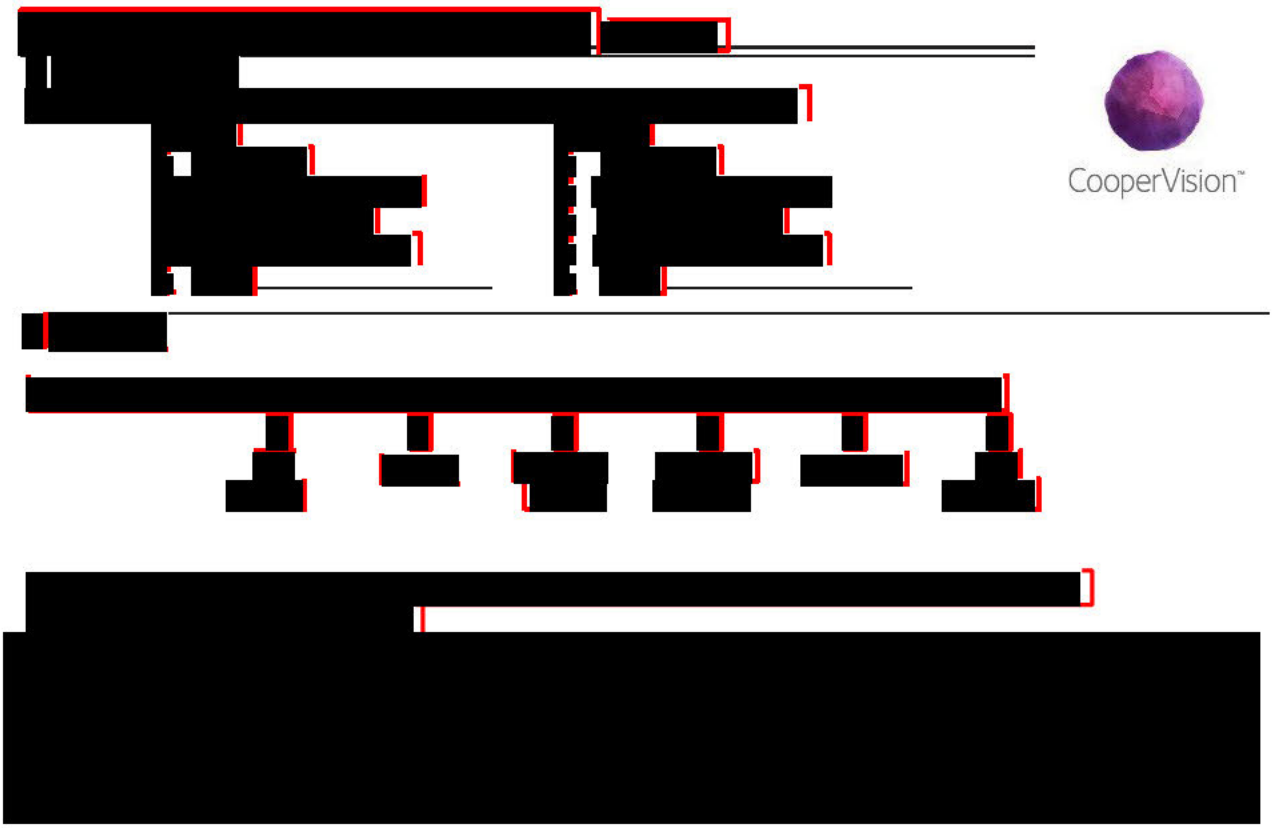


21 Appendix 6 – Lens Surface Assessments

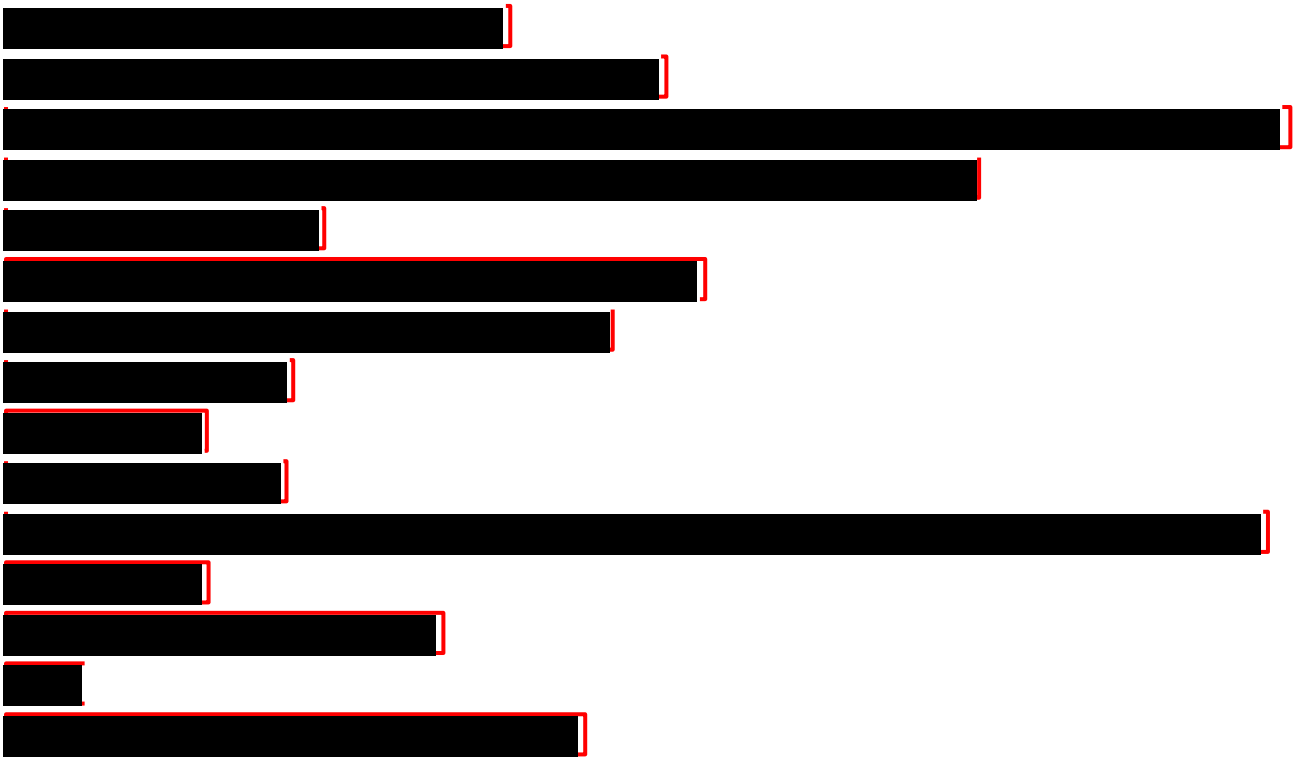




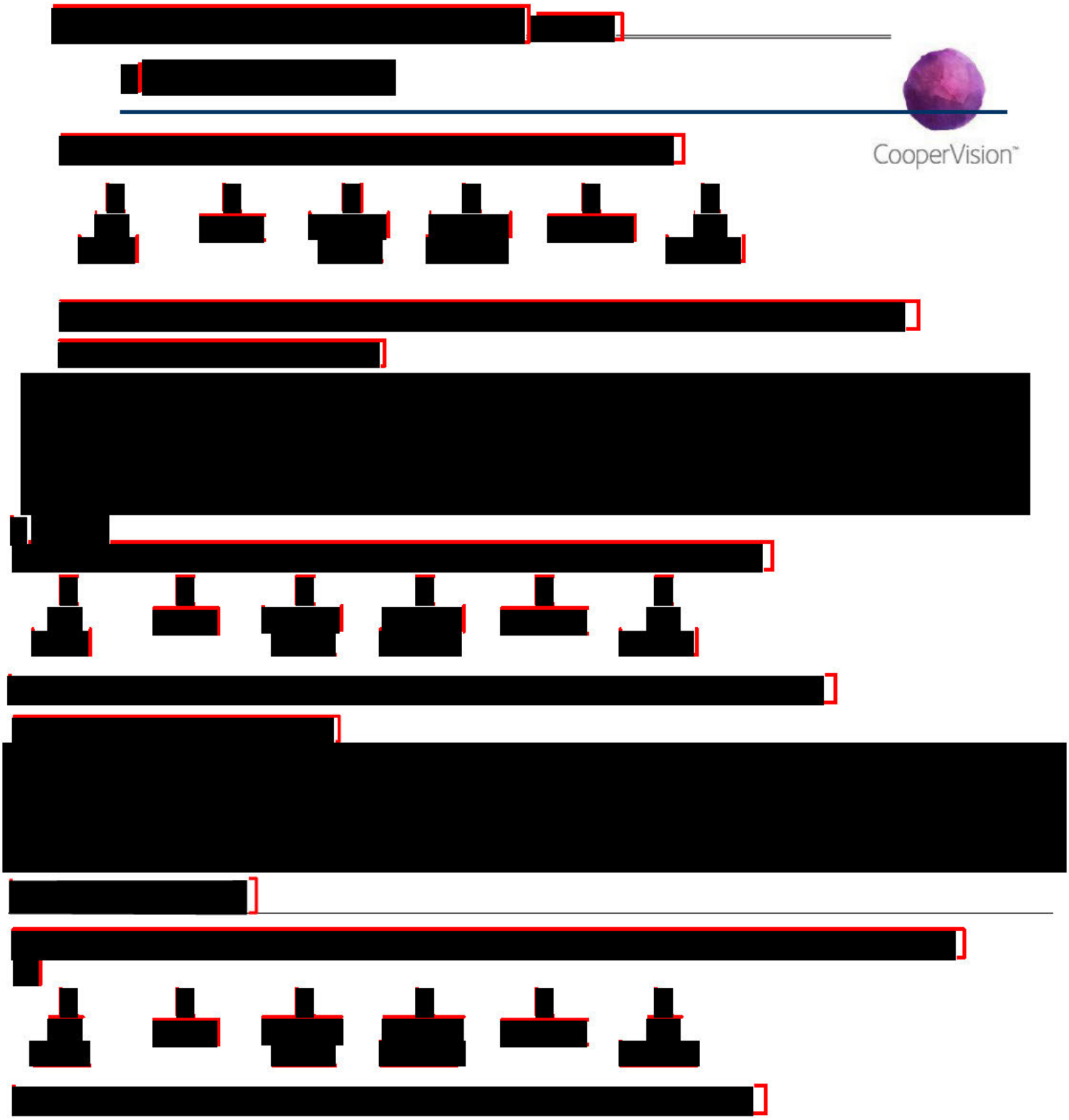
23 Appendix 8 – Post-Settling Questionnaire

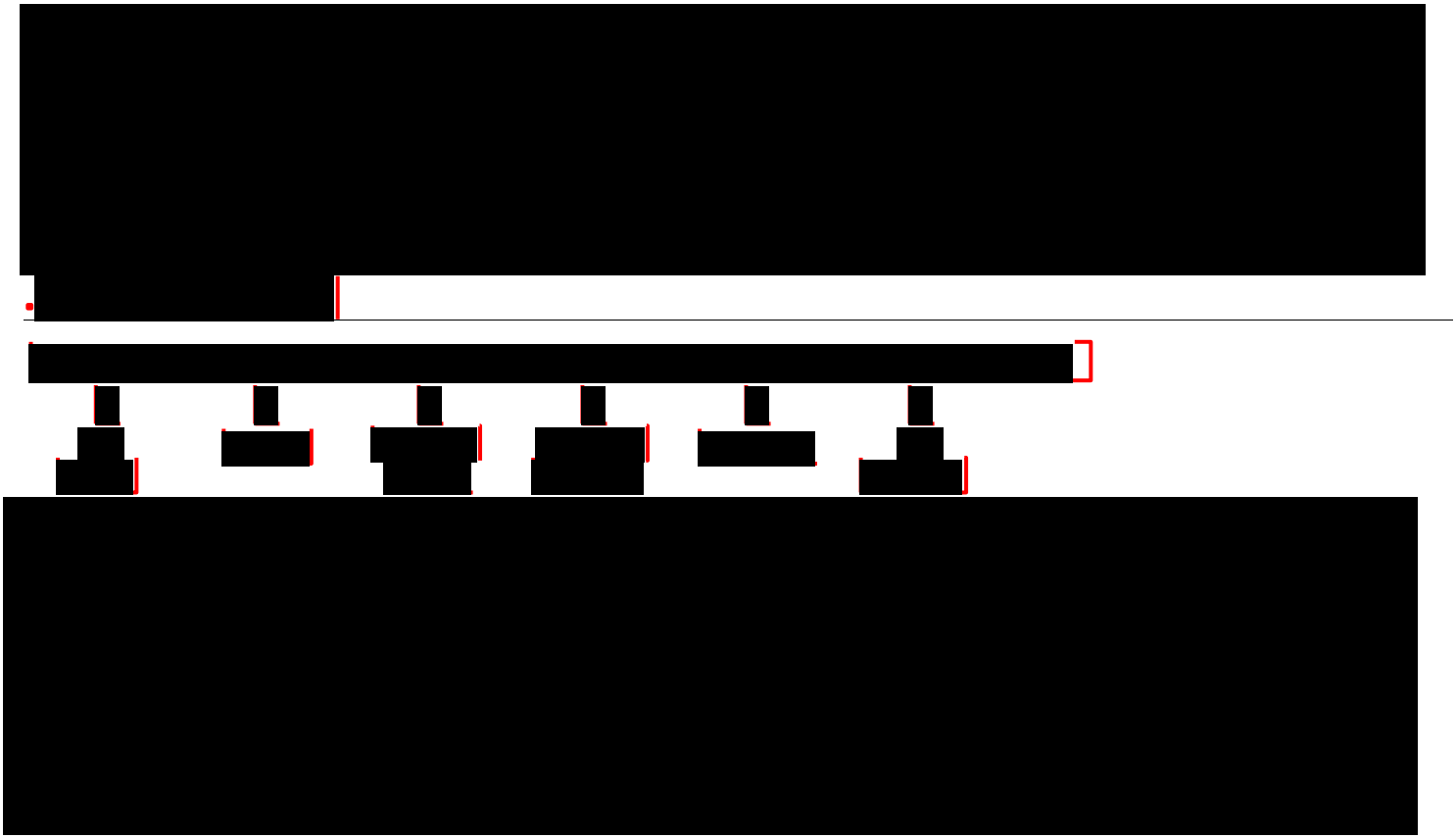


24 Appendix 9 – Interim Questionnaire



25 Appendix 10 – End of Day Questionnaire





26 Appendix 11 – Exit Questionnaire

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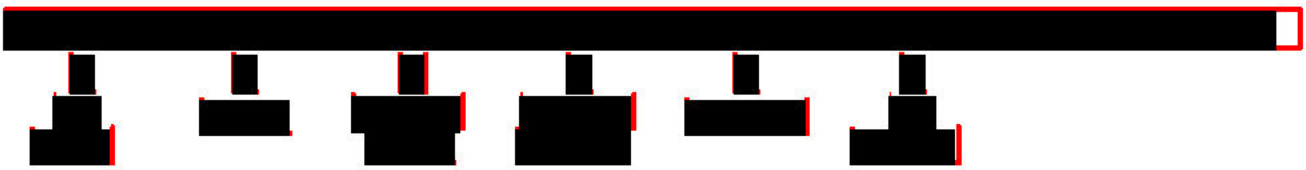

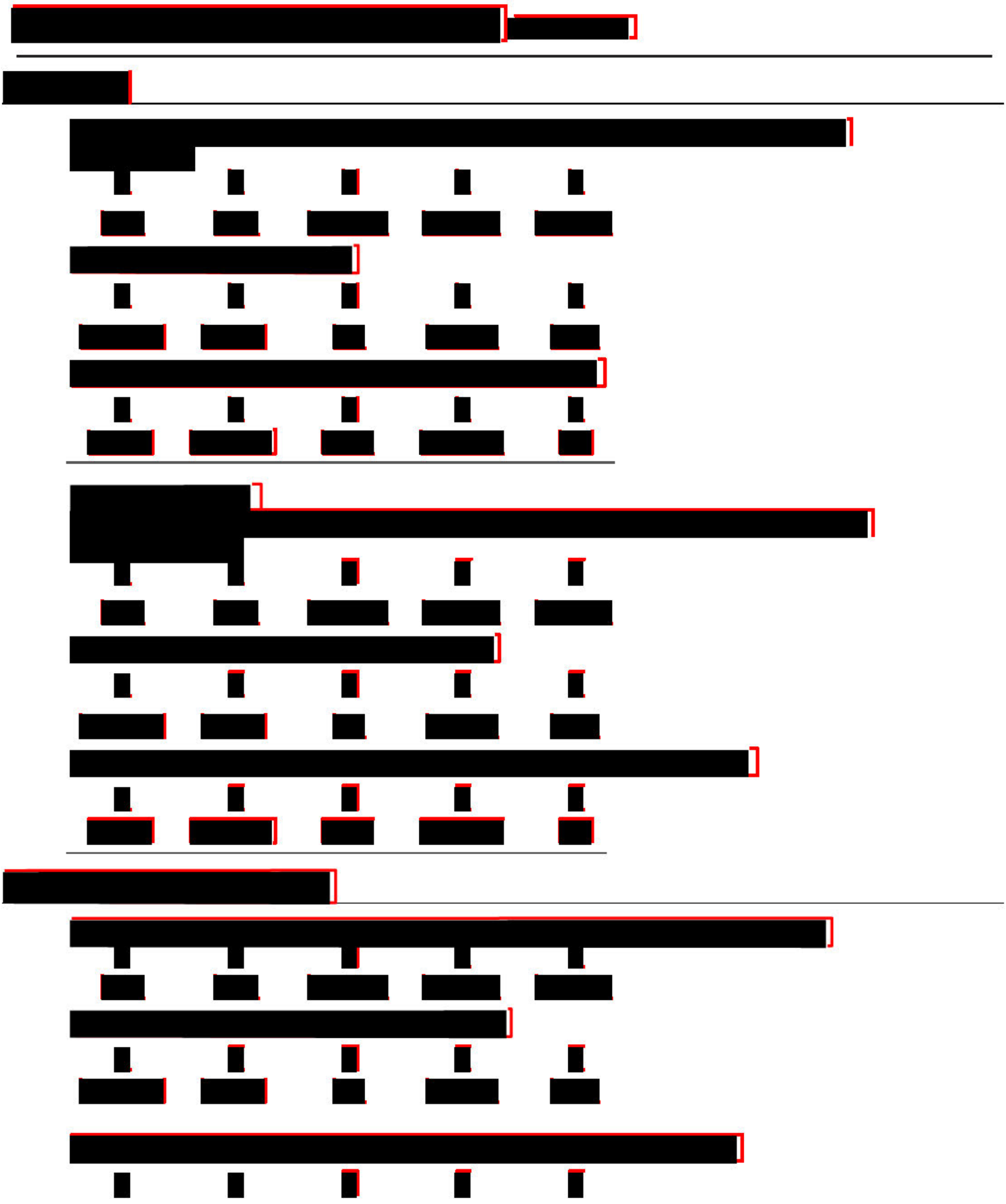

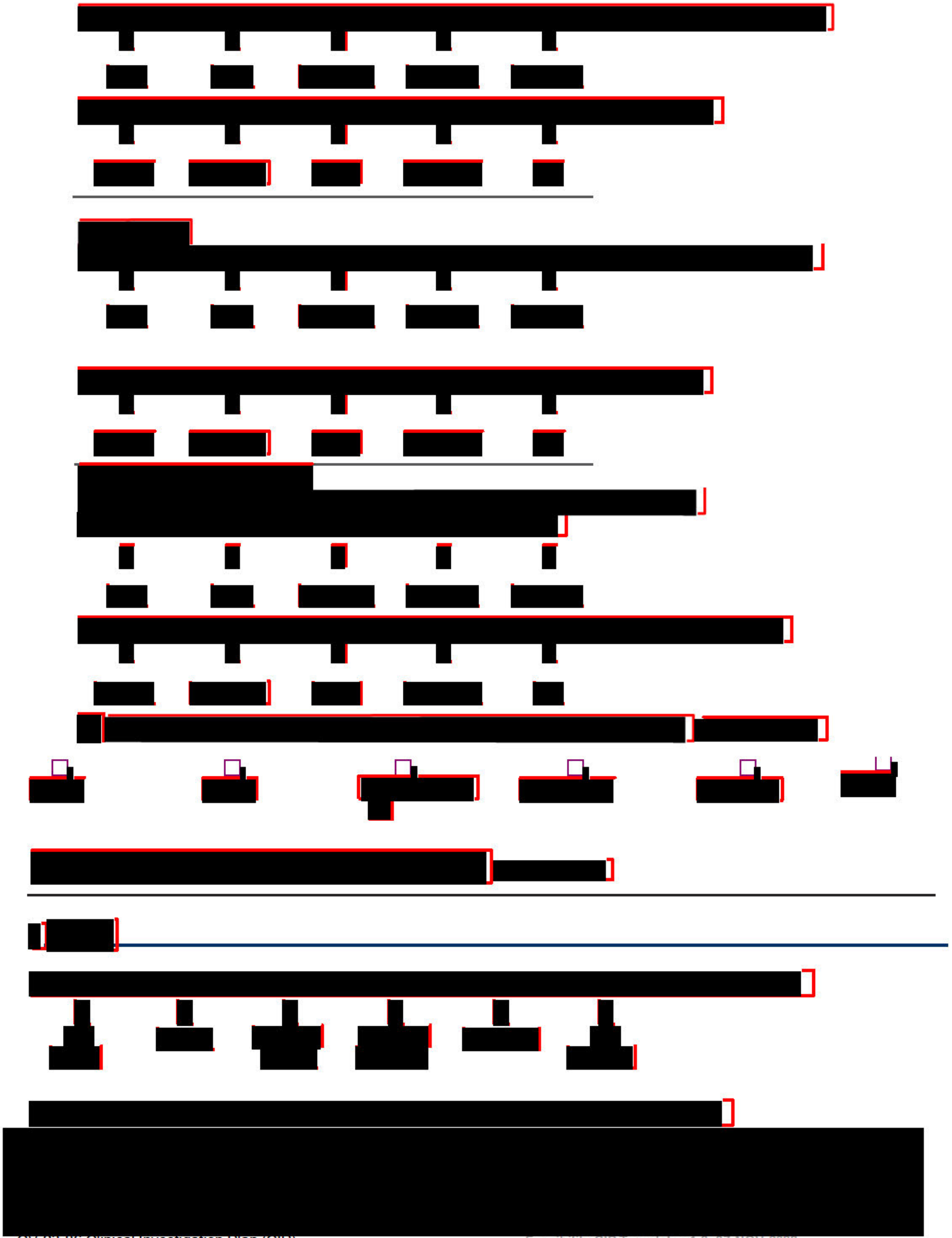

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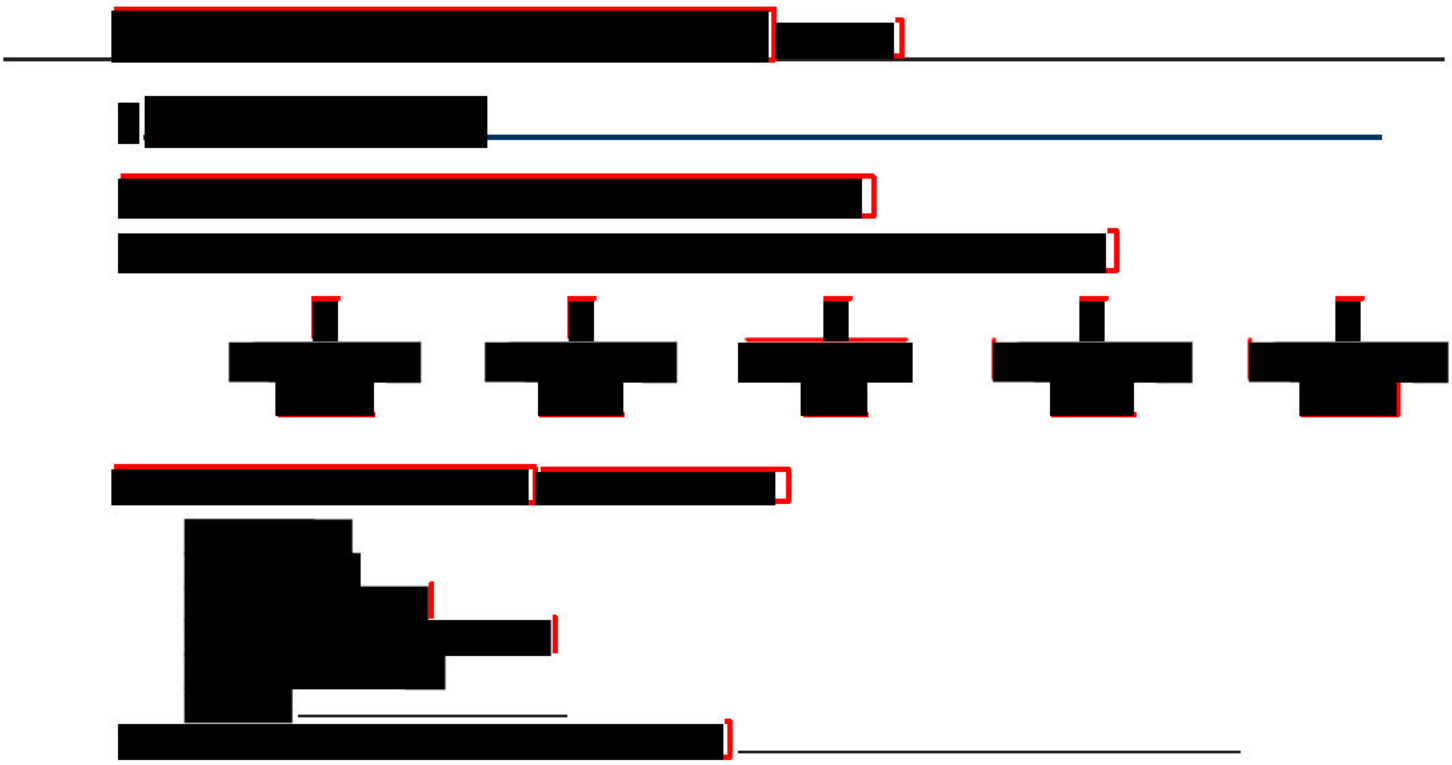
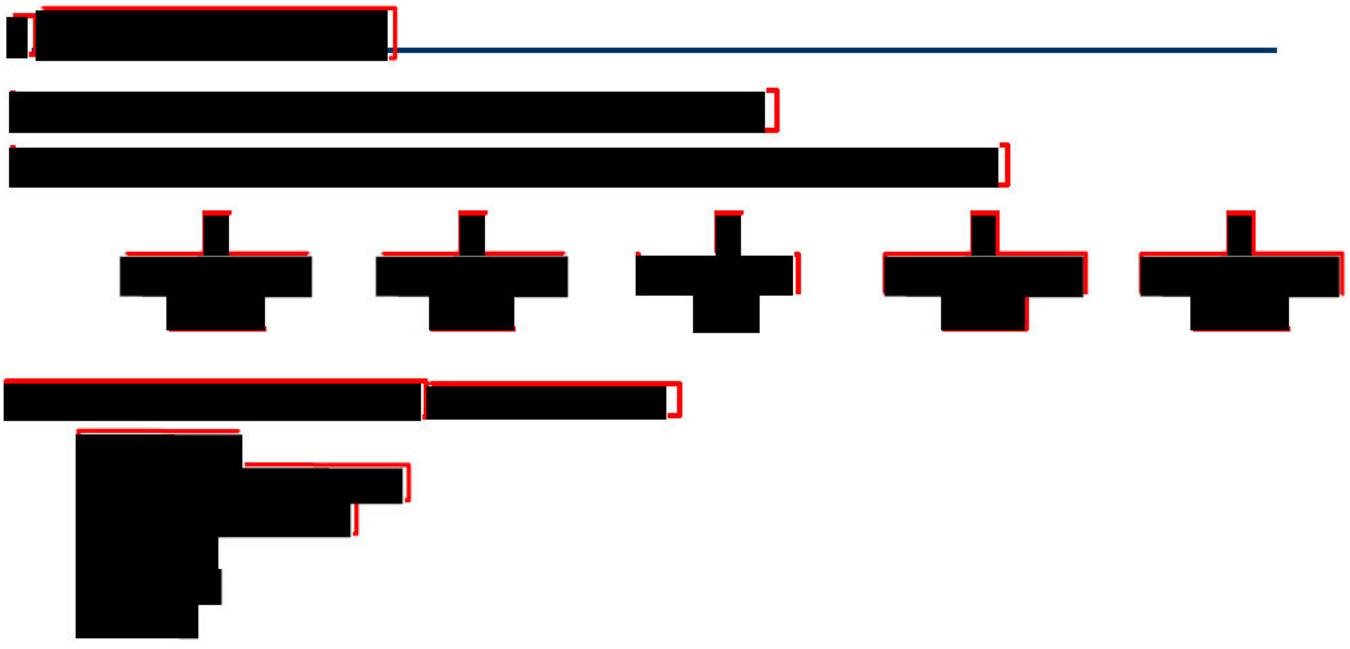
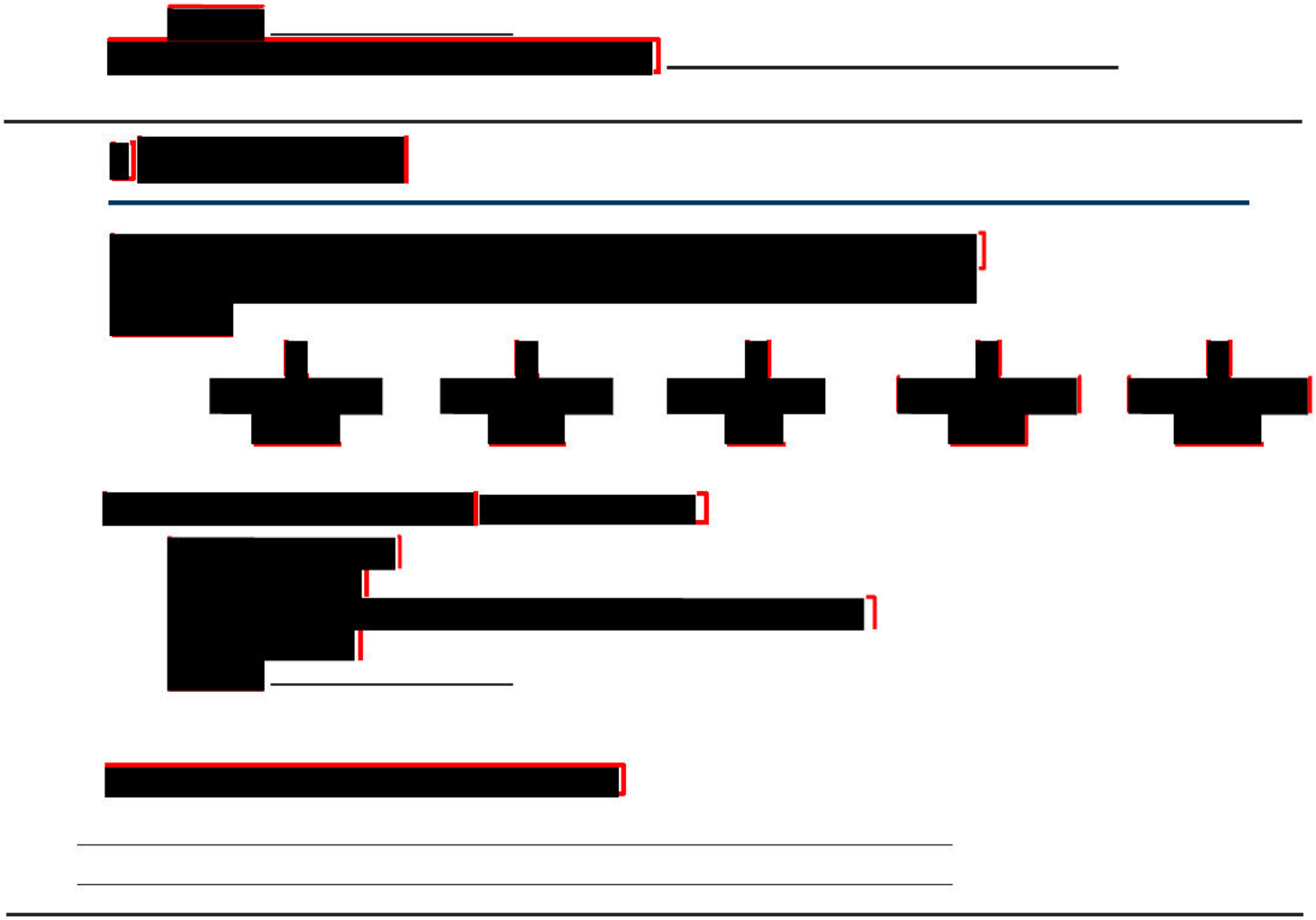
27 Appendix 12 – Preference Questionnaire







28 Appendix 13 – Principal Investigator and Study Site Information

28.1 Site #1

Protocol: CV-23-86

Study Title: Clinical Evaluation of comfilcon A Contact Lenses

Protocol Version: 1.1, Date: 02 NOV 2023

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 and the Institutional Review Board (IRB), 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 and trained on this protocol. 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 (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

Title:
Study Site:
Address:

Telephone:
Email:

28.2 Site #2

Protocol: CV-23-86

Study Title: Clinical Evaluation of comfilcon A Contact Lenses

Protocol Version: 1.1, Date: 02 NOV 2023

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 and the Institutional Review Board (IRB), 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 and trained on this protocol. 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 (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

Title:
Study Site:
Address:

Telephone:
Email:

28.3 Site #3

Protocol: CV-23-86

Study Title: Clinical Evaluation of comfilcon A Contact Lenses

Protocol Version: 1.1, Date: 02 NOV 2023

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 and the Institutional Review Board (IRB), 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 and trained on this protocol. 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 (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

Title:
Study Site:
Address:

Telephone:
Email:

28.4 Site #4

Protocol: CV-23-86

Study Title: Clinical Evaluation of comfilcon A Contact Lenses

Protocol Version: 1.1, Date: 02 NOV 2023

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 and the Institutional Review Board (IRB), 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 and trained on this protocol. 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 (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

Title:
Study Site:
Address:

Telephone:
Email:

28.5 Site #5

Protocol: CV-23-86

Study Title: Clinical Evaluation of comfilcon A Contact Lenses

Protocol Version: 1.1, Date: 02 NOV 2023

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 and the Institutional Review Board (IRB), 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 and trained on this protocol. 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 (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

Title:
Study Site:
Address:

Telephone:
Email:

28.6 Site #6

Protocol: CV-23-86

Study Title: Clinical Evaluation of comfilcon A Contact Lenses

Protocol Version: 1.1, Date: 02 NOV 2023

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 and the Institutional Review Board (IRB), 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 and trained on this protocol. 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 (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

Title:
Study Site:
Address:

Telephone:
Email: